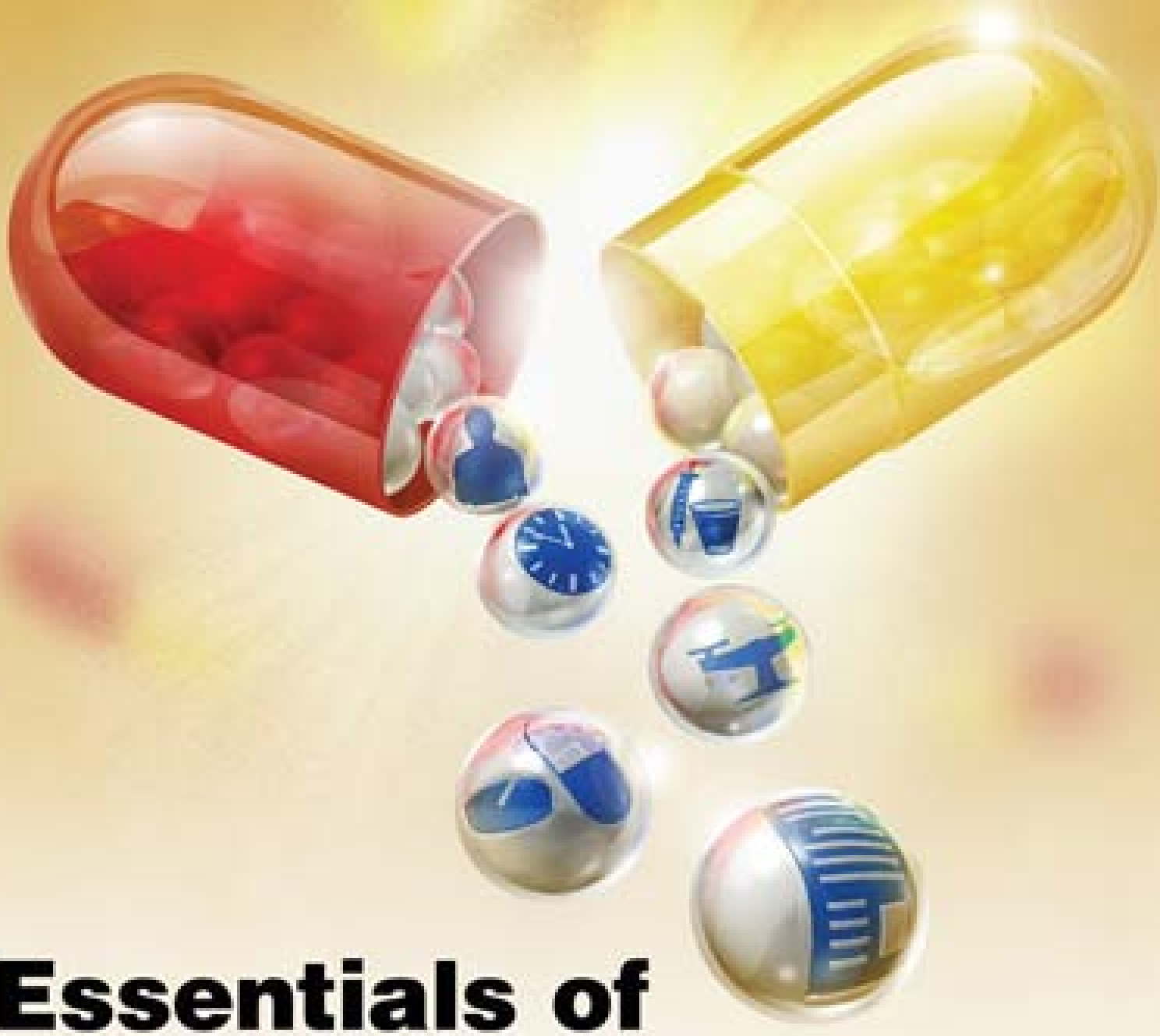


Essentials of Pharmacology for Health Occupations

Sixth Edition

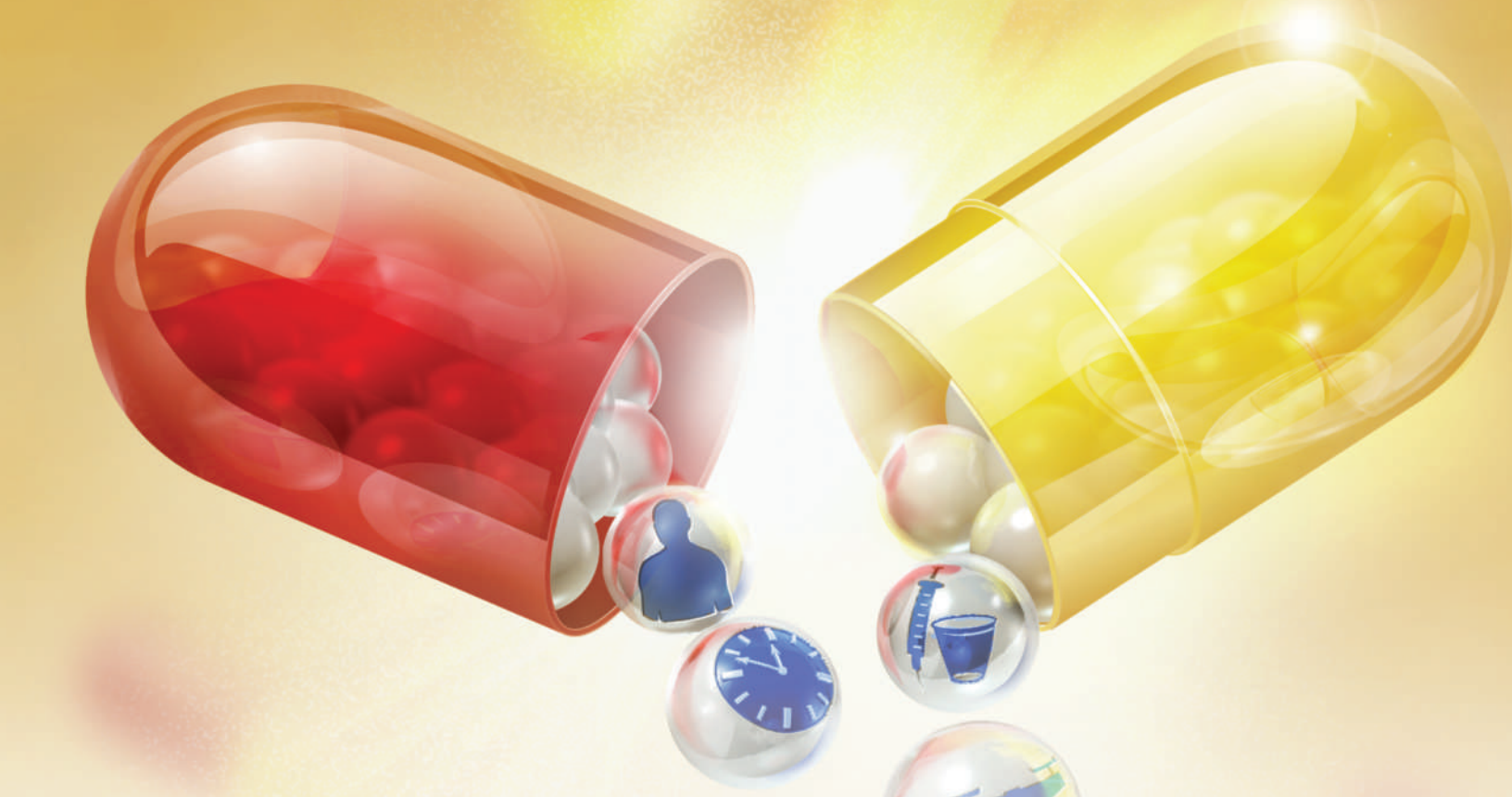
Ruth Woodrow, RN, BA, MA
Bruce J. Colbert, MS, RRT
David M. Smith, RPh, MS

Essentials of Pharmacology for Health Occupations

Sixth Edition

Supplements At-A-Glance

SUPPLEMENT:	WHAT IT IS:	WHAT'S IN IT:
StudyWARE™ CD-ROM	Software program (CD-ROM in the back of the book)	• Quizzes with immediate feedback • Additional quizzes with NCLEX-style questions • Medication administration and safety videos • Interactive games • Case studies • Audio Library • USP Quality Review No. 82 concerning look alike and/or sound alike drugs that can cause safety errors.
Study Guide	Print	• Review questions including multiple choice, fill-in-the-blank, true/false, and matching • Case studies
Mobile Downloads	Mobile downloads	• Mobile downloads with audio for drugs by generic and trade names, and text glossary terms
Flashcards	Print	• Over 1504 flashcards covering key terms and concepts from text
Instructor Resources	CD-ROM	• Electronic Instructor's Manual files • Electronic testbank • Slide presentations created in PowerPoint® with full-color art and video clips
WebTutor Advantage	Web access	• On Blackboard and WebCT platforms (other platforms available upon request) • Content and quizzes linked to each chapter • Comprehensive glossary • Medication administration video clips • StudyWARE™ interactive games • PowerPoint® slide presentations • Discussion questions • Mid-term and Final exams • Electronic Textbook files • Electronic Study Guide files



Essentials of Pharmacology for Health Occupations

Sixth Edition

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Essentials of Pharmacology for Health Occupations, Sixth Edition
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3	Oral Medications and their Administration
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4	Powdered Medications
4	Ointments and their Application
4	Needle Safety
4	Preparing an IV Solution
7	Medication Errors, Documentation, and Administration
8	Administering Rectal Medications
8	Oral Medications
9	Showing a Patient How to Use an Inhaler
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9	Filling the Syringe from a Vial
9	Drawing Meds from Two Vials
9	Subcutaneous Injections
9	Intramuscular Injection
9	Z-Track Method
9	Administering Eye Medications
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9	Administering an Intradermal Injection
10	How to Manage an Obstructed Airway
12	Ointments
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23	Blood Glucose Test
26	Using Oxygen

To my grandchildren, Ashton,
Jeff, Samantha, and Eric,
may they realize that knowledge is power and
seek to learn all of their lives.

Ruth Woodrow

To my loving wife Patty and two great sons,
Joshua and Jeremy.

Bruce J. Colbert

To Reggie, my loving wife of nearly 30 years,
I am extremely grateful for her patience,
support, and understanding during the
revision and updating of the sixth edition.

David M. Smith

Preface

This book is designed as:

- A basic text for learners studying nursing, medical assisting, and other allied health occupations.
- A continuing education update for practitioners in the health field.
- Part of a refresher program for practitioners returning to health occupations.
- A supplemental or reference book for practitioners wishing to extend their knowledge beyond basic training in specific health occupations.

The purpose of this book is to provide an extensive framework of knowledge that can be acquired within a limited time frame. It will be especially helpful to learners in one-year training programs with limited time allotted to the study of medications. For those in longer programs, it can be used as the basis for more extensive study. It is appropriate as a required text in training those who will administer medications. It has been especially designed to meet the needs of learners in nursing and medical assistant programs. However, learners in allied health programs will find the concise format adaptable to their needs also.

This text has been field tested in several classes with learners in various health occupations. Learners who have already used this book for updating or supplemental education include registered nurses, licensed practical nurses, medical assistants, and pharmacy technicians.

Those employed in health occupations now have increased responsibilities for providing the necessary information to patients regarding the safe administration of medications, side effects, and interactions. Patient education is presented in every chapter in Part II. Even if you are not involved directly in patient education, it is imperative you understand what information is being conveyed. The quantity of information could be overwhelming and confusing to the learner unless presented in a comprehensive and concise manner.

ORGANIZATION

The text's concise format eliminates unnecessary detail that may tend to overwhelm or confuse the learner. Outdated or rarely used medications, obsolete information, and complex descriptions are eliminated. The information is both factual and functional.

The textbook is broken down into two specific parts. ***Part I*** can stand alone as a basic but comprehensive review of pharmacologic principles. ***Part I*** introduces the learner to the fascinating subject of drugs, their sources, and their uses. Calculations are simplified into two optional, step-by-step processes. *Review questions* at the end of each chapter help the learner master the information. Medication preparation, supplies, and specific information on

each route of administration is covered. Administration checklists allow the learner to put the knowledge into practice. Illustrations and integrated videos on StudyWARE™ CD-ROM facilitate the visual learning process.

Part II organizes the drugs according to classifications, arranged in logical order. Each classification is described, along with characteristics of typical drugs, purpose, side effects, cautions, and interactions. Patient education for each category is highlighted.

Reference tables with each classification list the most commonly prescribed drugs according to generic and trade names, with dosage and available forms.

Case studies within each chapter in Part II stimulate critical thinking and help learners to put into practice the information they have mastered. A review quiz follows each chapter. Comprehensive review quizzes for Part I and Part II are at the end of the book.

An extensive glossary lists and defines key terms used in the text. A comprehensive index includes both generic and trade names.

CHANGES TO THE SIXTH EDITION

Global Changes

- Each drug classification has been updated with the latest and most frequently prescribed drugs available.
- Numerous tables have been added.
- Patient education boxes have been expanded.
- The glossary was expanded to include new terms. Illustrations were added and revised to reflect the rapid changes in pharmacology.
- Powerful videos have been added on the StudyWARE™ CD-ROM that allow learners to "see" what they just read. The "StudyWARE?™ Connection: See It In Action" feature in the textbook directs learners to the videos on the StudyWARE™ CD-ROM. These videos are also integrated within the instructor's PowerPoint presentations to enhance the classroom experience.
- The StudyWARE™ CD-ROM has also been expanded to include additional activities, case studies, and quizzes with NCLEX-style questions.

The following chapters in the text and on the StudyWARE™ CD-ROM have had significant additions with topics of current interest.

Chapter	Major Changes in Textbook	Videos Added to the StudyWARE™ CD-ROM
1	New information on orphan drugs and herbal medicine and dietary supplement regulation	• Managing Controlled Substances
2	Added table with examples of combination drugs	
3	New information on chemoinformatics, genetic engineering, recombinant DNA technology FDA Drug Pregnancy Categories were added	• Oral and Parenteral Medication Administration

Chapter	Major Changes in Textbook	Videos Added to the StudyWARE™ CD-ROM
4	New and updated information on implantable devices and the inhalation route	• Powdered medications, ointments and their application • Needle safety • Preparing an IV solution
7	Updated patient safety information	• Medication errors, documentation and administration
8		• Administering oral and rectal medications
9	Expanded information on dry powdered inhalers (DPI's)	• Showing a patient how to use an inhaler • The cartridge injection system • Filling a syringe from a vial Drawing meds from two vials • Subcutaneous injections • Intramuscular injections Z-track method • Administering eye and ear medications • Administering an interdermal injection
10	Expanded content on antidotes	• How to manage an obstructed airway
11	Updated and expanded content on vitamins, minerals, and herbal supplements	
12	Updated skin medications and added content on enzyme preparations	• Ointments and their application
14	New and updated information on radiation oncology and new drugs to treat cancer	
15	Updated urinary system agents	
16	Updated gastrointestinal agents with more information on probiotics	
17	Updated anti-infective agents with an emphasis on patient education. New information on vaccines and immunizations.	
18	Updated eye medications to include new antiglaucoma agents	• Administering eye medications
19	Updated information on analgesics, sedatives, and hypnotics	
20	Included new and updated information on ADHD products and antidepressants	

(continued)

Chapter	Major Changes in Textbook	Videos Added to the StudyWARE™ CD-ROM
21	Included the latest updates on osteoporosis prevention and therapy	
22	Updated the classification of seizures and added the latest treatments in Parkinson and Alzheimer's Disease	
23	Added the latest information on diabetic treatment	• Blood glucose test
25	Updated information, including the newest drugs, to treat cardiovascular disease	
26	Expanded information on drug aerosol delivery devices	• Using oxygen
27	Updated information on drugs and the older adult, and the listing of potentially inappropriate medications for older adults	

Resources to Accompany the Book Essentials of Pharmacology for Health Occupations, Sixth Edition StudyWARE™

The StudyWARE™ CD-ROM offers an exciting way to gain additional practice in learning pharmacology. Videos on various medication administration techniques and safe practices help learners visualize the concepts discussed in the textbook. The quizzes, games, and activities help reinforce even the most difficult concepts. See "*How to Use the Essentials of Pharmacology for Health Occupations*, Sixth Edition StudyWARE™" on page xxix for details.

Also Available: StudyWARE™ CD-ROM Stand-alone to accompany Essentials of Pharmacology, Sixth Edition (ISBN 1-1113-1372-5)

Study Guide

The Study Guide offers additional practice with review questions corresponding to each chapter in the text including: multiple choice, fill-in-the-blank, true/false, and matching questions. Case studies encourage you to apply the knowledge you have learned about drugs in Part II. Answers to all of the questions and case studies are included in the Instructor's Manual in the Electronic Classroom Manager.
Study Guide, ISBN 1-4354-8037-6

Flashcards

Review and learn essential pharmacology key terms and concepts with over 1504 flashcards. Flash cards are an effective study aid for use even when you only have a small amount of time.
ISBN 1-4354-8038-4

Premium Website

A premium website is available to accompany the text that includes the StudyWARE™, a link to Mobile Media, and slide presentations in PowerPoint®.

Redeeming an Access Code:

1. Go to: http://www.CengageBrain.com
2. Enter the Access code in the Prepaid Code or Access Key field, **Redeem**
3. Register as a new user or log in as an existing user if you already have an account with Cengage Learning or CengageBrain.com
4. Select **Go to MY Account.**
5. Open the product from the My Account page.

Also Available:

Premium Website PAC Stand-alone to accompany Essentials of Pharmacology for Health Occupations, Sixth Edition, (ISBN 1-1113-1369-5)

Premium Website IAC to accompany Essentials of Pharmacology, Sixth Edition, (ISBN 1-1113-1370-9)

Instructor Resources

With Delmar, Cengage Learning's Instructor Resources to Accompany Essentials of Pharmacology for Health Occupations, Sixth Edition by Ruth Woodrow, Bruce J. Colbert, and David M. Smith, preparing for class and evaluating learners has never been easier! As an instructor, you will find this CD-ROM offers invaluable assistance by giving you access to all of your resources – anywhere and at any time.

- **The Computerized Testbank in ExamView®** makes generating tests and quizzes a snap. With over 850 questions in a variety of formats to choose from, you can create customized assessments for your students with the click of a button. Add your own unique questions and print tests for easy class preparation.
- Customizable instructor slide presentations created in **PowerPoint®**, including video clips, and images, focus on key concepts from each chapter.
- **Electronic Instructor's Manual** includes the following tools:
  - Review quizzes with answers
  - Comprehensive Drug Worksheets
  - Alternate Comprehensive Exam Part II with answers
  - Answers to review quizzes and comprehensive review exams in the text
  - Answers to case studies in Part II in the text
  - Answers to review questions and case studies in the Study Guide

Instructor Resources CD-ROM, ISBN 1-4354-8034-1

Instructor Companion Site

An Instructor Companion Site is available that includes the Instructor Resources. To access the Instructor Companion Site, go to http://login.cengage.com/sso//.

WEBTUTOR™ Advantage

Designed to complement the text, WebTUTOR™ Advantage is a content-rich, Web-based teaching and learning aid that reinforces and clarifies complex concepts. The WebCT™ and Blackboard™ platforms also provide rich communication tools to instructors and learners, including a course calendar, chat, e-mail, and threaded discussions.

- WebTUTOR™ Advantage on Blackboard™, ISBN 1-4354-8035-X
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- WebTUTOR™ Advantage on WebCT™, ISBN 1-4354-8036-8
- Text Bundled with WebTUTOR™ on WebCT™, ISBN 1-1111-2197-4

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- IAC Cengage-Hosted Web Tutor to Accompany Essentials of Pharmacology, Sixth Edition (ISBN 1-1113-1374-1)
- PAC engage-Hosted Web Tutor to Accompany Essentials of Pharmacology, Sixth Edition (ISBN 1-1113-1375-X)

TO THE LEARNER STUDYING PHARMACOLOGY

Other learners, such as you, have helped me put this book together. They have learned that the study of medications can be a fascinating one. They tell me that this book has helped them to develop confidence and competence in dispensing medications and information about drugs to their patients. You will find this is only the beginning, a framework upon which you will build a vast store of useful knowledge.

Learners have told me that the objectives, review questions, and case studies were tremendously helpful to them. Organization is the key to acquiring large quantities of information. You will be amazed at all you have learned when you complete this book.

Keep growing and learning and questioning all of your life.

Ruth Woodrow

ACKNOWLEDGMENTS

I would like to acknowledge the support, encouragement, and technical assistance of my husband, Roger.

I am grateful to Bruce Colbert, a dedicated teacher and author, for taking over this sixth edition revision. Bruce shares my empathy for the student and the ideal of keeping it simple for successful learning. He has modernized the book and made it more user-friendly with the addition of video clips to facilitate the process of teaching and learning. A big thanks to Bruce for keeping me involved.

I wish to thank all of those at Delmar Cengage Learning who contributed in any way to this text. Appreciation is expressed particularly to Debra Myette-Flis, Senior Product Manager, for all of her guidance and support through the fourth and fifth editions, and especially for her understanding and assistance with this edition. She always goes above and beyond expectations.

I also wish to thank Matt Seeley, Acquisitions Editor, for finding Bruce Colbert, the perfect fit for this book.

Ruth Woodrow

First and foremost, I would like to thank Ruth Woodrow for her dedication to helping students learn. It was an honor to be offered to work on such a quality textbook and with such an inspiring author who maintains her passion for learning, teaching, mentoring, and volunteerism. She truly lives her values.

I would also like to thank David Smith, whom I haven't personally met yet, but have been so impressed with his work, knowledge, and professionalism. His updates with the latest and greatest information have been truly appreciated.

Luis Gonzalez, whom I consider not only a personal friend but one of the most dedicated and creative teachers I know, also deserves a thank you for his content expertise and wise advice.

Matt Seeley deserves a very large thank you for considering and believing in me for this project.

Last but certainly not least, I want to personally thank Debra Myette-Flis, for her tremendous assistance, organizational skills, professional knowledge, and guidance in helping to make this project a joy on which to work.

Bruce J. Colbert

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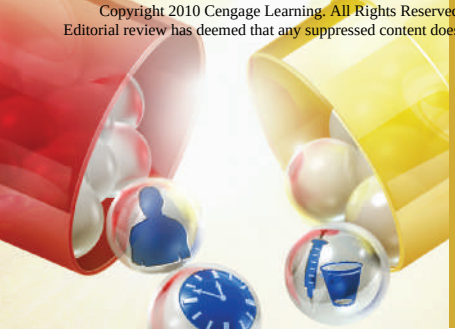


How to Use

Essentials of Pharmacology for Health Occupations, Sixth Edition helps you learn drug information in a concise format. Drugs are organized by classifications and include their purpose, side effects, cautions, and interactions. The following features are integrated throughout the book to assist you in learning and mastering core concepts and terms.

OBJECTIVES

The objectives alert you to core concepts you should understand after reading the chapter.

KEY TERMS AND CONCEPTS

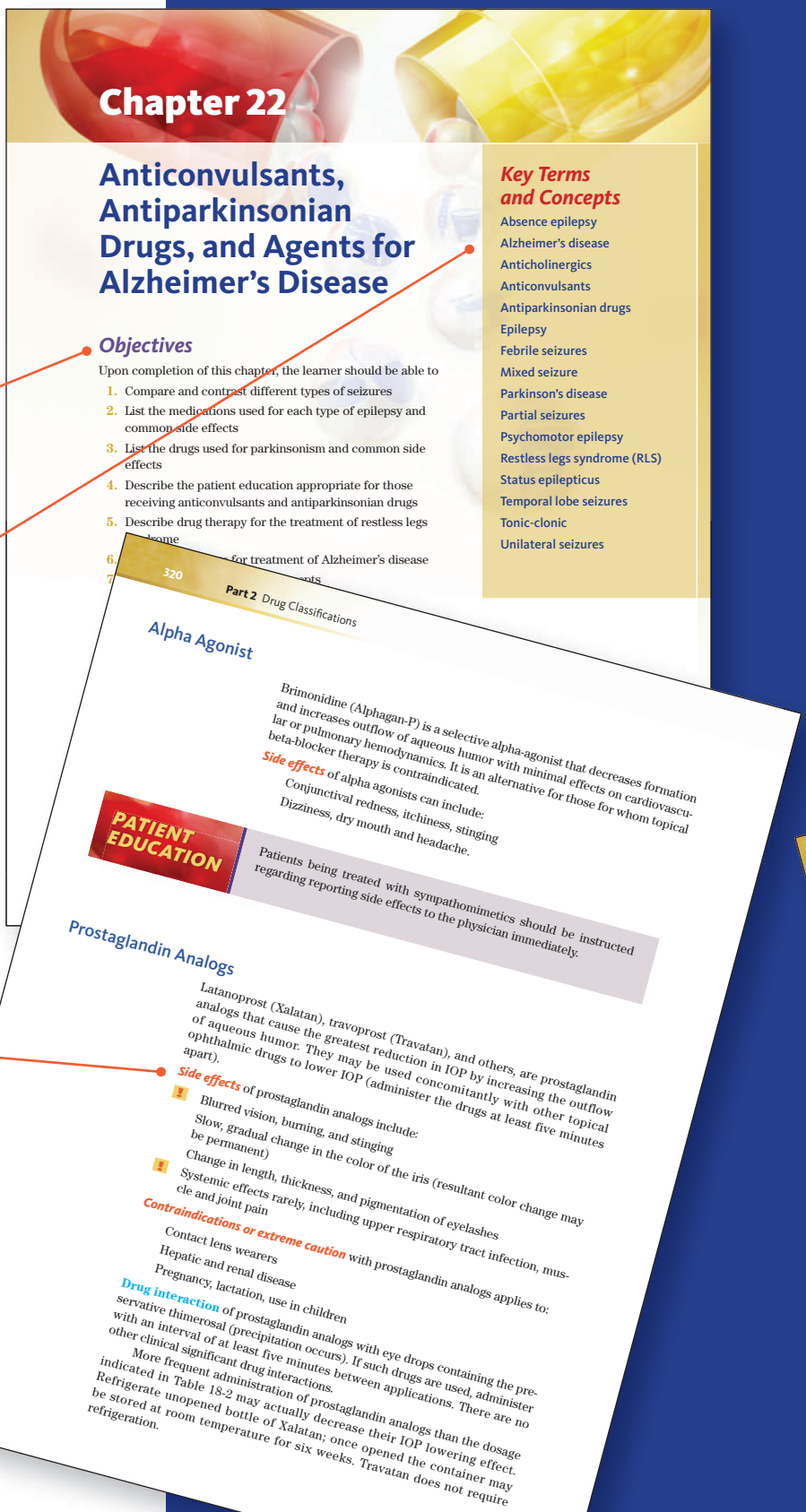
Key terms and concepts are highlighted and defined in the text the first time they are used. An extensive glossary lists and defines all key terms used throughout the book.

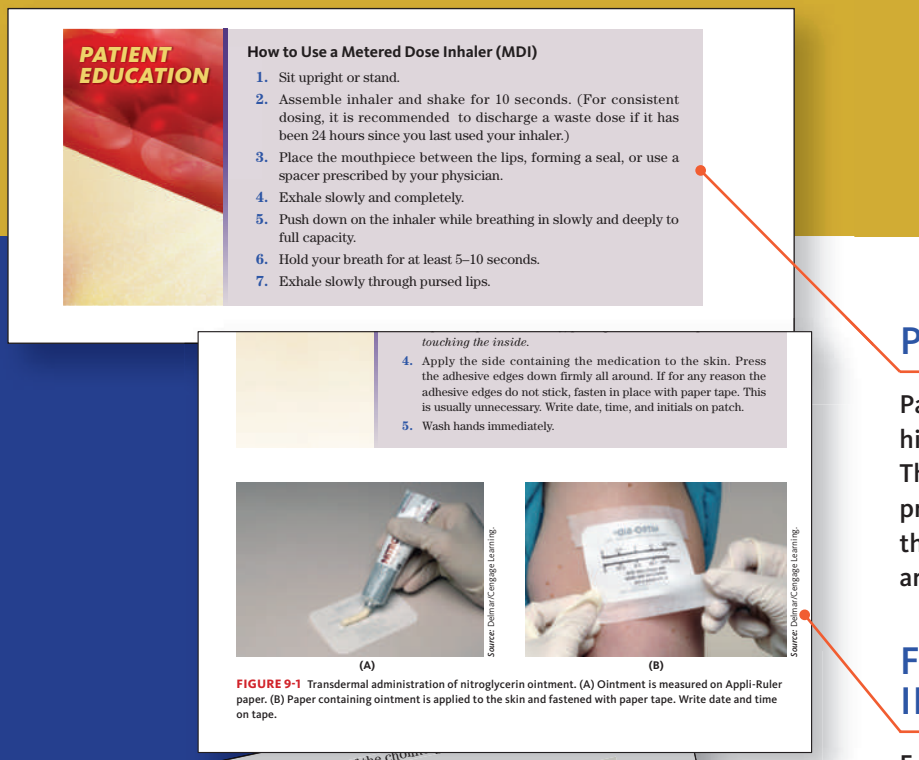
CLASSIFICATIONS

Drugs are organized according to classifications. Each classification is described, along with characteristics of typical drugs, purpose, side effects, cautions, and interactions.

SIDE EFFECTS OF DRUGS

A special icon identifies the most common and/or most important side effects of drugs. This special icon is meant to serve as a valuable guide for learners. Rather than memorizing every side effect for each drug, the icon emphasizes the side effects with which you should be familiar.




PATIENT EDUCATION

How to Use a Metered Dose Inhaler (MDI)

1. Sit upright or stand.
2. Assemble inhaler and shake for 10 seconds. (For consistent dosing, it is recommended to discharge a waste dose if it has been 24 hours since you last used your inhaler.)
3. Place the mouthpiece between the lips, forming a seal, or use a spacer prescribed by your physician.
4. Exhale slowly and completely.
5. Push down on the inhaler while breathing in slowly and deeply to full capacity.
6. Hold your breath for at least 5–10 seconds.
7. Exhale slowly through pursed lips.

touching the inside.

4. Apply the side containing the medication to the skin. Press the adhesive edges down firmly all around. If for any reason the adhesive edges do not stick, fasten in place with paper tape. This is usually unnecessary. Write date, time, and initials on patch.
5. Wash hands immediately.

Source: Delmar/Cengage Learning.

(A) (B)

Source: Delmar/Cengage Learning.

FIGURE 9-1 Transdermal administration of nitroglycerin ointment. (A) Ointment is measured on Appli-Ruler paper. (B) Paper containing ointment is applied to the skin and fastened with paper tape. Write date and time on tape.

Quinidine

See Table 13-3 for a summary of the cholin

Table 13-3 Cholinergics

GENERIC NAME	TRADE NAME	DOSAGE	COMMENTS
bethanechol	Urecholine	10–50 mg PO 4x per d	For postpartum or postoperative urinary retention, **not** with benign prostatic hypertrophy
neostigmine	Prostigmin	15–125 mg PO 3x per d 0.5–2 mg IM, subcu or IV q1–3h	Treatment for myasthenia gravis Neuromuscular blockade reversal
pilocarpine	Isopto Carpine	Ophthalmic gtt, dose varies	To lower intraocular pressure in glaucoma

CHAPTER REVIEW QUIZ

Fill in the blanks.

1. Parenteral includes any routes other than the _____.
2. Systemic effects are those affecting _____.
3. The four parenteral routes with systemic effects include: _____, _____, _____, _____.

Label the routes according to their action. Use R for rapid and S for slow. Match each route with the appropriate definition:

	Action		Definition
4. _____	Sublingual	_____	a. Given with a needle

CASE STUDY – A

Autonomic Nervous System Drugs

Shanelle Woods, a 33-year-old, receives epinephrine (Adrenalin) in the emergency room for a severe asthma attack. Health care personnel should have the following information.

1. Adrenalin has all of the following actions EXCEPT
   a. Peripheral vasodilator
   b. Dilation of pupils
   c. Bronchodilator
   d. Cardiac stimulant
2. All of the following doses of Adrenalin are appropriate EXCEPT
   a. 0.4 mL IM (deltoid)
   b. 0.3 mL subcu
   c. 5 mL subcu
   d. 1 mL IV
3. Epinephrine is also used to treat all of the following conditions EXCEPT
   a. Nosebleed
   b. Hypertension
   c. Anaphylaxis
   d. Cardiac arrest
4. Side effects can include all of the following EXCEPT
   a. Tremors
   b. Hypoglycemia
   c. Tachycardia
   d. Insomnia
5. She should be told all of the following about epinephrine EXCEPT
   a. May cause sedation
   b. Avoid alcohol
   c. May cause headaches
   d. Palpitations possible

PATIENT EDUCATION

Patient education is summarized and highlighted for each classification of drugs. These special boxes will assist health care professionals to instruct patients and answer their questions about the medications they are taking.

FULL-COLOR PHOTOS AND ILLUSTRATIONS

Full-color photographs and illustrations help explain and reinforce administration techniques and medication equipment.

REFERENCE TABLES

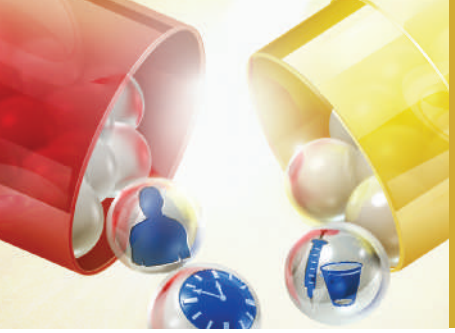
Reference tables within each classification list the most commonly prescribed drugs according to generic and trade names, with dosage and available forms.

REVIEW QUIZZES AND COMPREHENSIVE REVIEW EXAM

Review quizzes at the end of each chapter assist learners in identifying areas for further study. Two comprehensive review exams further help learners assess understanding of material learned.

CASE STUDIES

Case studies in Part II stimulate critical thinking through the presentation of reality-based situations regarding drug usage.

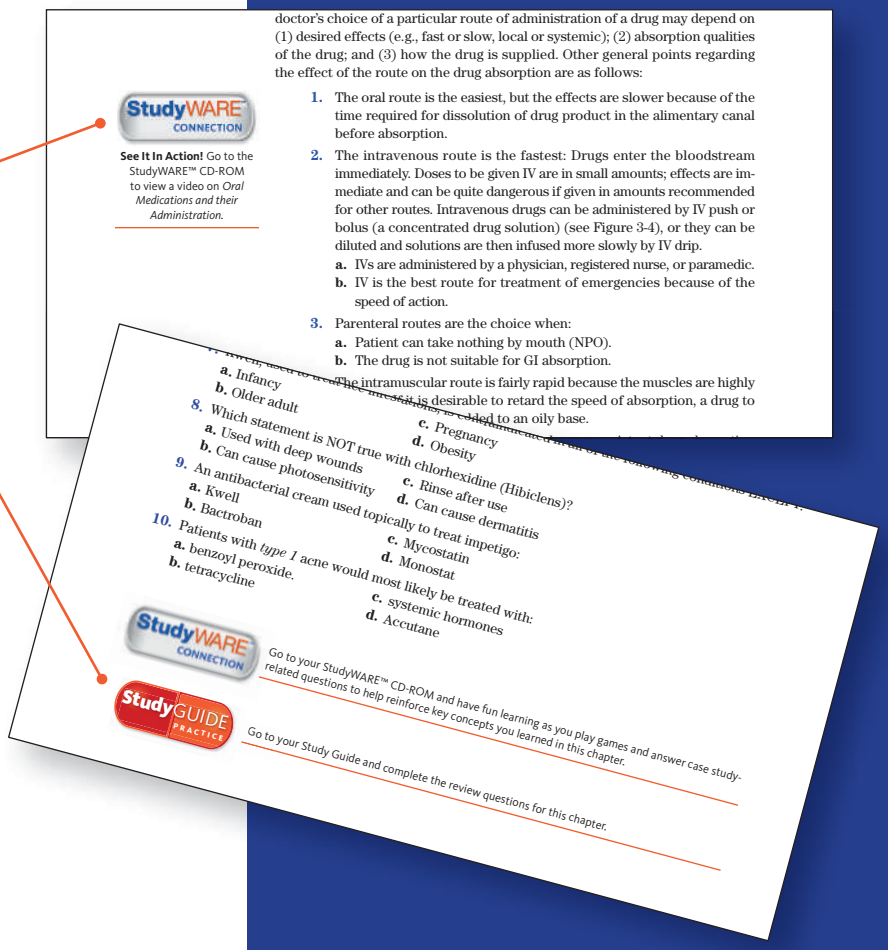


STUDYWARE™ CONNECTION

New! The StudyWARE™ Connection feature directs you to additional learning opportunities such as practice quizzes, medication administration videos, and interactive games on the CD-ROM that accompanies the book.

STUDY GUIDE PRACTICE

The Study Guide Practice feature reminds you to complete the additional practice questions and case studies for Part II found in the Study Guide.



How to Use *StudyWARE™ to Accompany Essentials of Pharmacology for Health Occupations*, Sixth Edition

LICENSE AGREEMENT

Refer to the license agreement on the StudyWARE CD. Refer to the set-up instructions and system requirements in the back of the book.

GETTING STARTED

The StudyWARE™ software helps you learn terms and concepts in *Essentials of Pharmacology for Health Occupations*, Sixth Edition. As you study each chapter in the text, be sure to explore the activity in the corresponding chapter in the software. Use StudyWARE™ as your own private tutor to help you learn the material in your *Essentials of Pharmacology for Health Occupations*, Sixth Edition textbook.

Getting started is easy. Install the software by inserting the CD-ROM into your computer's CD-ROM drive and following the on-screen instructions. When you open the software, enter your first and last name so the software can store your quiz results. Then choose a chapter from the menu to take a quiz or explore one of the activities.

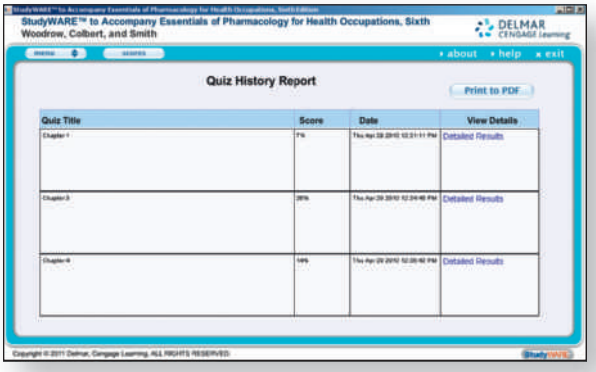
MENUS

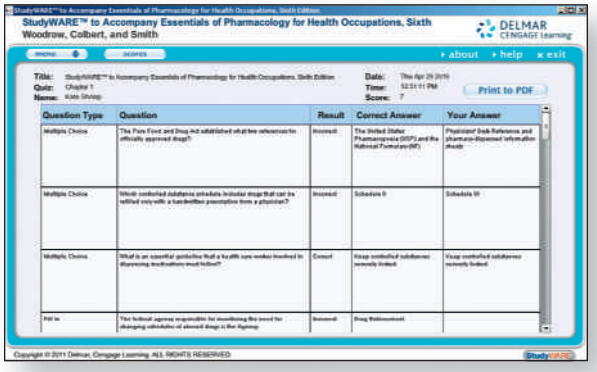
You can access the menus from wherever you are in the program.

Quizzes. Quizzes include fill-in-the-blank and multiple choice questions. You can take the quizzes in both Practice Mode and Quiz Mode. Use Practice Mode to improve your mastery of the material. You have multiple tries to get the answers correct. Instant feedback tells you whether you're right or wrong—and helps you learn quickly by explaining why an answer was correct or incorrect. Use Quiz Mode when you are ready to test yourself and keep a record of your scores. In Quiz Mode, you have one try to get the answers right, but you can take each quiz as many times as you want.

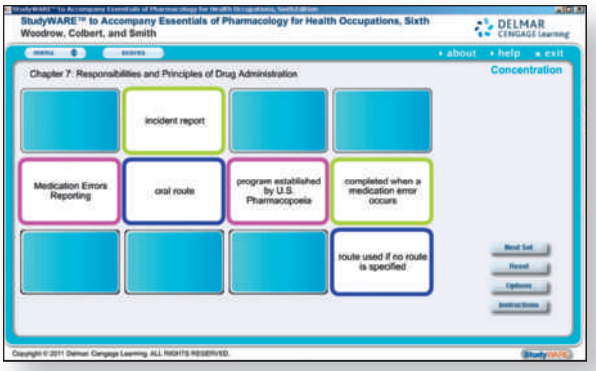
NCLEX-Style Quizzes. NEW to this edition are additional quizzes that contain NCLEX-style questions.

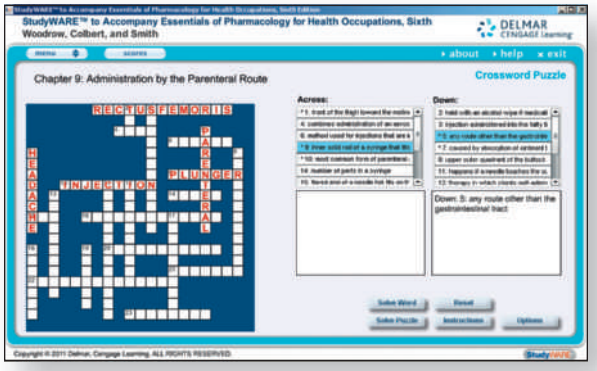
Scores. You can view your last scores for each quiz and print your results to hand in to your instructor.

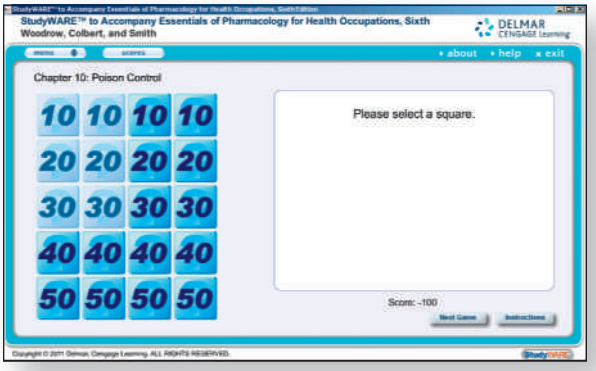




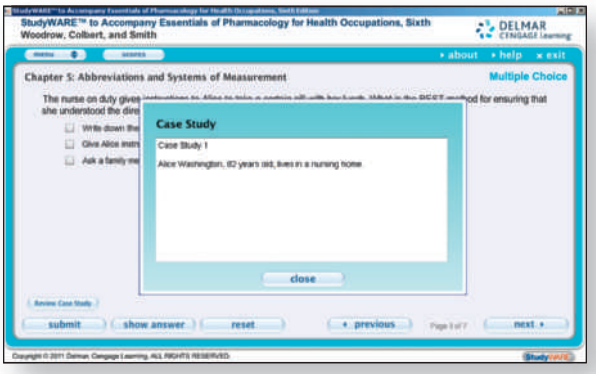
Activities. Activities include concentration, crossword puzzles, case studies, and championship. Have fun while increasing your knowledge!

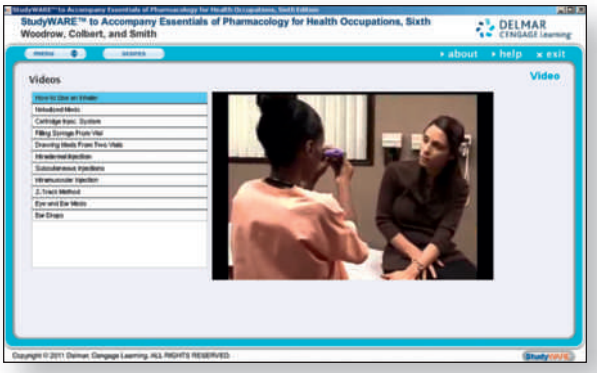




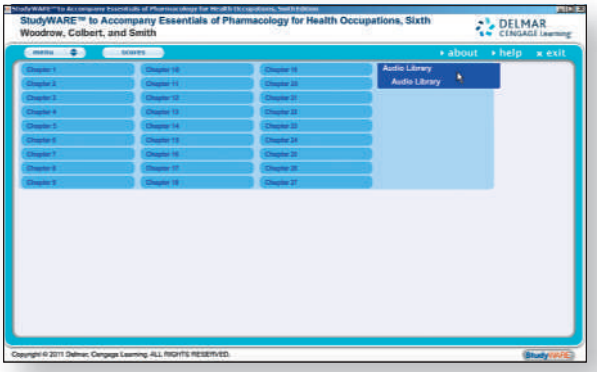


Case Studies. Case studies stimulate critical thinking through real-world situations and encourage you to apply the knowledge you have learned about drugs in Part II.

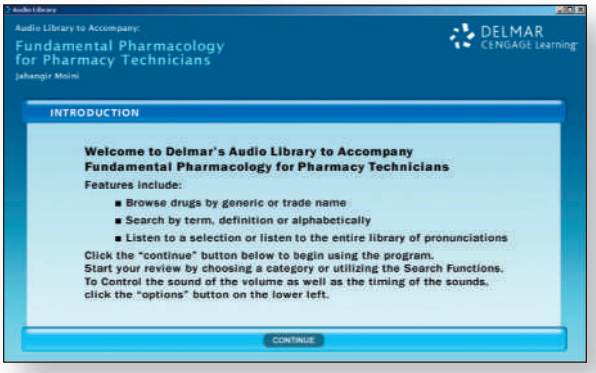


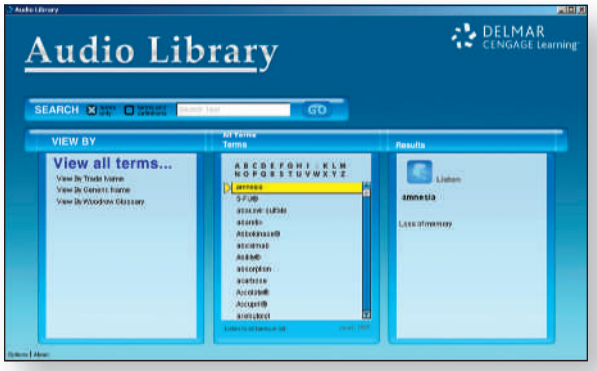


Videos. Videos on various medication administration techniques and safe practices help learners visualize the concepts discussed in the textbook.



Audio Library. The StudyWARE™ Audio Library is a reference that includes audio for drugs by generic and trade names, and text glossary terms.





USP Quality Review Report. USP Quality Review Report No. 82 is included for your reference. The report lists many similar drug names that have led to medication errors. USP Quality Review No. 82 is reprinted with permission from The United States Pharmacopeial Convention. Copyright 2009. *All Rights Reserved.*

PART 1

Introduction to Pharmacologic Principles

Chapter 1

Consumer Safety and Drug Regulations

Objectives

Upon completion of this chapter, the learner should be able to

1. Explain what is meant by drug standards
2. Name the first drug law passed in this country for consumer safety, and give the year it was passed
3. Summarize the provisions of the Federal Food, Drug, and Cosmetic Act of 1938, and identify the government agency that enforces the act
4. Interpret what is meant by USP/NF
5. Summarize the provisions of the Controlled Substances Act of 1970
6. Explain what is meant by a DEA number
7. Define schedules of controlled substances, and differentiate between C-I to C-V schedules
8. State several responsibilities you have in the dispensing of medications, as a direct result of the three major drug laws described in this chapter
9. Define the Key Terms and Concepts

Key Terms and Concepts

Controlled substances

Drug Enforcement Administration (DEA)

Drug standards

Food and Drug Administration (FDA)

Orphan drugs

Your decision to pursue a career in the health care field probably took a great deal of thought. No doubt you have questioned whether you will be able to handle the unique situations that arise in a clinic, health care facility, or physician's office. Have you ever stopped to consider the impact *you* will make on the lives of others as a health care practitioner? Not only can you make a tremendous difference in the efficiency of the facility where you work, but you can have a positive impact on your friends and family, as well as the patient or client.

It is inevitable that you will receive phone calls and questions about medications, prescriptions, and drug therapy. A great majority of patients are far too inhibited to tell their physician that there are things they do not understand about their medications. They feel much more at ease discussing their questions with the health care practitioner. Your potential for informing others with knowledgeable answers about medications can be quite an asset!

The key to reaching that potential is having knowledgeable answers. A serious, responsible attitude about all aspects of drug therapy is imperative. Consider yourself a potential prime resource of medication information for your friends, family, and future patients, as you begin to examine the foundations of facts about drugs. It may be necessary for you to clarify some of the layperson misunderstandings about the legalities of dispensing medications. Consider the following misconceptions and facts.

FALLACY	FACT
Only nurses can give medications to patients.	Trained and certified health care practitioners who may legally give medications include: physicians; physician assistants; paramedics; medical office assistants; practical, vocational, and registered nurses; and other allied health specialists such as respiratory therapists.
Only physicians may write prescriptions.	Dentists, physicians, physician assistants, veterinarians, nurse practitioners, and registered pharmacists may write prescriptions for their specific field of work, as governed by state law. For example, veterinarians write prescriptions for animal use only.
Prescriptions are required for narcotics only.	Specific drugs ruled illegal to purchase without the use of a prescription include: • Those that need to be **controlled** *because they are addictive and tend to be abused and dangerous* (e.g., depressants, stimulants, psychedelics, and narcotics). • Those that may cause dangerous health threats from side effects if taken incorrectly (e.g., antibiotics, cardiac drugs, tranquilizers).
All drugs produced in the United States are made in federally approved laboratories.	Numerous undercover illegal laboratories exist and operate within the United States today.
All herbal medicines and dietary supplements are safe.	Herbal remedies and other dietary supplements are not approved or production standards regulated by the Food and Drug Administration (FDA) and may have serious interactions with prescribed medications. Under the Dietary Supplement Health and Education Act of 1994 (DSHEA), the dietary supplement manufacturer is responsible for ensuring that a dietary supplement is safe before it is marketed. The FDA is responsible for taking action against any unsafe dietary supplement product after it reaches the market. (See Chapter 11.)

DRUG LAWS

The matter of dispensing drugs in the United States is specifically addressed by laws passed in the 1900s. Scientific advances, progress, and changes in society in the last century have made it necessary for drug laws to be set for our safety. Although substances have been taken into the body for their effects for centuries, so many are being produced today that consumer safety is now a critical issue.

Drug standards are rules set to assure consumers that they get what they pay for. The law says that all preparations called by the same drug name must be of *uniform strength*, *quality*, and *purity*.

Because of drug standardization, when you take a prescription to be filled, you are assured of getting the same basic drug, in the same amount and quality, no matter to which pharmacy or to which part of the country you take the prescription to be filled. According to drug standards, the drug companies must not add other active ingredients or varying amounts of chemicals to a specific drug preparation. They must meet the drug standards (federally approved requirements) for the specified strength, quality, and purity of the drug.

In the market of illegal (illicit) drugs, the lack of enforcement of drug standards is the consumer's danger. With no controls on the quality of illegal drugs, many deaths have occurred from overdose. Consider the heroin user, accustomed to very poor-quality heroin, who accidentally overdoses when given a much higher quality of heroin from a new source.

The laws that have evolved to provide consumer safety can be summed up by three major acts. They are described in the order in which they became necessary for consumer safety beginning with the 1906 Pure Food and Drug Act.

The importance of the timing of the 1938 Federal Food, Drug, and Cosmetic Act should be noted. It came about as the answer to a disastrous occurrence in 1937. A sulfa preparation, not adequately tested for safety, was responsible for 100 deaths that year. Thus the need was recognized for more proof of the safety and effectiveness of new drugs.

1906 PURE FOOD AND DRUG ACT

First government attempt to establish consumer protection in the manufacture of drugs and foods.

Required all drugs marketed in the United States to meet minimal standards of strength, purity, and quality.

Demanded that drug preparations containing dangerous ingredients have a labeled container indicating the ingredient. Originally there were eleven "dangerous" ingredients, such as morphine.

Established two references of *officially* approved drugs. Before 1906, information about drugs was handed down from generation to generation. No official written resources existed. After the 1906 legislation, two references specified the official U.S. standards for making each drug. Those references, listed below, have since been combined into one book, referred to as the USP/NF:

- United States Pharmacopeia (USP)
- National Formulary (NF)

1938 FEDERAL FOOD, DRUG, AND COSMETIC ACT AND AMENDMENTS OF 1951 AND 1962

Established the **Food and Drug Administration (FDA)** under the Department of Health and Human Services to enforce the provisions of the act.

Established *more specific* regulations to prevent adulteration of (tampering with) drugs, foods, and cosmetics:

- All labels must be accurate and must include a listing of all active and inactive ingredients. (Figure 1-1 shows an example of required product information for an over-the-counter [OTC] medication.)
- All new products must be approved by the FDA before public release.
- "Warning" labels must be present on certain preparations, for example, "may cause drowsiness," "may cause nervousness," and "may be habit-forming."
- Certain drugs must be labeled with the legend (inscription): "Caution—federal law prohibits dispensing without a prescription." Thus, the term *legend drug* refers to such preparations. The act also designated which drugs can be sold without a prescription.
- Prescription and nonprescription drugs must be shown to be *effective* as well as *safe*.

1970 CONTROLLED SUBSTANCES ACT

Established the **Drug Enforcement Administration (DEA)** as a bureau of the Department of Justice to enforce the provisions of the act.

Set much tighter controls on a specific group of drugs: *those that were being abused by society*; the name of the act indicates that such *substances needed to be controlled*. They include depressants, stimulants, psychedelics, narcotics, and anabolic steroids. The act:

- Isolated the abused and addicting drugs into five levels, or schedules, according to their medical value, harmfulness, and potential for abuse or addiction: C-I, C-II, C-III, C-IV, and C-V.
- Demanded security of **controlled substances**; anyone (e.g., pharmacists, hospitals, physicians, and drug companies) who dispenses, receives, sells, or destroys controlled substances must keep on hand special DEA forms, indicating the exact current inventory, and a two-year inventory of every controlled substance transaction.
- Set limitations on the use of prescriptions; guidelines were established for each of the five schedules of controlled substances, regulating the number of times a drug may be prescribed in a six-month period as well as for which schedules prescriptions may be phoned in to the pharmacy, and so on.
- Demanded that each prescriber of these substances register with the DEA and obtain a DEA registration number, to be present on their prescriptions of controlled substances; drug manufacturers must also be registered and identified with their own DEA numbers, as must pharmacists, physicians, veterinarians, and so on.

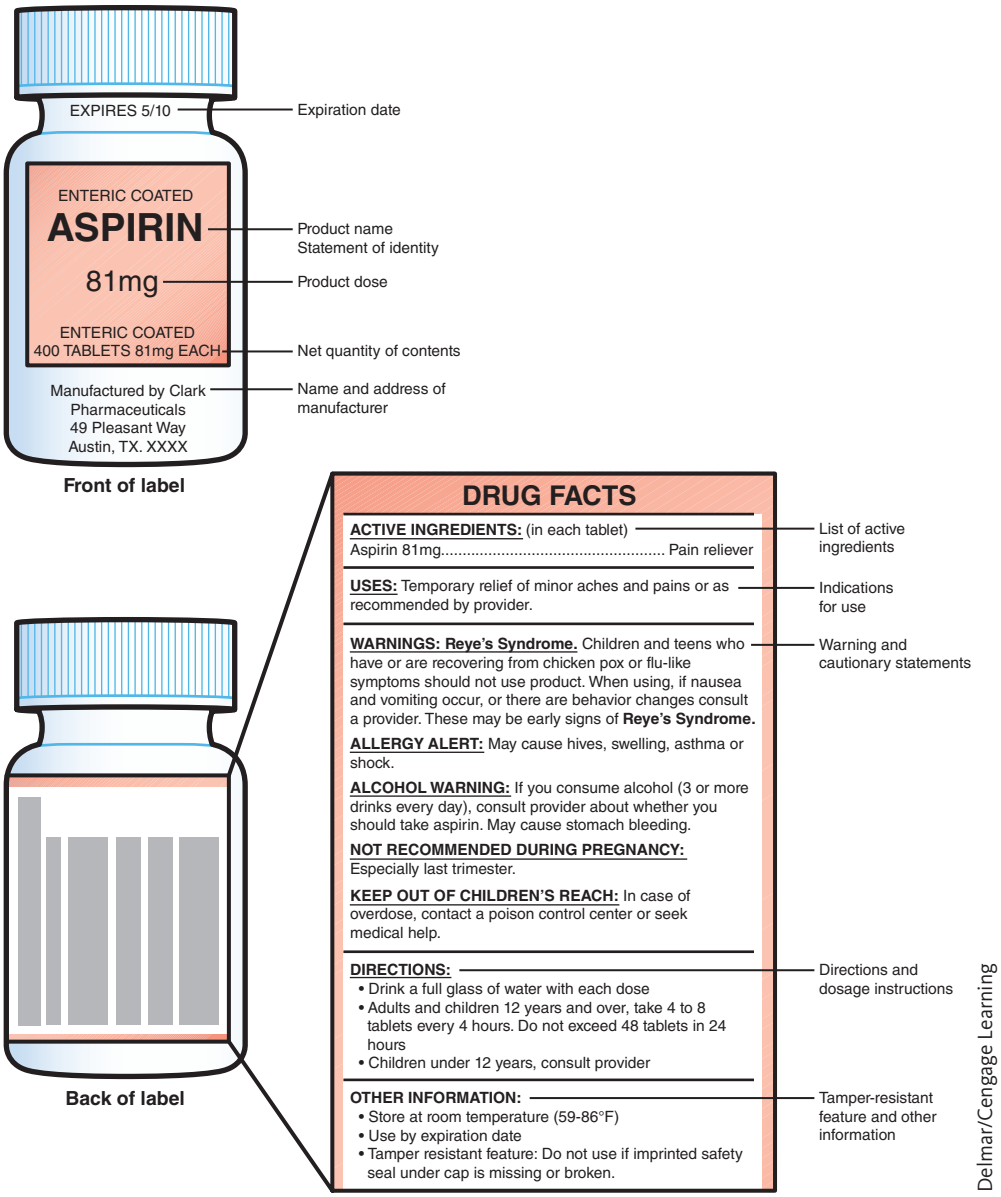


FIGURE 1-1 Consumer medication labels contain valuable information for safe and effective use of the drug.

The five schedules of controlled substances are arranged with the potentially most dangerous at level I and the least dangerous at level V. The lower the number, the stricter are the restrictions for control by the DEA. Thus, Schedule I drugs are illegal and not approved for medicinal purposes in the United States.

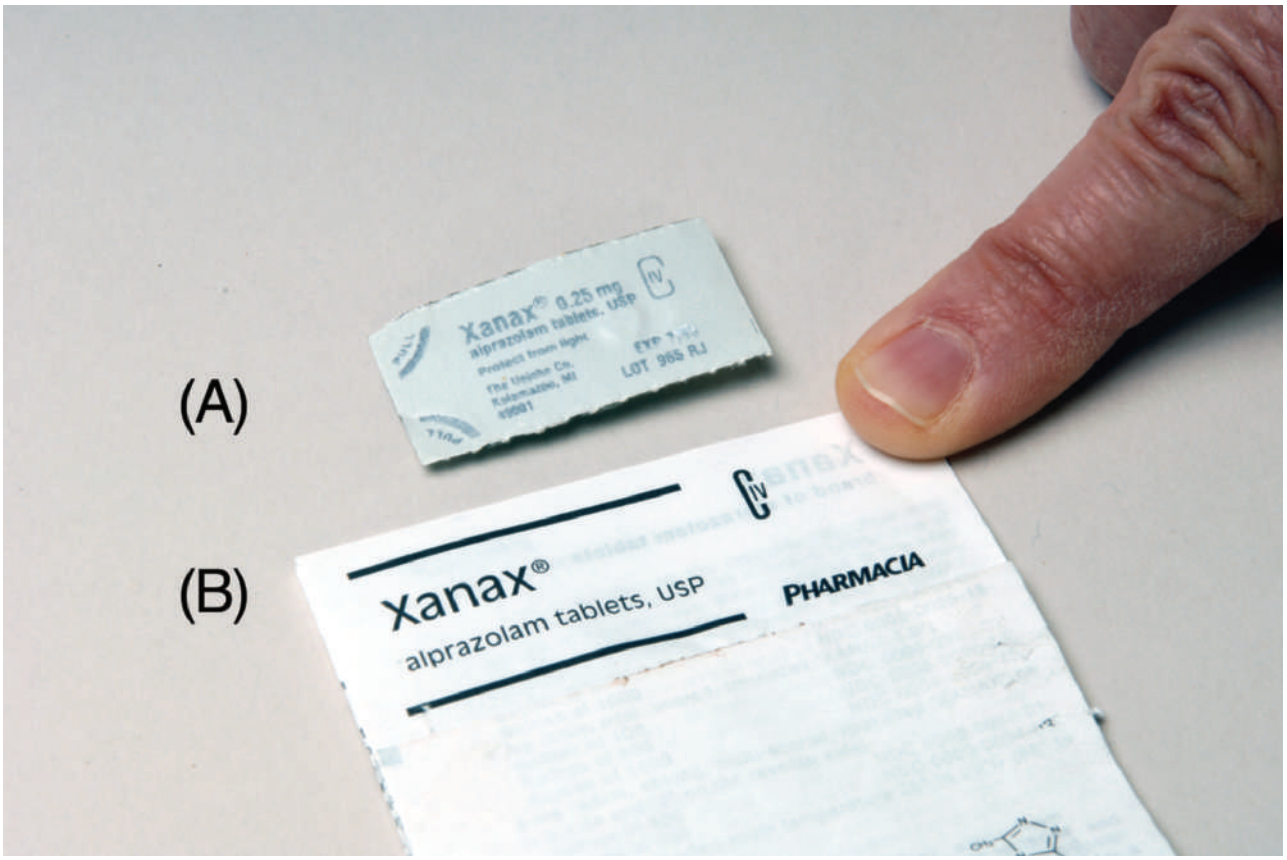
Drugs are frequently added, deleted, or moved from one schedule to another. If, for example, the DEA determines that drug A is becoming more of a societal problem, with an increased incidence of overdoses, drug A may be moved from the C-IV schedule to C-III. It is extremely important that the health care practitioner keep informed of any changes in drug scheduling. For the most part, using the most current drug reference book will keep you up to date.

You will recognize the schedule of a particular controlled substance by noting a *C* with either *I*, *II*, *III*, *IV*, or *V* after it. Some references show the capital C with the Roman numeral inside the curve of the C (Ⅽ). Labels on controlled substances are also designated with a C and a Roman numeral to indicate its level of control. Drug inserts (information leaflets accompanying drugs) are also marked with a C and the appropriate schedule number. (See Table 1-1 and Figure 1-2.)

Table 1-1 Five Schedules of Controlled Substances

SCHEDULE NUMBER	ABUSE POTENTIAL AND LEGAL LIMITATIONS	EXAMPLES OF SUBSTANCES
1, Ⅽ	High abuse potential Not approved for medical use in the United States	heroin, LSD, mescaline, ecstasy
2, Ⅽ	High abuse potential May lead to severe dependence Written prescription only No phoning in of prescription by office health care practitioner No refills without *new* written prescription May be faxed, but original prescription must be handed in to pick up prescription In emergency, physician may phone in, but handwritten prescription must go to pharmacy within 7 days	morphine, codeine, methadone, Percocet, Tylox, Dilaudid, Ritalin, cocaine, Oxycontin, meperidine (Demerol)
3, Ⅽ	May lead to limited dependence Written, faxed, or verbal (phoned in) prescription, by physician only May be refilled up to five times in 6 months	Codeine and Hydrocodone with aspirin or Tylenol, anabolic (muscle building) steroids
4, Ⅽ	Lower abuse potential than the above schedules Prescription may be written out by health care practitioner, but must be signed by the physician Prescription may be phoned in by health care practitioner or faxed May be refilled up to five times in 6 months	Valium, Ativan, Xanax, phenobarbital, Librium, Darvocet, Restoril, Ambien
5, Ⅽ	Low abuse potential compared to the above schedules Consists primarily of preparations for cough suppressants containing codeine and preparations for diarrhea (e.g., diphenoxylate)	Promethazine with codeine, Cheratussin AC, Lomotil

Note: Some states may have stricter schedules than the Federal regulations. You must be aware of the regulations in your area.



Delmar/Cengage Learning

FIGURE 1-2 Controlled substance schedule numbers appear in a variety of drug information resources, including (A) drug packages and (B) drug inserts. Schedule numbers are also found in drug reference books.

StudyWARE™ CONNECTION

See It In Action! View a video on *Managing Controlled Substances* on your StudyWARE™ CD-ROM.

Two significant pieces of drug legislation are important to mention here. The 1983 Orphan Drug Act gives pharmaceutical companies financial incentives to develop medications for diseases that affect only a small number of people. This encourages the companies to develop **orphan drugs** that would otherwise be of low profitability. The other legislation is the strangely named Omnibus Budget Reconciliation Act (OBRA) of 1990. This act mandates that all over-the-counter (OTC) drugs a patient is taking must be documented as part of the medical record. OBRA also mandates that pharmacists provide drug use review and patient counseling before dispensing prescriptions to a patient.

FDA AND DEA

The increase in the number of drugs produced for marketing brought dangers to the public. The federal Food and Drug Administration (FDA) was established to assure that some basic standards would be followed. Its responsibilities include:

- Overseeing testing of all proposed new drugs before they are released into the US market
- Inspecting plants where foods, drugs, medical devices or cosmetics are made

- Reviewing new drug applications and petitions for food additives
- Investigating and removing unsafe drugs from the market
- Ensuring proper labeling of foods, cosmetics, and drugs

When the need for better control of addictive drugs became urgent, the FDA had its hands full just trying to enforce basic drug standards. It became imperative to set up a new department, the Drug Enforcement Administration (DEA), in 1970 to handle all the needs and safety controls for the more dangerous drugs. Thus, the two agencies—FDA and DEA—were established with their own specific areas of drug control.

As a health care practitioner and an informed citizen, you must be aware of the latest developments concerning these two agencies. Hardly a week goes by without mention of the activities of the FDA or the DEA in the news. You should be able to recognize their separate areas of control.

FDA	Concerned with general safety standards in the production of drugs, foods, and cosmetics. Responsible for approval and removal of products on the market. Special note on drug withdrawals: In rare cases, the FDA may need to reassess and change its approval decision on a drug. A conclusion that a drug should no longer be marketed is based on the nature and frequency of the adverse events and how the drug's benefit and risk balance compares with treatment alternatives. When the FDA believes that a drug's benefits no longer outweigh its risks, the agency will ask the manufacturer to withdraw the drug. Interestingly, the FDA does not have the legal authority to withdraw a marketed drug product itself.
DEA	Concerned with controlled substances only. Enforces laws against drug activities, including illegal drug use, dealing, and manufacturing. Monitors need for changing the schedules of abused drugs.

HEALTH CARE PRACTITIONERS AND THE LAW

In some ways, you will be as involved as the physician in observing the restrictions of the drug laws. You will have the responsibility of keeping accurate records of the medications dispensed. You will maintain the supply of drugs at your facility. If you work in a doctor's office, clinic, or ambulatory care setting, you also will be involved with phoning in prescriptions and securing prescription forms at your facility.

The following guidelines should be followed by the health care practitioner involved in dispensing medications:

1. Keep a *current* drug reference book available at all times. You should be able to readily identify substances that must be controlled.

2. Keep controlled substances locked securely. Double-locking is required in most situations. This means:
   a. Placing the drugs in a locked safety box.
   b. Placing the locked box in a cupboard that is also locked.
3. Conceal and secure prescription pads at your office, clinic, or facility. Do not leave pads out in the open, especially in patient examining rooms. The prescription pads, with the physician's DEA registration number, are a possible source of fraud and drug tampering when forged and used illegally. Keep the pads locked up and in a designated location (e.g., a drawer), out of the public areas of the office or nursing station.
4. Keep accurate records of each controlled substance dispensed, received, or destroyed at your facility. These records, as well as the records from the previous two years, must be available at all times. Properly destroy expired drugs and old records.
5. Be responsible for keeping up to date with current news of the activities of the FDA and the DEA. If working for a physician, monitor the DEA registration renewal date. Keep informed of any changes in the scheduling of controlled substances.
6. Establish a working rapport with a pharmacist. A local pharmacist is an excellent resource for you when you are unsure of your legal responsibilities with drugs or have any uncertainties about drug therapy.
7. If you work in an office, maintain a professional rapport with the pharmaceutical representatives who leave drug samples there. They are also excellent resources for drug information.

CHAPTER REVIEW QUIZ

Complete the following statements.

1. The first major U.S. drug law was passed in the year _____ and was called the _____.
2. USP stands for _____.
3. NF stands for _____.
4. Which drug law established the USP and NF (which are now one)? _____
5. The agency that requires you to keep a record of each controlled substance transaction is the _____.
6. Prescriptions for schedule C-_____ drugs may be phoned in by the health care practitioner.
7. How long must you keep an inventory record of each controlled substance transaction at your office? _____
8. Three responsibilities of the FDA include:

   _____

   _____

   _____
9. What types of drugs are listed in the C-V schedule? _____
10. What method is recommended for securing the controlled substances at your office?

    _____
11. If a patient calls to request a refill of a Percocet (C-II) prescription, how would you reply?

    _____
12. Dawn Vasquez has a rare disease that requires medication for only a small population of patients. Which act has allowed her drug to be produced even though it is not profitable to the pharmaceutical industry? _____

Go to your StudyWARE™ CD-ROM and have fun learning as you play games and answer case study-related questions to help reinforce key concepts you learned in this chapter.

Go to your Study Guide and complete the review questions for this chapter.

Chapter 2

Drug Names and References

Objectives

Upon completion of this chapter, the learner should be able to

1. Differentiate among the following drug names: generic name, official name, trade name, and chemical name
2. Explain what is indicated by a number included in a drug trade name (e.g., Tylenol No. 3)
3. Define and explain the restrictions of drug sales implied by the following: OTC, legend drug, and controlled substance
4. List at least two drug references available today
5. Discuss several characteristics that you consider important in choosing the best drug reference
6. Identify the types of information listed on drug cards
7. Define the following side effects: ototoxicity, nephrotoxicity, tinnitus, and photosensitivity
8. Define the Key Terms and Concepts

Key Terms and Concepts

Actions
Adverse reactions
Cautions
Classifications
Contraindications
Generic names
Indications
Interactions
Pharmacology
Prototype
Side effects
Trade names

Pharmacology can be defined as the study of drugs and their origin, nature, properties, and effects on living organisms. We need to know why drugs are given, how they work, and what effects to expect. The thousands of drugs products on the market would make this subject difficult to tackle if it were not for:

- Numerous drug references, geared to a variety of levels of readers, from layperson to pharmacist
- Grouping of drugs under broad subcategories
- Continuity in the use of basic identifying terms for the names and actions of drugs

CLASSIFICATIONS

Each drug can be categorized under a broad *subcategory*, or *subcategories*, called **classifications** (see list on next page). While drugs can be classified several different ways, grouping them together according to their therapeutic

use is most helpful to the health care professional. Drugs that affect the body in similar ways are listed in the same classification. Drugs that have several types of therapeutic effects fit under several classifications. For example, aspirin has a variety of effects on the body. It may be given to relieve pain (analgesic), to reduce fever (antipyretic), or to reduce inflammation of tissues (anti-inflammatory). Therefore, aspirin is categorized under three classifications of drugs (as shown in parentheses).

Another drug, cyclobenzaprine (Flexeril), however, is known to be used for only one therapeutic effect: to relieve muscle spasms. Flexeril, therefore, is listed under only the one classification of muscle relaxant.

Examples of some common drug classifications are listed in Table 2-1 below. Are you familiar with any of them already?

The second part of this text compares the characteristics of the various major drug classifications. In each chapter, as a classification is explained, you will learn what general information to associate with drugs of that classification:

- Therapeutic uses
- Most common side effects
- Precautions to be used
- Contraindications (when *not* to use the drug)
- Interactions that may occur when taken with other drugs or foods
- Some of the most common product names, usual dosages, and comments on administration

You will also be given a prototype of each classification. A **prototype** is a *model example*, a drug that typifies the characteristics of that classification. Hopefully, each time you learn of a new drug, you will associate the prototype and its characteristics with the new drug, based on its classification.

You can find the classification, as well as the various names of the drug, by referring to a drug reference book.

Table 2-1 Examples of Common Drug Classifications

CLASSIFICATION	THERAPEUTIC USE	DRUG EXAMPLE(S)
Analgesics	Relieve pain without loss of consciousness	Ibuprofen, aspirin, Tylenol
Antacid	Neutralizes stomach acid	Mylanta, Milk of Magnesia
Anticoagulant	Prevents or delays blood clotting	Heparin, Coumadin
Antianxiety	Reduces anxiety	Valium, Xanax
Antitussive	Prevents or relieves cough	Codeine
Diuretic	Increases urinary output	Lasix
Hypoglycemic	Reduces blood glucose (sugar) levels	Insulin

IDENTIFYING NAMES

Drug names can seem very complicated because a single drug will have many names attached to it. Four specific names can apply to each approved drug:

1. ***Generic name.*** Common or general name assigned to the drug by the United States Adopted Name (USAN) Council; differentiated from the trade name by initial lowercase letter; never capitalized
2. ***Trade name.*** The name by which a pharmaceutical company identifies its product; is copyrighted and used exclusively by that company; can be distinguished from the generic name by capitalized first letter and is often shown on labels and references with the symbol ® after the name (for "registered" trademark)
3. ***Chemical name.*** The exact molecular formula of the drug; usually a long, very difficult name to pronounce and of little concern to the health care practitioner
4. ***Official name.*** Name of the drug as it appears in the official reference, the USP/NF; generally the same as the generic name

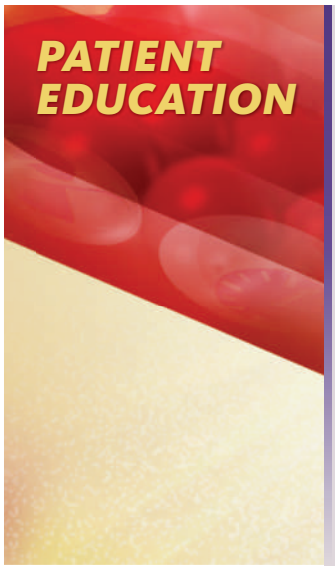
The use of **generic names** and **trade names** for drugs can be compared to the various names of grocery products. Two examples of generic names are orange juice and detergent. Corresponding trade names are Sunkist, Bird's Eye, Tropicana, and Minute Maid and Cheer, Tide, All, and Fab. While there is only one generic name, there may be many trade names.

When a company produces a new drug for the market, it assigns a generic name to the product. After testing and approval by the FDA, the drug company gives the drug a trade name (often something short and easy to remember when advertised). For 17 years, from the time the company submits a new drug application (NDA) to the FDA for approval, the company has the exclusive right to market the drug. Once approved, the drug is listed in the USP/NF by an official name, which is usually the same as the generic name. When 17 years have passed, and the patent has expired, other companies may begin to combine the same chemicals to form that specific generic product for marketing. Each company will assign their own specific trade name to the product or the drug can be offered simply by its generic name and strength, such as acetaminophen 325 mg. See Table 2-2 which compares the names for two drugs.

Table 2-2 Comparison of Drug Names

GENERIC NAME	CHEMICAL NAME	TRADE NAMES (DRUG COMPANY)
Tetracycline hydrochloride	4-(dimethylamino)-1,4,4a,5,5a,6,11,12a-octahydro-3,6,10,12,12a pentahydroxy-1,11 dioxi-naphthacene-2carboxamide	Sumycin (PD-RX Pharmaceuticals) Tetracycline HCL (IVAX)*
Propoxyphene hydrochloride	alpha-4 dimethylamino-3-methyl-1-2,2-diphenyl-2 butanol, propionate hydrochloride	Darvon (Xanodyne) Propoxyphene HCL (Mylan)*

*Some companies simply elect to market the product by the generic name.



Patients may ask you about the difference between generic and trade (brand) name products. The FDA regulates the manufacturing of generic drugs, so patients can be assured they are often safe and cost-effective alternatives. Generally, trade name products are more expensive, although the basic active ingredients (drug contents) are the same as in the generic. The higher price helps to pay for the costs of drug development and advertisements promoting the trade name. (Can you think of certain trade names that are heavily advertised in television commercials?)

Since generic drug equivalents may exist for both prescription and over-the-counter (OTC) drug products it is often economically wise to check for medicines that have the same generic components and strengths. For example, several cough syrups may have exactly the same contents, but the prices may vary widely.

Read and compare all ingredients on the labels.

Concerning prescription drugs, most states have enacted legislation encouraging physicians to let pharmacists substitute less expensive *generic equivalents* for prescribed brand name drugs. Specific provisions of drug *substitution laws* vary from state to state.

The physician may indicate "no substitutions" on the prescription, usually indicated by a DAW (dispense as written). Often physicians have preferences for certain products. Even though the drug contents are the same, the "fillers," or ingredients that are used to hold the preparation together, may be slightly different. This difference in fillers may affect how quickly the drug dissolves or takes effect. Dyes in some products may alter effects in some sensitive patients by leading to an allergic response.

Many products are combinations of several generic components. You will recognize this when you see several generic names (not capitalized) and corresponding amounts listed under one trade name (capitalized). Examples are given in Table 2-3.

It should be noted that a number may be part of the trade name. The number often refers to an amount of one of the generic components and helps to differentiate it from an almost identical product. Identify the significance of the numbers in comparing the following trade names:

Trade Name	*Generic Name and Amount*
Tylenol No. 2	acetaminophen 300 mg codeine 15 mg
Tylenol No. 3	acetaminophen 300 mg codeine 30 mg
Tylenol No. 4	acetaminophen 300 mg codeine 60 mg

Table 2-3 Examples of Combination Drugs

TRADE NAME	GENERIC NAME AND AMOUNT
Dyazide (used to treat high blood pressure)	hydrochlorothiazide 25 mg, triameterene 37.5 mg
Glucovance (used to treat Type 2 Diabetes mellitus)	glyburide 1.25 mg, metformin 250 mg
Robitussin DM 5 mL syrup	dextromethorphan, 10 mg; guiafenesin, 100 mg

Note that each product contains the same amount of acetaminophen, with varying amounts of the controlled substance codeine. *The larger the number in the name, the greater is the amount of controlled substance present.*

Many drug errors have occurred because the trade name was misinterpreted for the number of tablets to be given. So . . .

Be certain you can clearly read and understand the order!

Another type of drug error involves preventable allergic reactions to one of the generic components of a medication. The problem stems from:

Not consulting the patient's chart for the history of allergies before a new medication is ordered or given

Not checking a reference to find out if a medication being ordered or given contains any generic components to which the patient has a known allergy

For example, if a patient has an allergy to aspirin, do not administer the first dose of any new medication to the patient without finding out if the product contains aspirin. Although the doctor is in error for ordering the medication, you are also in error for administering a medication with which you are unfamiliar. A proficient health care practitioner should check the history and chart for known allergies, and pick up any discrepancies. Alertness is the key to safety in any setting.

According to the December 2008 issue of *Consumer Reports*, as much as 25% of drug errors occur when the name of one drug looks or sounds like another. For example, the generic drug clonidine for high blood pressure can be confused with the brand name drug Klonopin used for seizures; Celebrex for arthritis can be confused with Celexa for depression.

Always keep a drug reference handy, and use it when you are unfamiliar with the generic components of a drug ordered for a patient with known drug allergies. With experience, you will learn and remember the names of products most commonly used at your facility.

LEGAL TERMS REFERRING TO DRUGS

A drug may be referred to by terms other than its classification, generic name, trade name, chemical name, or official name. As mentioned in Chapter 1, the following terms imply the legal accessibility of the drug:

1. ***OTC.*** Over the counter; no purchasing restrictions by the FDA
2. ***Legend drug.*** Prescription drug; determined unsafe for over-the-counter purchase because of possible harmful side effects if taken indiscriminately; includes birth control pills, antibiotics, cardiac drugs, and hormones

The legend drug is so named because it requires a legend or warning statement that says, "Federal Law prohibits dispensing without a prescription."

3. ***Controlled substance.*** Drug controlled by prescription requirement because of the danger of addiction or abuse; indicated in references by schedule numbers C-I to C-V (see Chapter 1)

Figure 2-1 shows the information contained on a drug label including the trade name (Percocet) and the generic names of the two drugs (oxycodone and acetaminophen) that it contains.

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Test Yourself! Play interactive games concerning key terms and concepts in this chapter.

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FIGURE 2-1 Information contained on a drug label including the trade name (Percocet) and the generic names of the two drugs (oxycodone and acetaminophen) that it contains.

TERMS INDICATING DRUG ACTIONS

Most references follow a similar format in describing drugs. When you research drug information, you will find the following terms as headings under each drug. You will find specific information more quickly if you understand what is listed under each heading.

Indications. A list of medical conditions or diseases for which the drug is meant to be used (e.g., diphenhydramine hydrochloride [Benadryl], is a commonly used drug; indications include allergic rhinitis, mild allergic skin reactions, motion sickness, and mild cases of parkinsonism).

Actions. A description of the cellular changes that occur as a result of the drug. This information tends to be very technical, describing cellular and tissue changes. While it is helpful to know what body system is affected by the drug, this information is geared more for the pharmacist (e.g., as an antihistamine, Benadryl appears to compete with histamine for cell receptor sites on effector cells).

Contraindications. A list of conditions for which the drug should *not* be given (e.g., two common contraindications for Benadryl are breast-feeding and hypersensitivity).

Cautions. A list of conditions or types of patients that warrant closer observation for specific side effects when given the drug (e.g., due to atropine-like activity, Benadryl must be used cautiously with patients who have a history of bronchial asthma or glaucoma, or with older adults [see Chapter 27]).

Side Effects and Adverse Reactions. A list of possible unpleasant or dangerous secondary effects, other than the desired effect (e.g., side effects of Benadryl include sedation, dizziness, disturbed coordination, epigastric distress, anorexia, and thickening of bronchial secretions). This listing may be quite extensive, with as many as 50 or more side effects for one drug. Because it is difficult to know which are most likely to occur, choose a reference book that underlines or italicizes the most common side effects. Certain drugs may have side effects with which you are not familiar. Note the definitions of the following three side effects associated with specific antibiotics (Figure 2-2).

- Ototoxicity causes damage to the eighth cranial nerve, resulting in impaired hearing or ringing in the ears (tinnitus). Damage may be reversible or permanent.
- Nephrotoxicity causes damage to the kidneys, resulting in impaired kidney function, decreased urinary output, and renal failure.
- Photosensitivity is an increased reaction to sunlight, with the danger of intense sunburn.

Interactions. A list of other drugs or foods that may alter the effect of the drug and usually should not be given during the same course of therapy (e.g., monoamine oxidase [MAO] inhibitors will intensify the effects of Benadryl; you will find MAO inhibitors listed under interactions for many drugs; the term refers to a group of drugs that have been used for the treatment of depression; it has been found that they can cause serious

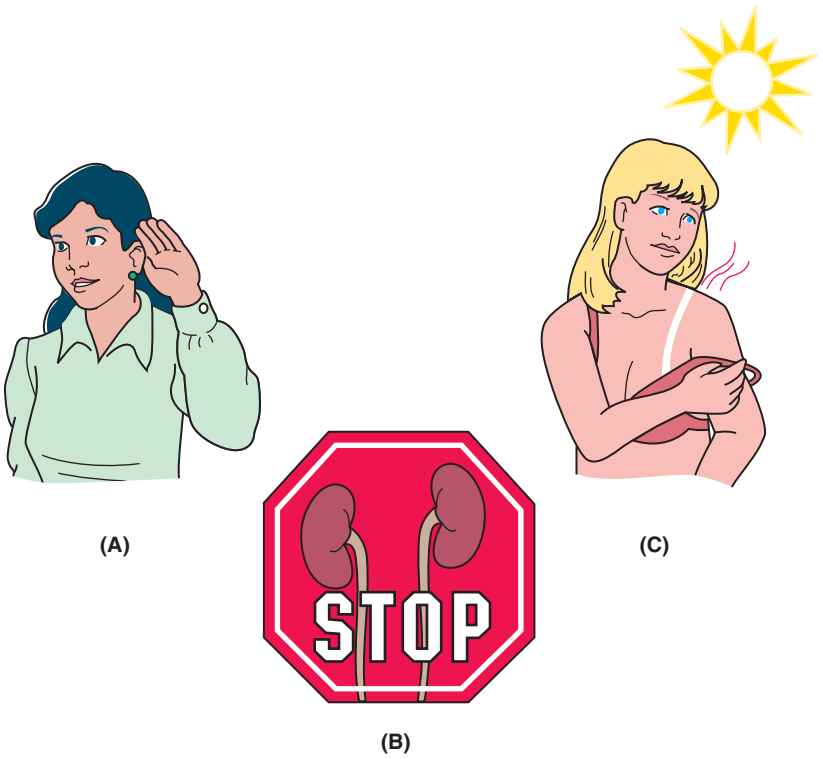


FIGURE 2-2 Side effects or adverse reactions can include (A) otoxicity, (B) nephrotoxicity, and (C) photosensitivity.

blood pressure changes, and even death, when taken with many other drugs and some foods).

Other headings often listed under information about a drug include "How Supplied" and "Usual Dosage." "How Supplied" lists the available forms and strengths of the drug. "Usual Dosage" lists the amount of drug considered safe for administration, the route, and the frequency of administration. For example:

How supplied: tablets (tabs): 20 mg and 40 mg; suppository: 20 mg

Usual dosage: 10 mg orally every 4 h (q4h)

For a listing of common abbreviations regarding drug administration and medication orders, see Tables 4-1 and 5-1 in the upcoming chapters.

DRUG REFERENCES*

The Physicians' Desk Reference (PDR) is one of the most widely used references for drugs in current use. It is an old standby found in every medical setting: offices, clinics, hospital units, pharmacies, and so on. As the name indicates, however, it is geared to the physician. Many new choices of references are available today. Three are compared here, including the PDR. You must find the reference most suitable for you, one that you can interpret quickly and easily. By becoming knowledgeable about the drugs you administer, you may prevent possible drug errors from occurring.

**References listed here were used to compile the information in this book.*

Physician's Desk Reference (PDR)†

PRO	CON
Distributed to practicing physicians; single hardback volume	Geared for physicians and pharmacists
Several supplements published throughout the year, with revised information or description of new products introduced after the previous edition went to press	Lengthy descriptions
All drugs cross-referenced, by several color-coded indexes, according to one of the following: • Company that makes the drug (white, "Manufacturers' Index") • Trade and generic names (pink, "Product Name Index") • Drug classification (blue, "Product Index")	Difficult to sort out what is most important to remember
Includes photographs of many drugs for product identification	No easily identified nursing implications
Includes a list of all U.S. Poison Control Centers, with addresses and phone numbers	Includes many code numbers in the description of "How Supplied," making it difficult to interpret
Includes a description of substances used for medical testing (green, "Diagnostic Product Information"), for example, barium, X-ray dyes, substances used for allergy testing	Contains only those drugs that manufacturers pay to have incorporated; incomplete with regard to OTC drugs, making it necessary to buy PDR OTC book

†Published annually by Biomedical Information Corp., New York, NY.

United States Pharmacopeia/Dispensing Information (USP/DI)*

PRO	CON
Two paperback volumes (and six updates on new drugs per year): • *Drug Information for the Health Provider*, drug information for the physician; includes up-to-date information on carcinogenicity (studies on the ability of drugs to cause cancer) • *Advice for the Patient*	No photographs of drugs
Easy-to-read, practical guidelines for the patient	Must be purchased, is not distributed freely
Stresses most important aspects of the patient's history for the physician to be aware of before prescribing the drug	
Stresses many tips for proper use of medication and what precautions to take	
Includes a pronunciation key for each drug name	

*Published annually by U.S. Pharmacopeial Convention, Inc., Rockville, Maryland.

AHFS Drug Information (American Health-System Formulary Service)†

PRO	CON
Distributed to practicing physicians; single paperback volume	Some parts (e.g., "Chemical Information" and "Drug Stability") not necessary for the health care practitioner
Good, concise information; easy to read	No photographs of drugs
Arranged by classifications, with a general statement about each classification at the beginning of each section	
Off-label drug indications are listed (not FDA-approved)	

†Published annually by American Society of Health-System Pharmacists, Bethesda, Maryland.

Other references (e.g., *The Pill Book*, *Handbook of Nonprescription Drugs*) may be found in bookstores, but they may not contain adequate information for the health care practitioner. Your school may recommend a specific drug reference other than the three listed in this text. Many new references geared to the nurse or health care practitioner are currently being published. Electronic drug references such as Lexi-Drugs and/or Epocrates (a free version of this) are also widely used.

THE INTERNET AS REFERENCE

The Internet offers a wealth of information regarding medications and the conditions they treat. However, there can be serious dangers associated with some online sources that may not be reliable, professional, or even legitimate. Therefore, care must be taken to identify and use only Web sites that are supervised and controlled, such as those under the auspices of government agencies or sponsored by professional pharmacist groups. It is important for the health care practitioner to obtain accurate information and also be able to direct the patient or client to reliable sources of information regarding medicines. It is the health care practitioner's responsibility to caution the layperson regarding the controversial and dangerous practices of "online prescribing" without ever evaluating the patient in person, or obtaining medicines without prescriptions through the Internet.

Remember that all Web sites are not created equal. Pay attention to a few simple rules when seeking the most reputable ones.

1. Check the source. Have scientific studies been done with a large enough sample? Are results reliable and valid? Are there links to a page listing professional credentials or affiliations?
2. Check the date of articles. Medicine is a rapidly evolving field. Information can go out of date quickly.
3. Be wary of information from forums and testimonials. Motivations are unknown. The information is not necessarily valid and there may be a hidden agenda.

The following Web sites are reliable professional sources of medical information:

http://www.aphanet.org	sponsored by the American Pharmaceutical Association (AphA), the national professional society of pharmacists.
http://www.fda.gov	U.S. Food and Drug Administration, includes "Human Drugs" and Center for Drug Evaluation and Research (CDER).
http://www.safemedication.com	sponsored by the American Society of Health System Pharmacists. Covers correct dosage, side effects, and optimal use of most prescriptions and over-the-counter drugs. Also offers reports on topics such as antibiotic-resistant bacteria.
http://www.uspdqi.org	U.S. Pharmacopeia/Dispensing Information (USP/DI) (See United States Pharmacopeia, previous page.)
http://www.cdc.gov/nip/	U.S. Centers for Disease Control and Prevention, National Immunization Program. Covers vaccines and immunizations.
http://medlineplus.gov/	A service of the U.S. National Library of Medicine and the National Institutes of Health. A great source for medicine and related health topics.

These sites provide links to other Web sites that can be accessed through the Internet.

DRUG CARDS

As a learner of pharmacology, you may find it helpful to prepare drug cards because there are so many drugs to learn. Many educational programs require drug cards with the curriculum. You may use 3×5 or 5×7-inch index cards stored in a recipe card box or other similar file. Included on the cards should be the information most useful to medical personnel. Although the cards should be updated periodically, using them saves valuable time compared to using the larger drug references. Preparing drug cards also reinforces learning. Certain information should be included on the drug card:

1. Generic and trade name of the drug
2. Classification or classifications of the drug
3. Forms and routes of administration
4. Drug action
5. Indications
6. Side effects
7. Contraindications
8. Interactions
9. Dosage range and customary dosage
10. Any special instructions for giving the medication

In addition to making it easier and faster to locate information on drugs, drug cards constitute an ideal method of becoming more knowledgeable about

drugs, classifications, and other pharmaceutical terminology. Keep in mind that handheld electronic devices are also extremely useful for storing large amounts of drug information and making it readily available to the user.

Pharmaceutical salespeople and drug company representatives frequently have drug inserts or package brochures that are also useful. Such material can be attached to index cards or filed separately. It is especially important that drug cards be prepared on those drugs used predominantly at your medical facility.

The following is a sample drug card. Note that a number of abbreviations are used to save space. Common abbreviations regarding drug administration and medication orders appear in Tables 4-1 and 5-1 and you will soon become familiar with all the abbreviations and terms stated in this sample drug card.

Drug. Nitroglycerin (Nitro-Bid, Nitrostat).

Classification. Vasodilator.

Form and Route. Sublingual tablet, timed-release tablets or capsules, ointment, dermal patches, and IV.

Action. Relaxes smooth muscles, dilates arterioles and capillaries.

Uses. Management of acute angina pectoris episodes.

Side Effects and Toxicities. Headache with throbbing, dizziness, weakness, blurred vision, dry mouth, tachycardia, and postural hypotension.

Contraindications. Glaucoma, intracranial pressure, and hypotension.

Interactions. With alcohol, PDE inhibitors (Viagra), and contraindicated with nitrates.

Dosage. Sublingual, one tablet under tongue or in buccal pouch, may be repeated three times (X3) if necessary; timed-release capsule, two or three times a day at 8–12-h intervals; ointment, apply to any convenient skin area and spread in thin, uniform layer 1–2 inches, may be applied every 6 hours around-the-clock.

Special Instruction. Severe headache may occur; flushing, dizziness, or weakness is usually transient; if blurred vision or dry mouth occurs, discontinue use.

CHAPTER REVIEW QUIZ

Match the definition with the term.

1. _____ List of conditions for which a drug is meant to be used
2. _____ Subcategories of drugs based on their effects on the body
3. _____ Description of the cellular changes that occur as a result of a drug
4. _____ Conditions for which a drug should not be given

a. Contraindications
b. Precautions
c. Indications
d. Prototype
e. Actions
f. Classifications

Refer to the following drug description to answer questions 5–8.

Pyridium®
(phenazopyridine HCl tablets, USP)
Product of Warner-Chilcott, Inc.
Description: Pyridium (phenazopyridine HCl) is a urinary tract analgesic agent, chemically designated 2.6-pyridinediamine, 3-(phenylazo), monohydrochloride.

5. The generic name of the drug is _____.
6. The chemical name of the drug is _____.
7. The trade name of the drug is _____.
8. What is indicated by the ® symbol after the drug name?

_____

9. List three drug references:

_____

_____

_____

10. Explain the difference between these two medication orders:

a. Give two Tylenol, PO.

b. Give one Tylenol No #2 PO.

_____

_____

11. An elderly male was found unconscious in his bedroom with several pink and blue pills beside his bed but no labeled pill bottle can be found. He is rushed to the emergency department for treatment. What drug reference source will be most helpful in this situation?

Go to your StudyWARE™ CD-ROM and have fun learning as you play games and answer case study-related questions to help reinforce key concepts you learned in this chapter.

Go to your Study Guide and complete the review questions for this chapter.

Chapter 3

Sources and Bodily Effects of Drugs

Objectives

Upon completion of this chapter, the learner should be able to

1. Identify the five sources of drugs
2. Differentiate between the following: drug actions and drug effects, systemic effects and local effects, loading dose and maintenance dose, and toxic dose and lethal dose
3. Define the following processes as they relate to the passage of drugs through the body and give conditions that may decrease the effectiveness of each: absorption, distribution, metabolism, and excretion
4. Define the following terms: selective distribution, toxicity, placebo, synergism, potentiation, and antagonism
5. List several variables that may affect the action of drugs
6. Identify the fastest route of drug administration
7. Define the following undesirable drug effects: teratogenic effect, idiosyncrasy, tolerance, dependence, hypersensitivity, and anaphylactic reaction
8. Define the Key Terms and Concepts

Key Terms and Concepts

Adverse drug effects
Dosage
Drug interactions
Drug processes
Effects of drugs
Source of drugs
Therapeutic range
Variables

SOURCES OF DRUGS

Any chemical substance ingested or applied on the body for the purpose of affecting body function is referred to as a drug. In earlier times, these substances were found in nature, sometimes accidentally. Plants were the primary **source of drugs** used on the human body. Berries, bark, leaves, resin from trees, and roots were found to aid the body and are still very important drug sources today (Figure 3-1).

Minerals from the earth and soil also found their way into human use as drugs. Iron, sulfur, potassium, silver, and even gold are some of the minerals used to manufacture drugs.

More sophisticated sources of drugs emerged as human beings progressed. Research led to the use of substances from *animals* as effective drugs.

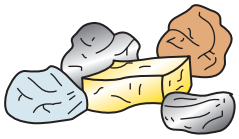
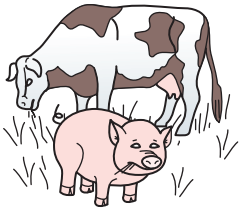
Sources of Drugs	Example	Trade Name	Classification
 Plants	Cinchona Bark	Quinidine	Antiarrhthymic
	Purple Foxglove Plant	Digitalis	Cardiotonic
	Poppy Plant (Opium)	Morphine, Codeine	Analgesic Analgesic, Antitussive
 Minerals	Magnesium	Milk of Magnesia	Antacid, Laxative
	Zinc	Zinc Oxide Ointment	Sunscreen, Skin Protectant
	Gold	Auranofin	Anti-inflammatory; Used in the Treatment of Rheumatoid Arthritis
 Animals	Pancreas of Cow, Hog	Insulin: regular, NPH, PZI	Antidiabetic Hormone
	Stomach of Cow, Hog	Pepsin	Digestive Hormone
	Thyroid Gland of Animals	Thyroid, USP	Hormone
 Synthetic	Meperidine	Demerol	Analgesic
	Diphenoxylate	Lomotil	Antidiarrheal
	Co-Trimoxazole	Bactrim, Septra	Anti-infective Sulfonamide; Used in the Treatment of Urinary Tract Infections (UTI) and Some Other Infections
 DNA	Hepatitis B vaccine, insulin, and growth hormone	"not applicable"	Vaccine, hormone and hormone respectively

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FIGURE 3-1 **Sources of drugs: plant, mineral, animal, synthetic, and recombinant DNA.**

Substances lacking in the human body can be replaced with similar substances from the glands, organs, and tissues of animals. The origin of drugs from an animal source even now includes human extractions. The pituitary gland from cadavers can be used to make a drug for the treatment of growth disorders.

Chemists use synthetic sources to make drugs to market for human consumption. The *synthetic* (manufactured) sources evolved with human skills in laboratories and advanced understanding of chemistry. Today, through advances in computers, millions of potential drug candidates can be screened on computers quickly and efficiently using a process called *chemoinformatics*. Chemoinformatics is the application of computer technology, statistics, and mathematics to study information about the structure, properties, and activities of molecules. This method is probably the most actively pursued source of drugs by major companies today. Competitive research is a big industry in experimenting with chemicals to discover cures for current medical problems. Numerous antibiotics are synthetic or semisynthetic, the results of researchers meeting the need for better treatment of infections. Someday the cure for cancer or human immunodeficiency virus (HIV) may be found from a synthetic source developed in a laboratory.

Genetic engineering and the recently developed technique of *recombinant DNA technology* has allowed for the production of biological active substances that are in the body and can be used to treat certain diseases. DNA is the genetic material of the cells, and the DNA sequence determines the genetic code. Genetic engineering refers to the alteration of genes done in a lab setting.

Recombinant DNA techniques involve combining the DNA of two or more different organisms for a desired change or improvement. Some examples of therapeutic agents derived by recombinant DNA technology are: Hepatitis B vaccine, insulin, and growth hormone. One of the areas of most current interest in recombinant DNA technology is gene therapy. This consists of essentially inserting normal genes into a human chromosome to counteract the effects of an abnormal or missing gene. This has huge implications for preventive medical therapy as well as ethical considerations.

Investigational New Drugs (INDs)

During the 1990s, the emphasis on investigational new drugs (INDs) was on the development of drugs for the treatment of life-threatening or other very serious conditions, for example, HIV infection/AIDS, various malignancies, and Alzheimer's disease. Three of the many INDs developed in the 1990s include:

- Zidovudine (AZT) (Retrovir), which slows the progression of HIV infection in some patients. It is not a cure.
- Interferon (Roferon A), which has been used to treat many different malignancies and also has been used in the management of AIDS-related Kaposi's sarcoma.
- Tacrine (Cognex), which has been used to slow the progression of dementia in some patients with Alzheimer's disease. However, this product was removed from the market due to liver toxicity.

In the twenty-first century, several of the INDs developed recently include:

- Combination drugs that treat more than one disease at a time. For example, **Caduet®**, which combines Norvasc and Lipitor for

simultaneous treatment of high blood pressure and high cholesterol (two major risk factors for cardiovascular disease), was the first product to treat these conditions with a single tablet.

- **Avastin**™, an antiangiogenesis drug, is indicated as a first-line treatment for patients with metastatic colorectal cancer. A monoclonal antibody, it is the first FDA-approved product that prevents the formation of new blood vessels, a process known as angiogenesis. When tumors are unable to form new blood vessels, they are denied blood, oxygen, and other nutrients needed for their growth and metastasis. Avastin extended patient's lives longer when it was given with standard drugs for colon cancer.
- Many exciting developments have recently occurred in insulin delivery that will enhance the quality of life for insulin users. These products include an inhaled insulin product called Exubera that was marketed by Eli Lilly and approved by the FDA, but due to lung toxicity the product was withdrawn from the market. Further studies are underway.

Research continues with the implantable insulin pump, transdermal patch, and many other INDs in the treatment of many very serious diseases.

EFFECTS OF DRUGS

No matter how different the sources, the common characteristic of all drugs is the ability to affect body function in some manner. When introduced into the body, all drugs cause cellular changes (drug actions), followed by some *physiological change* (**effects of drugs**). Generally, drug effects may be categorized as systemic or local:

1. ***Systemic effect.*** Reaches widespread areas of the body (e.g., acetaminophen [Tylenol] suppository, although given rectally, has the ability to be absorbed and distributed throughout the body to cause a general reduction in fever and pain).
2. ***Local effect.*** Is limited to the area of the body where it is administered (e.g., dibucaine ointment [Nupercainal], applied rectally, affects only the rectal mucosa to reduce hemorrhoidal pain).

DRUG PROCESSING BY THE BODY (PHARMACOKINETICS)

Kinetics means "movement" and therefore *pharmacokinetics* literally means what happens to the drug as it moves throughout our bodies.

Within the body, drugs undergo several changes. From start to finish, the biological changes consist of four **drug processes** **(abbreviated ADME)**:

1. ***Absorption.*** Passage of a substance through a membrane into the bloodstream
2. ***Distribution.*** Moving from the bloodstream into the tissues and fluids of the body
3. ***Metabolism.*** Physical and chemical alterations that a substance undergoes in the body
4. ***Excretion.*** Eliminating waste products of drug metabolism from the body

Many variables affect how quickly or successfully substances go through the body via these four processes. If any of the four processes is hindered, the drug action and effects will be impeded. Table 3-1 lists conditions that may hamper each process.

Directions for the administration of one drug versus another may vary widely because the physical properties of the drugs may vary widely. The specific directions ("Usual Dosage and Administration," "Contraindications," and "Warnings") that accompany each drug are given to enhance the absorption, distribution, metabolism, and excretion of the drug. For example, directions to "Give on an empty stomach" ensure the most effective means of absorption. "Use cautiously in patients with renal dysfunction" implies possible effects on the excretion of a drug. "Decrease dose in patients with hepatic dysfunction" implies possible effects on the metabolism of a drug. *Read all labels carefully, and caution the patient to do so as well* (Figure 3-2).

Table 3-1 Processing of Drugs within the Body

PROCESS	PRIMARY SITE OF PROCESS	CONDITIONS THAT MAY HAMPER PROCESS
Absorption	Mucosa of the stomach, mouth, small intestine, or rectum; blood vessels in the muscles or subcutaneous tissues; or dermal layers	Incorrect administration may destroy the drug before it reaches the bloodstream or its site of action (e.g., giving certain antibiotics after meals instead of on an empty stomach).
Distribution	Circulatory system, through capillaries and across cell membranes	Poor circulation (impaired flow of blood) may prevent drug from reaching tissues.
Metabolism	Liver	Hepatitis, cirrhosis of liver, or a damaged liver may prevent adequate breakdown of drug, thus causing a build-up of unmetabolized drug.
Excretion	Kidneys, sweat glands, lungs, or intestines	Renal damage or kidney failure may prevent passage of drug waste products, thereby causing an accumulation of the drug in the body.

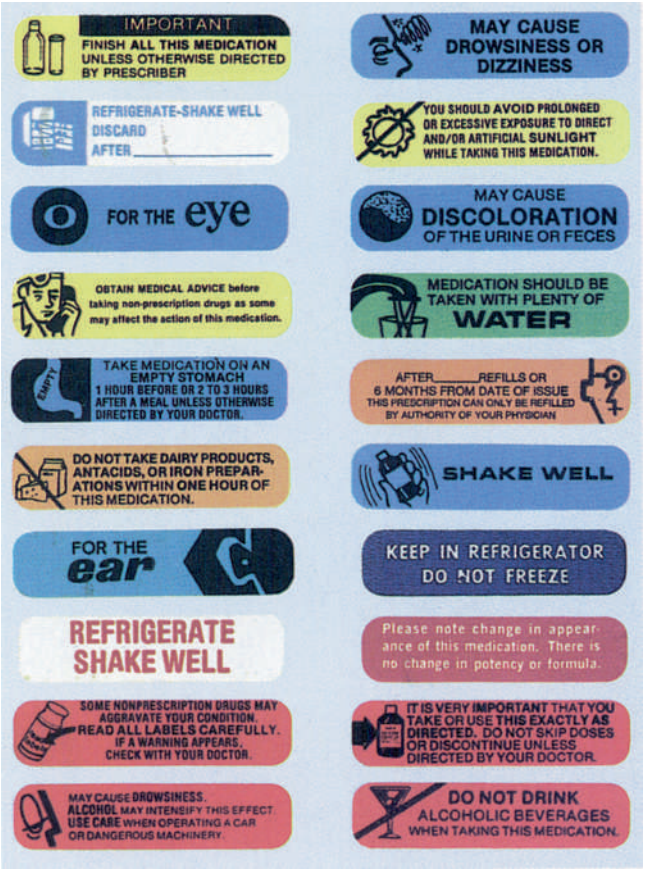

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FIGURE 3-2 Warning labels are placed on prescription medication containers. Patients should be advised to read and follow the precautions or instructions.

ABSORPTION

The site of absorption of drugs varies according to the following physical properties of each drug:

1. ***pH.*** Drugs of a slightly acidic nature (e.g., aspirin and tetracycline) are absorbed well within the acidic stomach environment. Drugs of an alkaline pH are not absorbed well through the stomach, but are readily absorbed in the alkaline environment of the small intestine. The antibiotic tetracycline is not recommended to be given in the presence of milk, dairy products, or antacids, since it will not be properly absorbed. (This is due to *chelation*, which is the formation of an insoluble complex of tetracycline with calcium in dairy products. pH effect may also play a role. It varies with the specific antacid used.) Oral medications for infants (syrups and solutions) may not be absorbed well after infant feedings. The milk or formula neutralizes the acidity of the stomach. Thus, absorption may be enhanced when the infant is given medications on an empty stomach.

2. ***Lipid (fat) solubility.*** Substances high in lipid solubility are quickly and easily absorbed through the mucosa of the stomach. Alcohol and substances containing alcohol are soluble in lipids. They are rapidly absorbed through the gastrointestinal (GI) tract. Substances low in lipid solubility are not absorbed well through the stomach or intestinal mucosa and are absorbed best when given by a means other than the GI tract. An exception is the drug neomycin, which is not lipid soluble and yet is given orally. It is indicated for suppression of intestinal bacteria before intestinal or bowel surgery or in the treatment of bacterial diarrhea. By giving neomycin orally, it passes through the GI tract, unable to be absorbed. As a result, it tends to build up and accumulate in the bowel. There, the trapped antibiotic kills the bacteria in the bowel, for the desired effect.
3. ***Presence or absence of food in the stomach.*** Food in the stomach tends to slow absorption due to a slower emptying of the stomach. If a fast drug effect is desired, an empty stomach will facilitate quicker absorption. On the other hand, giving some medications on an empty stomach is contraindicated. Medications that are irritating to the stomach can be buffered by the presence of food. Directions may indicate "Give after meals" or "Take with food" to decrease side effects (e.g., nausea and gastric ulcers) on the GI tract.

DISTRIBUTION

The movement of a drug from the bloodstream into the tissues and fluids of the body is also affected by specific properties of the drug. Reaching sites beyond the major organs may depend on the drug's ability to cross a lipid membrane. Some drugs pass the "blood-brain barrier" or the "placental barrier," whereas others do not. You may read about drugs contraindicated for lactating mothers because the drug has the ability to pass through the cell membranes into the milk.

Some drugs have a *selective distribution* (Figure 3-3). This refers to an affinity, or attraction, of a drug to a specific organ or cells. For example, amphetamines have a selective distribution to cerebrospinal fluid (CSF). The human chorionic gonadotropin (hCG) hormone, which is used as a fertility drug, has a selective distribution to the ovaries.

By virtue of their properties, some drugs are distributed more slowly than others. Thus, while two drugs may be categorized in the same drug classification, one may be known to act on the cells and achieve the effect more quickly than the other.

METABOLISM

When transformed in the liver (biotransformation), a drug is broken down and altered to more water-soluble by-products (metabolites). Thus the drug may be more easily excreted by the kidneys.

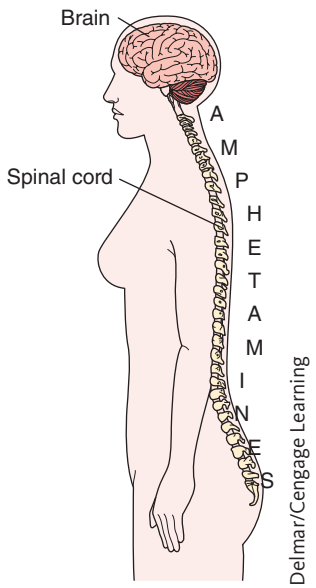

FIGURE 3-3 **Distribution. One example of selective distribution is the attraction of amphetamines to the cerebrospinal fluid.**

If hepatic disease is present, a patient may exhibit toxic (poisonous) effects of a drug. This occurs because the drug is not being broken down properly by the inefficient liver. It may accumulate, unchanged by the liver, and may be unable to pass out of the body's excretory system.

It is possible for some drugs to bypass the process of metabolism. They reach the kidneys virtually unchanged and may later be detected in the urine.

EXCRETION

While it is possible for some drugs to be eliminated through the lungs (e.g., exhaled gases and anesthetics) or through perspiration, feces, bile, or breast milk, most are excreted by the kidneys.

If a drug is not excreted properly before repeated doses are given, a cumulative effect due to a drug build-up may eventually occur. A *cumulative effect* is an increased effect of a drug demonstrated when repeated doses accumulate in the body. Patients with decreased kidney function may be at risk of drug accumulation. If unnoticed, the cumulative effect may build to a dangerous, or toxic, level. This can be of particular concern with older adults. (See Chapter 27.)

Toxicity refers to a condition that results from exposure to either a poison or a dangerous amount of a drug that is normally safe when given in a smaller amount. In drug therapy, the goal is to give just enough of the drug to cause the desired (therapeutic) effect while keeping the amount below the level at which toxic effects are observed. It should be noted that toxicity can develop even with properly dosed or small amounts of a drug.

Digoxin is a cardiac drug that must be given cautiously because of its potential for causing a cumulative effect. Normally, digoxin slows the heart

rate, but if the drug accumulates, the heart rate may slow to a dangerously low level. Circulation and renal function must be adequate, or the digoxin will accumulate, leading to digoxin toxicity.

Keep in mind that the purpose of most medication treatment is to have a desired effect by maintaining a drug level within a **therapeutic range**. The therapeutic range is the range of drug levels in the blood that will give the desired effect without causing serious side effects.

OTHER VARIABLES

Many **variables** affect the speed and efficiency of drugs being processed by the body. The physical properties of the drugs themselves and the condition of the body systems have been discussed. Other variables affecting drug action and effect follow.

Age

Metabolism and excretion are slower in older adults, and therefore attention must be paid to possible cumulative effects. Children have a lower threshold of response and react more rapidly and sometimes in unexpected ways; therefore, frequent assessment is imperative.

Weight

Generally, the bigger the person, the greater the dose should be. However, there is great individual variation in sensitivity to drugs. Many drug dosages are always calculated on the basis of the patient's weight.

Gender

Women respond differently than men to some drugs. The ratio of fat per body mass differs, and so do hormone levels. If the female is pregnant or nursing, drugs should be selected that are safe to use for both the mother and her child.

Psychological State

It has been proven that the more positive the patient feels about the medication he or she is taking, the more positive the physical response. This is referred to as the *placebo effect*.

A *placebo* is an inactive substance that resembles a medication, although no drug is present. For example, a sugar tablet or a saline solution for injection may be used as a placebo in a research study program.

Placebos are most often used in blind study experiments in which groups of people are given either a drug or a placebo. (Needless to say, placebos are not administered if doing so would risk serious or irreversible harm to those taking them.) The individuals, unaware of which they have been given, are studied for the effects. Often, by virtue of strong belief or by the natural fluctuation

of a disease (e.g., headaches may get better without treatment), the placebo-administered individuals achieve the desired effect associated with the drug they think they have received.

It is also possible for a drug's effect to decrease when the attitude of a patient toward a medication is negative.

Attitudes toward medicines can also be influenced positively or negatively by cultural or religious beliefs. The caregiver needs to understand the importance of these beliefs to the patient.

The significance for you, the health care practitioner, is to recognize that your attitude regarding a medication may be picked up by the patient and indirectly may affect the patient's response to the drug.

Drug Interactions

Often patients are prescribed multiple drugs. Whenever more than one drug is taken, it is possible that the *combination* may alter the normal expected response of each individual drug. One drug may interact with another to increase, decrease, or cancel out the effects of the other.

The following terms are used to describe drug interactions:

Synergism. The action of two drugs working together in which one helps the other simultaneously for an effect that neither could produce alone. Drugs that work together are said to be synergistic.

Potentiation. The action of two drugs in which one prolongs or multiplies the effect of the other. Drug A may be said to potentiate the effect of drug B. (See Chapter 19, Analgesics Interactions.)

Antagonism. The opposing action of two drugs in which one decreases or cancels out the effect of the other. Drug A may be referred to as an antagonist of drug B.

It is extremely important for the prescribing physician to know of all medications that a patient is taking in order to prevent undesirable **drug interactions**. On the other hand, it may be intentionally ordered that two drugs be taken together, because some drug interactions are desirable and beneficial. Compare the following situations, describing both desirable and undesirable drug interactions:

Desirable synergism. Simvastatin (Zocor) (lowers high cholesterol) and gemfibrozil (Lopid) (lowers high triglycerides) are very effective in treating patients who have both high cholesterol and triglyceride levels (collectively called high lipids). By giving small amounts of each together, high lipid levels can be treated more effectively.

Undesirable synergism. Sedatives and barbiturates given in combination can depress the central nervous system (CNS) to dangerous levels, depending on the strengths of each.

Desirable potentiation. To build up a high level of some forms of penicillin (an antibiotic) in the blood, the drug probenecid (antigout medication) can be given simultaneously. Probenecid potentiates the effect of penicillin by slowing the excretion rate of the antibiotic.

Undesirable potentiation. Toxic effect may result when cimetidine (Tagamet) (a gastric antisecretory) is given simultaneously with Tofranil (an antidepressant). Tagamet potentiates the level of antidepressant concentrations in the blood.

Desirable antagonism. A narcotic antagonist (e.g., naloxone, Narcan) saves lives from drug overdoses by canceling out the effect of narcotics.

Undesirable antagonism. Antacids taken at the same time as tetracycline may alter the pH and/or form chelates, which are insoluble complexes that prevent the absorption of tetracycline. Antacids may interact with many medications so a current drug reference should be consulted for potential interaction considerations.

Dosage

Different dosages of a drug may bring about variations in the speed of drug action or effectiveness. **Dosage** is defined as the amount of drug given for a particular therapeutic or desired effect. Terms of various dosage levels are:

1. ***Minimum dose.*** Smallest amount of a drug that will produce a therapeutic effect
2. ***Maximum dose.*** Largest amount of a drug that will produce a desired effect without producing symptoms of toxicity
3. ***Loading dose.*** Initial high dose (often maximum dose) used to quickly elevate the level of the drug in the blood (often followed by a series of lower maintenance doses)
4. ***Maintenance dose.*** Dose required to keep the drug blood level at a steady state in order to maintain the desired effect
5. ***Toxic dose.*** Amount of a drug that will produce harmful side effects or symptoms of poisoning
6. ***Lethal dose.*** Dose that causes death
7. ***Therapeutic dose.*** Dose that is customarily given (average adult dose based on body weight of 150 lb); adjusted according to variations from the norm

You may be familiar with the use of a high loading dose followed by a lesser maintenance dose. If you have taken antibiotics, you may have been instructed to take two tablets or capsules initially and then to take one tablet every six hours. It is frequently desirable to give a loading dose of antibiotics to build up a high level and get the process of killing the bacteria started.

Routes of Administration

The route of administration is probably the most significant factor in the speed of drug action.

The route of drug administration can be compared to the route of travel. In planning a trip from point A to point B, you may have a map that shows several courses of travel to reach the destination. The course you select is optional, depending on your choice for the quickest, cheapest, safest, or most scenic route.

Options for routes of drug administration are much the same. There are a number of methods by which drugs may be given to reach their destination. Sometimes the route selected is based on the degree of speed, cost, or safety of administration. Sometimes there is no choice of routes because some medications can be given only by one route. Often this is because absorption occurs by that route only, or the substance is dangerous or toxic when given by another route. Insulin, for example, may be given only by injection (inhalation route still under investigation). Much research has been done to produce an oral form of insulin, but attempts have failed because the drug is destroyed by gastric juices.

The most common routes of administration may be grouped into two main categories:

1. *Enteral or GI tract routes*
   - **a.** Oral (PO)
   - **b.** Nasogastric tube (NG)
   - **c.** Rectal (R)
2. *Parenteral routes*, which include any other than the gastrointestinal tract
   - **a.** Sublingual (SL) (under the tongue) or buccal (cheek: absorbed through mucosa, not swallowed) (note: some classify SL and buccal as oral routes)
   - **b.** Injection routes
     - **i.** Intravenous (IV)
     - **ii.** Intramuscular (IM)
     - **iii.** Subcutaneous (subcu)
     - **iv.** Intradermal (ID)
     - **v.** Intracardiac, Intraspinal, Intraventricular, Intracapsular*
   - **c.** Topical (T)
     - **i.** Dermal (D)
     - **ii.** Mucosal
     - **iii.** Transdermal (skin patches that allow the drug to be slowly absorbed systemically.)
   - **d.** Inhalation

The term *enteral* means within or by way of the intestine. The term *parenteral* is derived from the Greek term *para* "apart from" plus *eneteron*, "the intestine." Therefore, parenteral means any route other than the gastrointestinal (GI) tract.

**The latter four injection routes are less common and are administered by the physician.*

There are advantages and disadvantages in the use of each route. The doctor's choice of a particular route of administration of a drug may depend on (1) desired effects (e.g., fast or slow, local or systemic); (2) absorption qualities of the drug; and (3) how the drug is supplied. Other general points regarding the effect of the route on the drug absorption are as follows:

StudyWARE CONNECTION

See It In Action! Go to the StudyWARE™ CD-ROM to view a video on *Oral Medications and their Administration.*

1. The oral route is the easiest, but the effects are slower because of the time required for dissolution of drug product in the alimentary canal before absorption.
2. The intravenous route is the fastest: Drugs enter the bloodstream immediately. Doses to be given IV are in small amounts; effects are immediate and can be quite dangerous if given in amounts recommended for other routes. Intravenous drugs can be administered by IV push or bolus (a concentrated drug solution) (see Figure 3-4), or they can be diluted and solutions are then infused more slowly by IV drip.
   a. IVs are administered by a physician, registered nurse, or paramedic.
   b. IV is the best route for treatment of emergencies because of the speed of action.
3. Parenteral routes are the choice when:
   a. Patient can take nothing by mouth (NPO).
   b. The drug is not suitable for GI absorption.
4. The intramuscular route is fairly rapid because the muscles are highly vascular. If it is desirable to retard the speed of absorption, a drug to be given IM may be added to an oily base.

StudyWARE CONNECTION

See It In Action! Go to the StudyWARE™ CD-ROM to view a video on *Parenteral Medications.*

5. The transdermal route allows for slower consistent drug absorption over time allowing the patient to usually place one patch on in the morning for the entire day.
6. The inhalation route is fast acting due to the large surface area of the lung and rich blood supply which allows the drug to enter the bloodstream quickly. This route often requires more involved patient cooperation and therefore education to be effective.

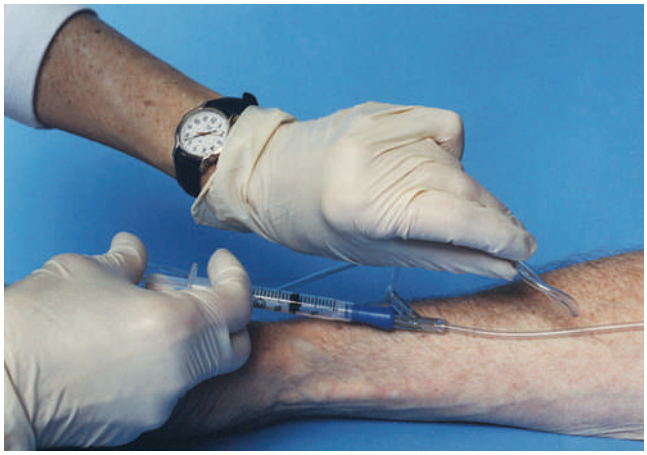

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FIGURE 3-4 Intravenous push or bolus, IV drugs are administered slowly over a specified period of time (usually one to seven minutes).

UNEXPECTED RESPONSES TO DRUGS

Unintended side effects from medications are termed Adverse Drug Reactions (ADR's) and can include a host of reactions such as cough, pain, tremors, headaches, dizziness, change in lab values, and photosensitivity. Several other terms must be defined in order to complete your awareness of the bodily effects of drugs. These terms refer to **adverse drug effects**.

Teratogenic effect. Effect from maternal drug administration that causes the development of physical defects in a fetus. See Table 3-2, which describes the FDA pregnancy categories.

Idiosyncrasy. Unique, unusual, and unexpected response to a drug.

Paradoxical. Opposite effect from that expected. For example, a patient may have a paradoxical reaction to a particular tranquilizer if it causes agitation and excitement rather than tranquility.

Tolerance. Decreased response to a drug that develops after repeated doses are given. To achieve the desired effect, the drug dosage must be increased or the drug replaced.

Dependence. Acquired need for a drug that may produce psychological or physical symptoms of withdrawal when the drug is discontinued.

- Psychological dependence involves only a psychological craving; no physical symptoms of withdrawal other than anxiety.
- Physical dependence exists when cells actually have a need for the drug; symptoms of withdrawal include retching, nausea, pain, tremors, and sweating.

Table 3-2 FDA Drug Pregnancy Categories

CATEGORY	DESCRIPTION
Pregnancy Category A	Drug studies on pregnant women have not demonstrated risk to fetus.
Pregnancy Category B	Drug studies not performed on pregnant woman; animal studies have not shown fetal risk.
Pregnancy Category C	Conclusive drug studies have not yet been performed in pregnant women or animals.
Pregnancy Category D	Drug studies have revealed adverse risk to fetus and the benefit to risk ratio must be established before use during pregnancy.
Pregnancy Category X	Drug studies have shown teratogenic effects and the drug is contraindicated during pregnancy.

Hypersensitivity. Immune response (allergy) to a drug may be of varying degrees.

- May be mild with no immediate effects; rash or hives may appear after three to four days of drug therapy.
- May develop after uneventful previous uses of a drug.
- More likely to exist in patients with other known allergies.

Note Nausea, vomiting, and diarrhea are not considered signs of allergies.

Extreme caution should be taken when giving a medication, especially antibiotics, to a patient for the first time, particularly if the patient has a history of other allergies.

Anaphylactic reaction. Severe, possibly fatal, allergic (hypersensitivity) response

- Signs include itching, urticaria (hives), hyperemia (reddened, warm skin), vascular collapse, shock, cyanosis, laryngeal edema, and dyspnea.
- Treatment includes cardiopulmonary resuscitation (CPR) if indicated and drugs as required: epinephrine (Adrenalin) and fluids to raise blood pressure; corticosteroid (Solu-Medrol) to reduce inflammation and the body's immunological response; or antihistamine (Benadryl) to suppress histamine, thereby reducing redness, itching, and edema.
- Anaphylaxis has been noted often with the following: antibiotics, especially penicillin; X-ray dyes containing iodides (IVP [intravenous pyelogram] dye, angiogram dye, gallbladder dyes, etc.); foods (shellfish, onions, peanuts, etc.); and insect stings (bees and ants).

Knowledge of any adverse reactions to drugs should be included in the patient's history. This information can be helpful in preventing repeated episodes. Getting an accurate drug history and clearly listing known allergies is a critical function of the health care practitioner.

Persons who have had an anaphylactic reaction to a substance should always wear a Medic-Alert tag or bracelet to identify the substance to which they are extremely allergic. Persons who have had hypersensitivity reactions to a substance are more at risk for reactions to other substances as well. Allergies should be listed on a card and carried in the wallet of the sensitive individual.

CHAPTER REVIEW QUIZ

Fill in the blanks.

1.

Drug Sources	Example	Trade Name	Classification

2. Drugs that are distributed throughout the body have _____ effects.

3. Drugs whose action is limited to a specific location have _____ effects.

4. As drugs pass through the body, they undergo four processes:

Process	Definition of Process

5. Factors that may affect the passage of drugs through the body:

Process	Primary Site of Process	Conditions Hampering Process

6. If circulation is poor, metabolism faulty, or excretion inadequate, drugs may build up in the system, leading to _____ effects, causing poisonous, or _____ levels of the drug.

7. Variables affecting the efficiency of drug action include _____, _____, _____, and _____.

Match the term with the definition.

8. Synergism _____
9. Antagonism _____
10. Potentiation _____
11. Lethal dose _____
12. Toxic dose _____
13. Maintenance dose _____
14. Idiosyncrasy _____
15. Tolerance _____
16. Dependence _____
17. Teratogenic _____

a. Amount of drug required to keep drug level steady
b. Amount of drug that can cause death
c. Amount of drug that can cause dangerous side effects
d. One drug making the effect of another drug more powerful
e. Drugs working together for a better effect
f. Drugs working against each other or counteracting each other's effect
g. Acquired need for a drug, with symptoms of withdrawal when discontinued
h. Unusual response to a drug, other than expected effect
i. Effects on a fetus from maternal use of a drug
j. Decreased response after repeated use of a drug, increased dosage required for effect

Fill in the blanks.

18. An allergy or immune response to a drug is called

_____

19. Allergic reactions to drugs may be *mild*, with symptoms such as

_____

_____

20. Allergic reactions to drugs are more common in patients with

_____

21. *Severe* allergic reaction with shock, laryngeal edema, and dyspnea is called

_____

22. Treatment of severe analphylactic reactions can include the following: _____, _____, and _____.

Go to your StudyWARE™ CD-ROM and have fun learning as you play games and answer case study-related questions to help reinforce key concepts you learned in this chapter.

Go to your Study Guide and complete the review questions for this chapter.

Chapter 4

Medication Preparations and Supplies

Objectives

Upon completion of this chapter, the learner should be able to

1. Differentiate between various oral drug forms: sublingual tablet versus buccal tablet, solution versus suspension, syrup versus elixir, enteric-coated tablet versus scored tablet, and timed-release capsule versus lozenge
2. Explain what is meant by parenteral
3. List four classifications of drugs that are commonly given by the rectal route
4. Define the following types of injections and explain how they differ in administration and absorption rate: IV, IM, and ID
5. Compare the IV injections referred to as IV push, IV infusion, and IV piggyback
6. List and define at least eight drug forms used for topical (both dermal and mucosal) administration
7. Explain the advantages of administering drugs via a dermal patch
8. Identify various supplies used in the preparation of medications
9. Define the Key Terms and Concepts

Key Terms and Concepts

Drug form
Inhalable drug forms
Injectable drug forms
Oral drug forms
Parenteral
Rectal drug forms
Route of delivery
Topical drug forms
Transdermal

The forms in which drugs are prepared are as numerous as the routes of administration. **Drug form** refers to the type of preparation in which the drug is supplied. Pharmaceutical companies prepare each drug in the form or forms most suitable for its intended **route of delivery** and means of absorption. *Drug form* and *drug preparation* are synonymous. The *PDR* lists the forms available for each drug under the heading "How Supplied." See Table 4-1 for abbreviations of some of the drug forms and routes of administration.

Table 4-1 Abbreviations for Drug Administration

DRUG FORMS		ROUTES	
Cap	capsule	IM	intramuscular
Elix	elixir	IV	intravenous
Gtt	drop	TOP	topical
supp	suppository	PO, po, per os	oral
susp	suspension	R	rectal
Tab	Tablet	subcu	subcutaneous

NONTRADITIONAL DRUG FORMS AND DEVICES

Great advances in developing new drug forms have revolutionized the way a number of drugs are administered. One of the recent drug forms that have gained a lot of popularity is the dermal patch or **transdermal** delivery system. Dermal patches were first taken on the space shuttles during the 1990s for the prevention of nausea. The key to the transdermal system is that the drug molecules are present in a variety of sizes and shapes that allow for absorption through the skin at various rates. Thus, a patch can provide a constant, even flow of a drug over a long period of time—hours or days. The drug, being released at a consistent rate, remains at an effective level in the blood, as opposed to rising and falling, as happens with pills. Advantages of this method of administration include:

- Easy application, with no discomfort or undesirable taste
- Effectiveness for long periods of time, hours for some drugs and days for others
- Consistent blood level of drug because drug is released at varying rates, rather than all at one time

Dermal patches vary in size, shape, and color (Figure 4-1). They are most commonly seen today on patients for the prevention of angina. Current marketing of dermal patches also includes others for the prevention of motion sickness (may be applied before traveling), for management of chronic pain (e.g., Duragesic; see Chapter 19), as a smoking deterrent (e.g., Habitrol and Nicoderm), and for estrogen replacement (e.g., Estraderm). Research is ongoing in the development of dermal patches for birth control, high blood pressure, ulcers, allergies, and heart conditions. Probably not all drug molecules will be adaptable to this drug form, but it certainly has opened new doors in the area of drug administration.

Implantable devices are available in a variety of sizes and are placed just below the skin near blood vessels where the medication can readily be absorbed into the bloodstream. One example is the small infusion pump implanted in a diabetic patient's waist to deliver a continuous supply of insulin.

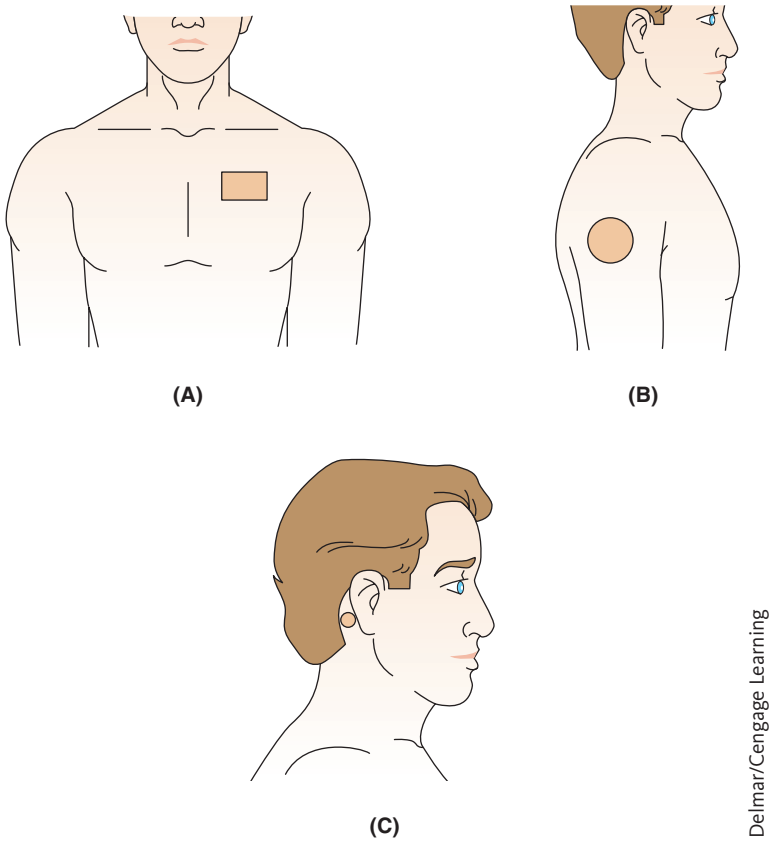

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FIGURE 4-1 Transdermal drug delivery. Dermal patches vary in size, shape, and color (A, B). For prevention of angina pectoris, for management of chronic pain, and (C) for prevention of motion sickness.

Implantable devices are also used to deliver contraceptives and to administer chemotherapeutic drugs to cancer patients.

Another recent and innovative drug form entails sandwiching the drug between very thin plastic membranes and then placing it under the patient's eyelid. This administration permits a controlled release of medicine over an extended time period. Pilocarpine, which is used to treat glaucoma, has been successfully administered in this manner with little or no discomfort.

STANDARD DRUG FORMS

You probably have received medications in many of the standard forms at some time during your life. Each form is defined and listed in the following sections according to the routes of administration. Figure 4-2 illustrates some examples of oral drug forms. As you read in Chapter 3, drugs may be administered through the gastrointestinal (GI) tract or parenterally. GI routes include oral, nasogastric or gastrostomy tube, and rectal. **Parenteral** refers to any route not involving the GI tract, including injection, topical (skin or mucosal), and inhalation routes.

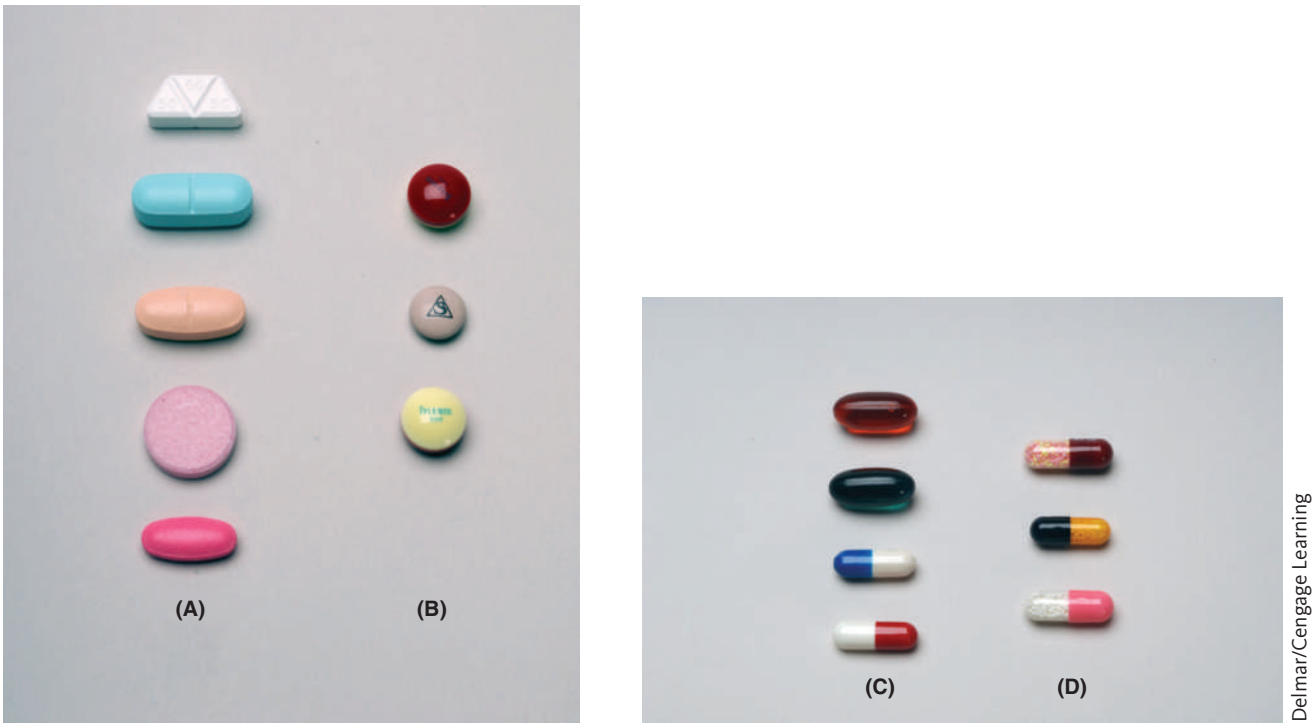

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FIGURE 4-2 Oral drug forms. Tablets and capsules vary in size, shape, and color. (A) Tablets, scored and unscored; (B) enteric-coated tablets; (C) gelatin capsules; and (D) timed-release capsules.

Oral Drug Forms

Oral drug forms include:

Tablet. Disk of compressed drug; may be a variety of shapes and colors; may be coated to enhance easy swallowing; may be *scored* (evenly divided in halves or quarters by score lines) to enhance equal distribution of drug if it has been broken.

Enteric-coated tablet. Tablet with a special coating that resists disintegration by gastric juices. The coating dissolves further down the GI tract, in the enteric, or intestinal, region. Some drugs that are irritating to the stomach, such as aspirin, are available in enteric-coated tablets. To be effective, the coating must never be destroyed by chewing or crushing when it is administered.

Capsule. Drug contained within a gelatin-type container.

- Easier to swallow than non-coated tablets.
- Double chamber may be pulled apart to add drug powder to soft foods or beverages for patients who have difficulty swallowing (unless specifically contraindicated for absorption).

Timed-release (sustained-release) capsule. Capsule containing drug particles that have various coatings (often of different colors) that differ in the amount of time required before the coatings dissolve. This form of drug preparation is designed to deliver a dose of drug over an extended period of time. An advantage of taking a drug in the timed-release form is

the decreased frequency of administration. For example, the antihypertensive Cardizem may be administered in tablet form 60 mg tid (three times daily) or in the timed-release form (Tiazac, 180 mg) only once daily. Because of the significance of the various coatings that encapsulate the drug particles, it is important that the small colored pellets *not* be crushed or mixed with foods. Damage to the coatings of drug pellets allows the drug to be released all at one time as it is administered. Such immediate release of drug is a potential overdose. Timed-release capsules should be swallowed whole, with no physical damage to the contents of the capsule.

Lozenge (troche). Tablet containing palatable flavoring, indicated for a local (often soothing) effect on the throat or mouth.

- Patient is advised not to swallow a lozenge; it should be allowed to slowly dissolve in the mouth.
- Patient is also advised *not* to drink liquids for approximately 15 minutes after administration, to prevent washing of the lozenge contents from the throat or mouth.

Suspension. Liquid form of medication that must be shaken well before administration because the drug particles settle at the bottom of the bottle. The drug is not evenly dissolved in the liquid.

- A cephalosporin (Keflex) suspension is a commonly used antibiotic suspension for children. This form is more easily ingested by children than are capsules of Keflex.

Emulsion. Liquid drug preparation that contains oils and fats in water.

Elixir, fluid extract. Liquid drug forms with alcohol base.

- Should be tightly capped to prevent alcohol evaporation.
- Should not be available to alcoholics.

Syrup. Sweetened, flavored liquid drug form. Cherry syrup drug preparations are common for children.

Solution. Liquid drug form in which the drug is totally and evenly dissolved. Appearance is clear, rather than cloudy or settled (as with a suspension).

Many drug forms for the oral route are commonly available over-the-counter and include thousands of trade name products. The oral route is the easiest and probably the cheapest for administration. It is, however, *not* the route of choice for treatment of emergencies, acute pain, NPO patients (ordered to have nothing by mouth), or patients unable to swallow. Other routes, especially the parenteral routes, produce a more rapid absorption rate and drug effect due to their often direct absorption into the bloodstream.

Rectal Drug Forms

Rectal drug forms include:

Suppository. Drug suspended in a substance, such as cocoa butter, that melts at body temperature.

Enema solution. Drug suspended in solution to be administered as an enema.

The rectal route of administration is often the choice if the patient is ordered to have nothing by mouth (NPO) or cannot swallow. The most common classifications of drugs given rectally include sedatives, antiemetics (prevent vomiting), and antipyretics (reduce fever). A local analgesic effect may also be achieved by this route.

Injectable Drug Forms

Injectable drug forms include:

Liquid. Drug suspended (suspension, must be shaken before given to a patient) or dissolved (solution) in a sterile vehicle.

- Quite often the solutions have a sterile water base and are thus referred to as aqueous (aq) (waterlike) solutions.
- Some solutions have an oil base, which tends to cause a more prolonged absorption time. The oily nature of these solutions makes them thick; thus they are referred to as viscous (thick) solutions.

See It In Action! Go to the StudyWARE™ CD-ROM to view a video on *Powdered Medications.*

Powder. Dry particles of drugs. The powder itself cannot be injected. It must be mixed with a sterile diluting solution (sterile water or saline solution) to render an injectable solution. This is termed *reconstitution* of a drug. Drugs are supplied undiluted in powder form because of the short period of time they remain stable after dilution.

The various injection routes differ according to the type of tissues into which the drug is deposited and the rate of absorption.

Intravenous. Injected directly into a vein. Immediate absorption and availability to major organs renders this route a dangerous one. IV drugs are usually administered by physicians, paramedics, or registered nurses. Types of intravenous injections include:

- IV push, a small volume of drug (bolus) injected into a peripheral saline lock (PRN adapter), attached to a vein (Figure 4-3A). An IV push medication can also be injected into a port on a primary (continuous) injection line (Figure 4-3B).
- IV infusion or IV drip, a large volume of fluids, often with drugs added, that infuses continually into a vein (Figure 4-3C).

Note

When adding a medication to an IV solution bag through the injection port, take the bag down and invert it a few times to disperse the drug throughout the solution instead of concentrated at the bottom of the bag.

See It In Action! Go to the StudyWARE™ CD-ROM to view a video on *Preparing an IV Solution.*

- IV piggyback (IVPB), a drug diluted in moderate volume (50–100 mL) of fluid for intermittent infusion at specified intervals, usually q6–8h; the diluted solution is infused (piggyback) into a port on the main IV tubing or into a rubber adapter on the IV catheter (Figure 4-3D).

Intramuscular. Injected into a muscle, by positioning the needle and syringe at a 90-degree angle from the skin (Figure 4-4). Absorption is fairly rapid due to the vascularity (presence of many blood vessels) in muscle.

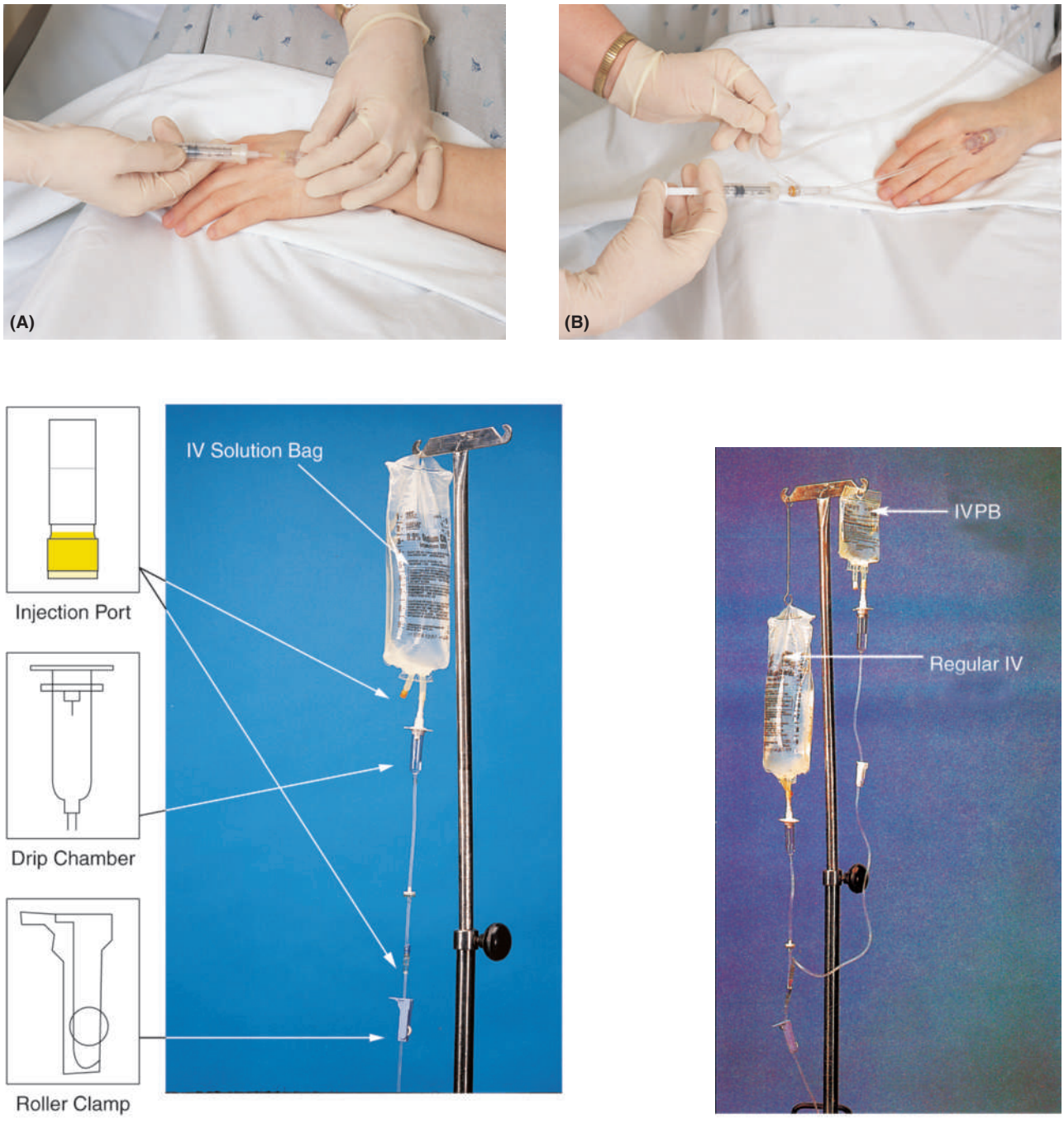

FIGURE 4-3 Intravenous administration. Different forms of IV injection include: (A) IV push, injecting a bolus of medication into a peripheral saline lock; (B) pinch closed the IV tubing of a primary infusion line to administer an IV push medication; (C) IV infusion (continuous); and (D) IV piggyback (IVPB) intermittent.

Subcutaneous. Injected into the fatty layer of tissue below the skin by positioning the needle and syringe at a 45-degree angle from the skin (Figure 4-5). This may be the route of choice for drugs that should not be absorbed as rapidly as through the IV or IM routes. Sometimes, especially with self-administration and/or a shorter needle, a 90-degree angle is used.

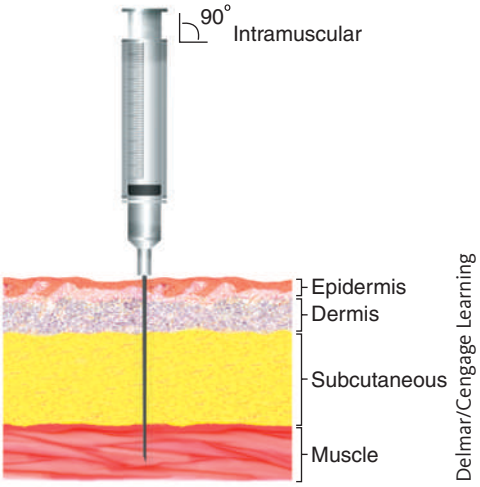

FIGURE 4-4 Intramuscular (IM) injection. Needle is inserted at a 90-degree angle.

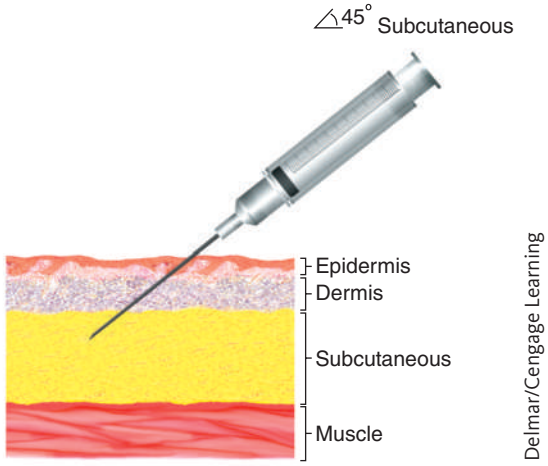

FIGURE 4-5 Subcutaneous injection. Needle is usually inserted at a 45-degree angle. Sometimes, with a shorter needle (3/8), a 90-degree angle is used.

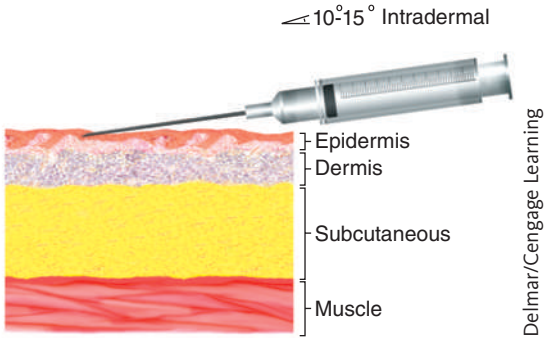

FIGURE 4-6 Intradermal injection. Needle is inserted just beneath the skin at a 10–15-degree angle. Bevel of needle is up.

Intradermal. Injected just beneath the skin, by positioning the needle bevel up and the syringe at a 15-degree angle from the skin (Figure 4-6). This route is used primarily for allergy skin testing. Because of the lack of vascularity in the dermis, absorption is slow. The greatest reaction is in the local tissues rather than systemic. When a small amount (0.1–0.2 mL) of drug is injected intradermally, the amount of redness that develops around the injection site can be used to determine whether a person is sensitive to the drug. Tuberculin (TB) skin tests (PPD) are also administered intradermally, and the site is inspected 48–72 hours later for hardness (induration) and swelling. Redness (erythema) alone, *without swelling*, does not indicate a positive test result with PPD. The *raised area (induration)* is measured with a special ruler and the number of millimeters (mm) is documented. Check with your local Public Health Department regarding appropriate protocol with a positive PPD test result.

Epidural. Injected into a catheter that has been placed by an anesthesiologist in the epidural space of the spinal canal. Medications for pain can be

administered into the catheter by bolus (a measured amount of solution in a syringe) or by continuous infusion through tubing attached to a bag of solution. Epidural catheters have long been used for administration of opioid analgesics for chronic intractable pain and for chemotherapy. Epidurals have become a popular and widely accepted vehicle for the management of acute, postoperative pain.

The less common parenteral routes, which are limited to a physician's administration, are:

Intraosseous. Injected directly into the marrow of long bones. This route may be used to administer medications during a cardiac arrest. (Intracardiac no longer recommended in Advanced Cardiac Life Support [ACLS] guidelines.)

Intraventricular. Drugs injected directly into the heart's ventricle. In critical care, antibiotics can be given via an intraventriculostomy tube.

Intraspinal. Injected into the subarachnoid space, which contains cerebrospinal fluid (CSF) that surrounds the spinal cord. Drugs injected by this route are frequently anesthetics, which render a lack of sensation to those regions of the body distal to the intraspinal injection.

Intracapsular (intra-articular). Injected into the capsule of a joint, usually to reduce inflammation, as in bursitis. Arthritic or bursitic joints often injected with anti-inflammatory drugs include shoulders, elbows, wrists, ankles, knees, and hips.

Topical Drug Forms

Topical drug forms include drugs for dermal application and drugs for mucosal application. Those for *dermal* application include:

Cream or ointment. A semisolid preparation containing a drug, for external application. Note: Creams and ointments are not the same. The dose used differs for each.

Rule of thumb: If skin is wet, use cream; if skin is dry, use ointment. (Follow the physician's order. Contact the physician with questions.)

Lotion. A liquid preparation applied externally for treatment of skin disorders. Unlike hand lotions, medicated lotions (e.g., calamine lotion) should be *patted*, not rubbed, on the affected skin.

Liniment. Preparation for external use that is rubbed on the skin as a counterirritant. As such, the liniment creates a different sensation (e.g., tingling or burning) to mask pain in the skin or muscles.

Dermal patch. Skin patch containing drug molecules that can be absorbed through the skin at varying rates to promote a consistent blood level between application times.

Both the dermal patch and ointment are common forms for administration of nitroglycerin. Nitroglycerin is a vasodilator used for the treatment of angina (chest pain related to narrowing of the coronary arteries). The advantage of the external applications of nitroglycerin is their ability to *prevent* angina by the slow, consistent release of the drug over a period of time. Before the

external applications became available, nitroglycerin was primarily available in the form of a sublingual tablet to be taken at the time of an angina attack. Now all three forms are used—the tablet, the ointment, and the patch—with the external forms focusing on the prevention of angina. They are applied at regular intervals, as follows:

Ointment: One to two inches applied q8h (every eight hours) measured and applied on special Appli-Ruler paper (Figure 4-7).

Dermal patch: One patch (available in varied doses) usually applied every 24 hours for angina. Other types of patches are applied every 24–72 hours depending on the condition treated (Figure 4-1). (See Chapter 9 for administration instructions.)

StudyWARE™ CONNECTION

See It In Action! Go to the StudyWARE™ CD-ROM to view a video on *Ointments and Their Application.*

Other drug preparations considered topical are those that are applied to *mucosal membranes.* Some are administered for local effect (at the site of application) and, in other cases, a systemic (affecting the whole body) effect is desired. The *mucosal drug forms* include:

Eye, ear, and nose drops (gtt). Drugs in sterile liquids to be applied by drops (referred to as instillation of drops).

Eye ointment. Sterile semisolid preparation, often antibiotic in nature, for ophthalmic use only.

Vaginal creams. Medicated creams, often of antibiotic or antifungal nature, that are to be inserted vaginally with the use of a special applicator.

Rectal and vaginal suppositories. Drug suspended in a substance, such as cocoa butter, that melts at body temperature, for local effect. Some rectal suppositories are also used for systemic effects, for example, Tylenol suppository for fever (Figure 4-8).

Douche solution. Sterile solution, often an antiseptic such as povidone iodine solution and sterile water, used to irrigate the vaginal canal.

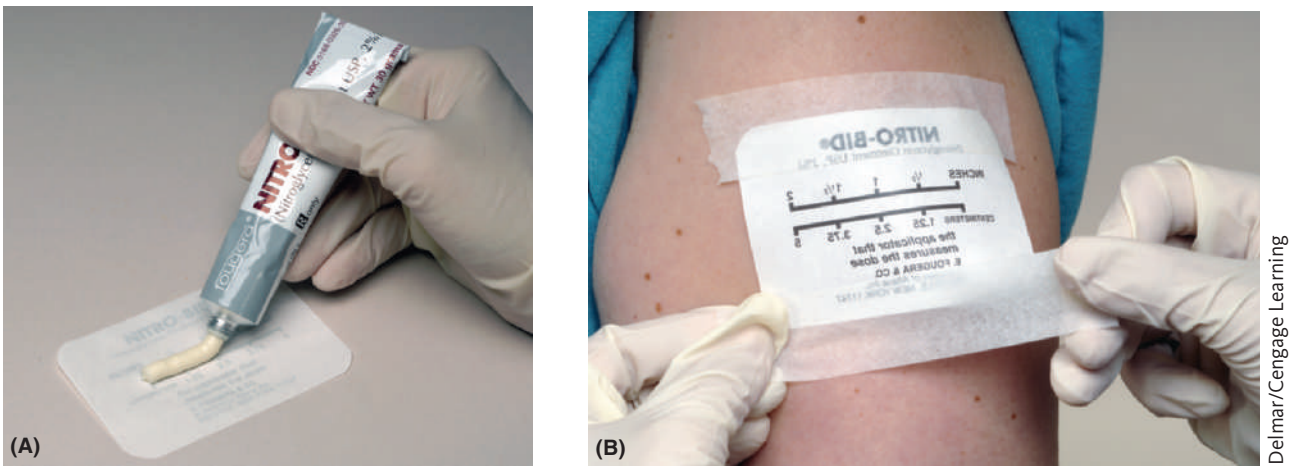

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FIGURE 4-7 Topical administration. Dermal application includes creams and liquids placed on the skin. (A) Nitroglycerin ointment is measured on Appli-Ruler paper. (B) Paper containing ointment is applied to the skin and taped in place. Mark date and time on tape.

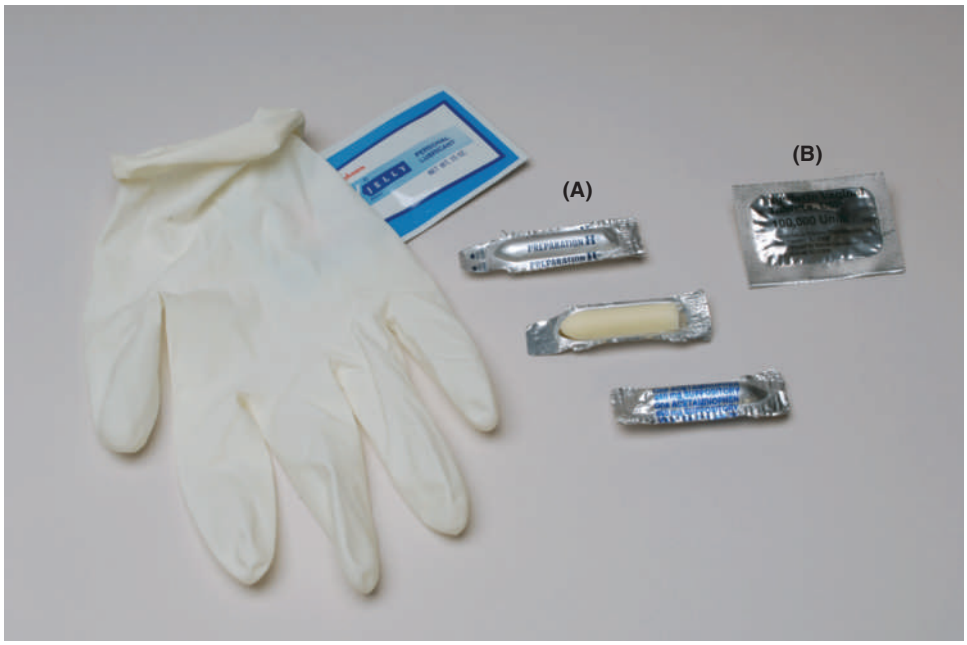

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FIGURE 4-8 Topical administration via mucous membranes. Suppositories come in various shapes and sizes, for example, (A) rectal suppositories, wrapped in foil and unwrapped, and (B) vaginal suppository, wrapped in foil. Lubricant and a glove will be needed for administration.

Buccal tablet. Tablet that is absorbed *via the buccal mucosa* in the mouth.

- Patient is told *not* to swallow tablet; it is to be placed between the cheek and gums, and allowed to dissolve slowly.
- Not commonly used today. Sublingual preferable.

Sublingual tablet. Tablet that is absorbed via the mucosa under the tongue.

- Patient is told not to swallow tablet; it is to be placed under the tongue and allowed to dissolve slowly.
- The most common sublingual tablet is nitroglycerin. Given for the treatment of angina, this drug reaches the bloodstream immediately via the rich vascular supply of sublingual capillaries. Angina may be relieved within one to five minutes after sublingual nitroglycerin is administered.

Inhalable Drug Forms

The inhalation route is a very fast acting (second to IV route) and effective route for delivering humidification and/or medication directly into the respiratory system. Usually, a liquid drug is placed in a device that will create a fine mist or aerosol that contains tiny droplets of medication. The medication is rapidly absorbed into the respiratory system due to the large surface area

and vast blood supply of pulmonary capillaries. The drug forms used for the inhalation route include:

Spray or mist. Liquid drug forms that may be inhaled as fine droplets via the use of spray bottles, nebulizers, or metered dose inhalers.

- In the hospital setting, respiratory therapists instill a liquid into a chamber of a nebulizer for a patient's breathing treatment. Often the liquid contains a bronchodilator, a mucolytic agent, or sterile saline solution for moisture.
- In the home, the patient may instill aerosol sprays via a small volume nebulizer (SVN), metered dose inhaler (MDI), or a dry powdered inhaler (DPI). These inhaler devices and how to use them will be explained in Chapter 26. Patients with moderate to severe asthma rely on these devices to keep their airways open by inhaling the mist of a bronchodilator to open constricted airways and the mist of an anti-inflammatory agent to reduce swollen airways. Patients with mild asthma will use their inhalers when needed (PRN) to treat or prevent mild episodes.

SUPPLIES

Considering the variety of drug forms you may be administering, you must become familiar with various supplies to be used.

Medicine cup. Two types of disposable cups are commonly used. Paper cups are used for dispensing tablets and capsules. Plastic 1-oz medicine cups with measurements (mL, tsp, tbsp, dr, or oz) marked on the side are used for dispensing oral liquid medications. (See Table 5-1 [in the next chapter] for a list of common abbreviations used in medication orders.)

Metal pillcrusher and pill cutter. Used in most institutions (Figure 4-9).

(A)

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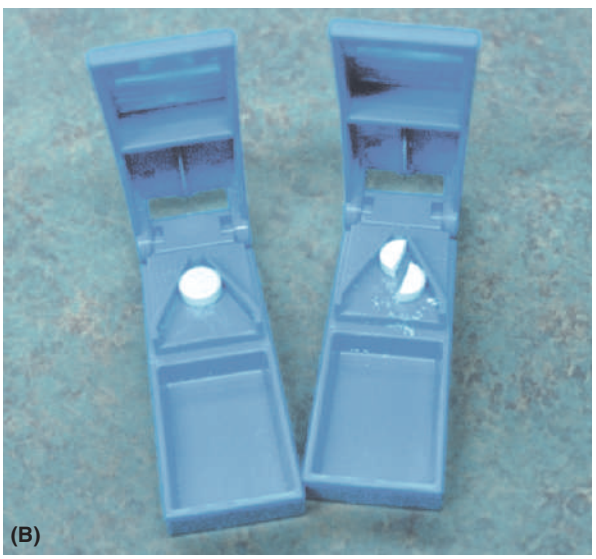

(B)

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FIGURE 4-9 (A) Metal pillcrusher. Place paper soufflé cup in well of the device and place tablet to be crushed in the paper cup. Then place another paper cup on top of the tablet before bringing down handle. (B) Scored tablets may be broken, if necessary.

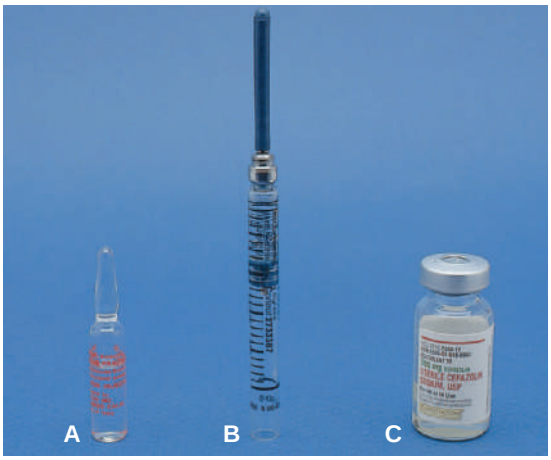

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FIGURE 4-10 Medications given parenterally. (A) Ampule. (B) Sterile cartridge with premeasured medication. (C) Vial of powder for reconstitution.

Note
In some areas, a physician's order is required for pill crushing. Check the regulations in your area.

Mortar and pestle. The mortar is a glass cup in which tablets (excluding enteric-coated tablets) may be placed to be crushed using a club-shaped glass tool called a pestle.

Various other pill-crushing devices are available.
Medication for injection is contained in an ampule, vial, or prefilled syringe (Figure 4-10):

Ampule. Small glass container that holds a single dose of sterile solution for injection. The ampule must be broken at the neck to obtain the solution.

Vial. Glass container sealed at the top by a rubber stopper to enhance sterility of the contents. Contents may be a solution or a powdered drug that needs to be reconstituted. Vials may be multiple dose or unit dose.

- Multiple-dose vials contain large quantities of solution (up to 50 mL) and may be entered repeatedly through the rubber stopper to remove a portion of the contents.
- Unit-dose vials contain small quantities of solution (1–2 mL) that are removed during a single use. Unit-dose vials are widely used today as a means of controlling abuse or removal of excess amounts of solution from a drug vial.

Needles. Needles for injections have two measurements that must be noted (Figure 4-11).

- Length varies from short (3/8 inch) to medium (1–1½ inch) for standard injections. Long needles (5 inch) may be used by the physician for intraspinal or intraosseous routes. Needles 2–5 inches long are used by the physician for intra-articular injections (into the joint).
- Gauge is a number that represents the diameter of the needle lumen (opening). Needle gauges in common use by health care practitioners vary from 16 (largest) to 27 (smallest), with the higher gauge number representing the smaller lumen. Occasionally, larger needles may be used, for example, physicians sometimes use a larger needle gauge for certain biopsies.

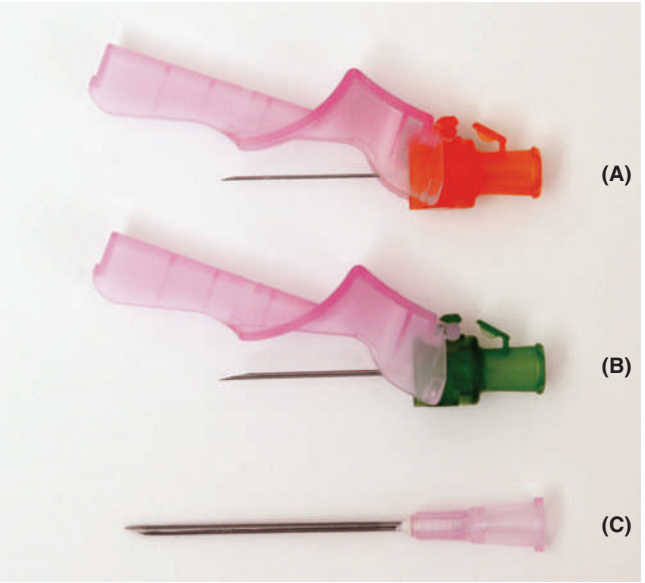

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FIGURE 4-11 Examples of some various gauges and lengths of needles. (A) 25-gauge, 1-inch needle with safety cap; (B) 21-gauge, 1-inch needle with safety cap; (C) 18-gauge, 1 ½-inch needle.

- ***Syringes.*** The three most common disposable syringes for parenteral administration of drugs are the standard hypodermic syringe, the tuberculin (TB) syringe, and the insulin syringe (Figure 4-12).
- The standard hypodermic syringe has a capacity of 2–3 mL. Most companies prepackage this type of syringe with a needle attached. You may use this type of syringe for either subcutaneous or intramuscular injections, so you must choose the package with the needle length and gauge appropriate for the route and depth of injection you will give. All hypodermic syringes are marked with 10 calibrations per milliliter (mL). Thus, each small line represents 0.1 mL. When preparing for an injection with this syringe, you must know the amount of solution needed to the nearest 0.1 mL (an additional scale on the syringe shows calibrations in minims, which is discussed in Chapter 9).
- The TB syringe is very narrow and is finely calibrated. The total capacity is only 1 mL. There are 100 fine calibration lines marking the capacity. Thus, each line represents 0.01 mL. Every tenth line is longer, to indicate 0.1-mL increments. Very precise small amounts of solution may be measured with the TB syringe. It is most commonly used for newborn and pediatric dosages and for intradermal skin tests. When preparing for an injection with this syringe, you must know the amount of solution needed to the nearest 0.01 mL.
- The insulin syringe is used strictly for administering insulin to diabetics. Insulin should be measured only in an insulin syringe. Like the TB syringe, the standard insulin syringe has only a 1-mL capacity, which is equivalent to 100 units of U-100 insulin. The standard U-100 syringe has a dual scale: even numbers on one side

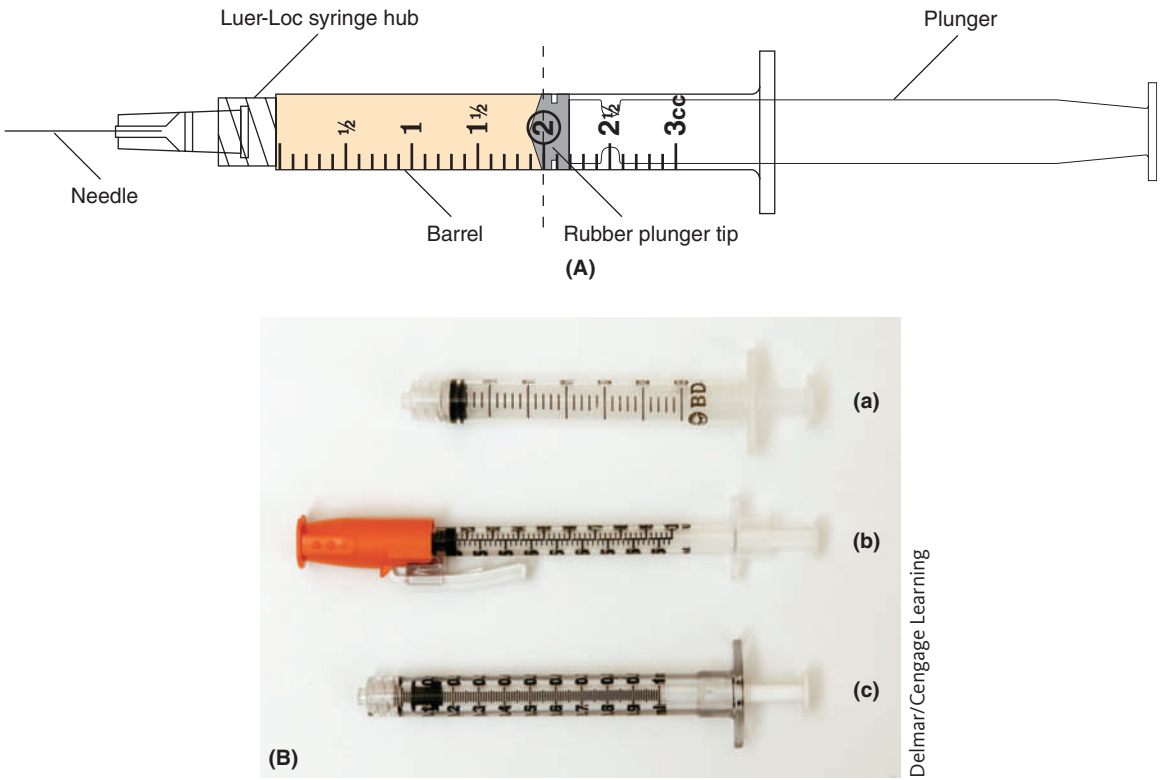


FIGURE 4-12 (A) Parts of a syringe. (B) Types of syringes: (a) 3 cc Syringe; (b) Standard U-100 Insulin; (c) 1 mL Tuberculin with Leur-Lok.

and odd numbers on the other side. Look carefully at the calibrations on each side. Count each calibration (on one side only) as two units (Figure 4-13B).

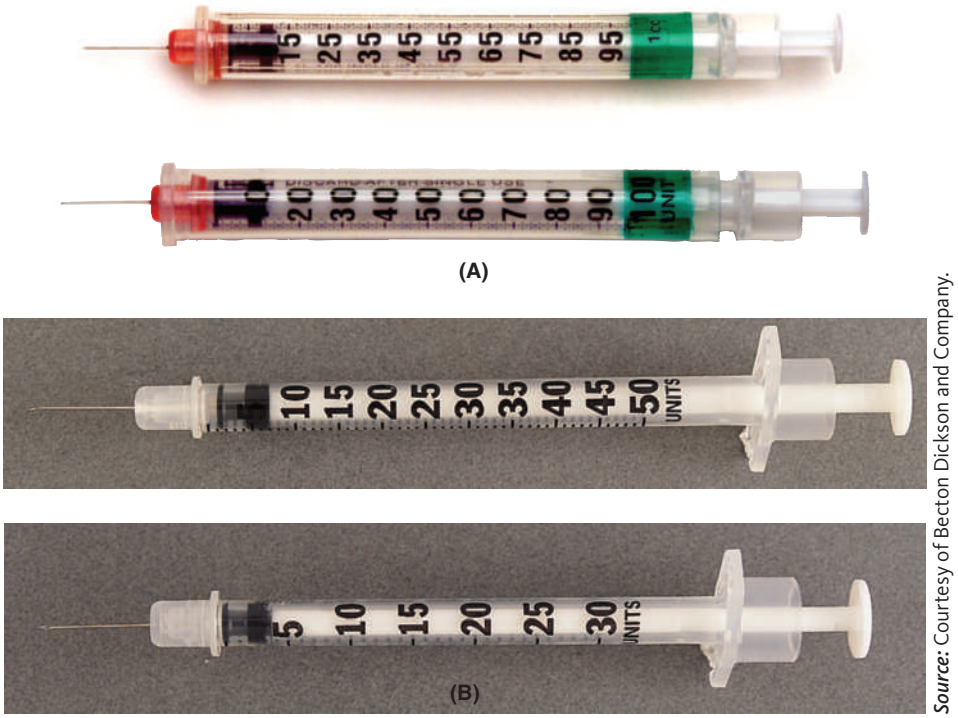
There are also smaller insulin syringes to more accurately measure small amounts of insulin, such as for children (Figure 4-13B for Lo-Dose Insulin Syringes 50 Units and 30 Units). Look carefully at the calibrations. In these Lo-Dose syringes, each calibration counts only *one* unit.

It is extremely important that you can interpret the value of the calibrations on each of the syringes. Study the calibrations each time you prepare for an injection to prevent a medication error from negligent misinterpretation. ***All insulin dosages should be double-checked by two caregivers before administration.***

Oral syringes. Health care practitioners should be aware that some oral liquid medications are dispensed from the pharmacy in disposable plastic syringes with rubber or plastic covers on the tip. These syringes are labeled "Not for injection" or "For oral use only."

Safety Devices

The Occupational Safety and Health Administration (OSHA) has mandated that every effort must be made to reduce the risk of needle-stick injuries that could lead to exposure to blood borne pathogens, such as the human



Source: Courtesy of Becton Dickson and Company.

FIGURE 4-13 Insulin syringes. (A) Opposite sides of the same standard U-100 insulin syringe; note the numbers; (B) Lo-Dose insulin syringes, 50 units and 30 units.

immunodeficiency virus (HIV), hepatitis B virus (HBV), or hepatitis C virus (HCV). Therefore, the following equipment is included in OSHA recommendations:

- Safety needles with a protective sheath that covers the needle automatically immediately after administration, or others that retract into the syringe upon administration
- Needleless devices that can be used to access intravenous tubing for the administration of IV push medications or IV piggybacks.

Safety devices vary depending on the company manufacturing the equipment. Therefore, it is important that you familiarize yourself with the safety equipment used in your facility.

StudyWARE™ CONNECTION

See It In Action! Go to the StudyWARE™ CD-ROM to view a video on *Needle Safety.*

CHAPTER REVIEW QUIZ

Fill in the blanks.

1. **a.** Which route of administration is used most often? Why?

_____

b. Which route is fastest? _____

Complete with the appropriate drug form.

2. A tablet placed under the tongue: _____
3. A tablet placed in the cheek pouch: _____
4. A tablet dissolved in the mouth for local action: _____
5. A coated tablet that dissolves in the intestines instead of in the stomach:

_____

6. A capsule that has delayed action over a longer period of time:

_____

7. A liquid drug form with an alcohol base: _____
8. A liquid medication that must be shaken before administration:

_____

9. Drugs given by the rectal route include _____ _____.
10. The parenteral route refers to any route other than the gastrointestinal route. Name four parenteral routes:

_____

_____

_____

_____

Fill in the blanks.

11. Topical drug forms include those applied to the _____ and _____.
12. To administer a rectal suppository, you need a _____ and _____.

13. Medicine for injection is contained in two types of glass containers:

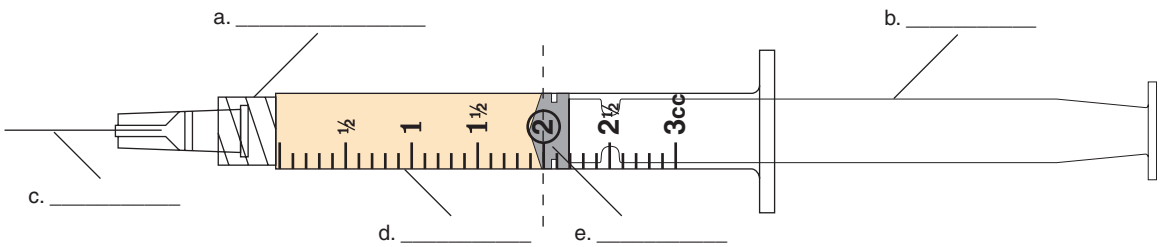
a. With rubber stopper on top: _____

b. All glass to be broken at the neck: _____

14. Needles are selected according to two measurements: _____ and _____.

15. The three most commonly used syringes for injections are: _____, _____, and _____.

16. Label the parts of a syringe



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Go to your StudyWARE™ CD-ROM and have fun learning as you play games and answer case study-related questions to help reinforce key concepts you learned in this chapter.

StudyGUIDE PRACTICE

Go to your Study Guide and complete the review questions for this chapter.

Chapter 5

Abbreviations and Systems of Measurement

Key Terms and Concepts

Abbreviations

Conversion

Medication orders

Metric system

Objectives

Upon completion of this chapter, the learner should be able to

1. Identify common abbreviations and symbols used for medication orders
2. List the six parts of a medication order and the two additional items required on a prescription blank
3. Describe the responsibilities of the health care practitioner regarding verbal and telephone orders for medications
4. Interpret medication orders correctly
5. Compare and contrast the three systems of measurement
6. Convert dosages from one system to another by use of the tables for metric, apothecary, and household equivalents
7. Describe appropriate patient education for those who will be measuring and administering their own medications
8. Define the Key Terms and Concepts

ABBREVIATIONS

Interpretation of the medication order is the first responsibility when preparing medication for administration. Knowledge of **abbreviations** and symbols is essential for accurate interpretation of the physician's order. The abbreviations and symbols in Table 5-1 must be memorized. Orders may vary in the use of capital versus lowercase letters. You may occasionally see other abbreviations not included in this list. *When in doubt, always question the meaning. Never guess!*

Table 5-1 Common Abbreviations for Medication Orders

ABBREVIATION	MEANING	ABBREVIATION	MEANING
a	before	NG	nasogastric
ac	before meals	noc	night
ad lib	as desired	NPO, npo	nothing by mouth
AM, am	morning	NS, N/S	normal saline (sodium chloride, 0.9%)
amp	ampule		
bid	twice a day	Ø	none
c̄	with	oint	ointment
cap	capsule	OTC	over the counter
Cl	chloride	oz	ounce
cm	centimeter	p	after
DC, D/C	discontinue	pc	after meals
DS	double strength	PCA	patient controlled analgesia
DW	distilled water	PM, pm	afternoon
D5W	dextrose 5% in water	po, PO	by mouth, orally
EC	enteric coated	PRN, prn	whenever necessary
elix	elixir	pt	pint, patient
ER	extended release	qh	every hour
Fe	iron	q2h	every 2 hours
fl	fluid	q3h	every 3 hours
gr	grain	q4h	every 4 hours
Gm, g	gram	qid	four times a day
gtt	drop	QNS	quantity not sufficient
h, hr	hour	qs	quantity sufficient
IM	intramuscular	qt	quart
IV	intravenous	R, pr	rectal, per rectum
IVPB	intravenous piggyback	RL, R/L	Ringer's lactate
K	potassium	s̄	without
KCL	potassium chloride	SL	sublingual
kg, Kilo	kilogram	sol	solution
KVO	keep vein open	SR	sustained release
L	liter	stat	immediately and once only
LA	long acting	subcu*	subcutaneous
LR	Lactated Ringer's	supp	suppository
lb	pound	tab	tablet
mEq	milliequivalent	tbsp, T, tbs	tablespoon
mcg	microgram	tid	three times daily
mg	milligram	TO	telephone order
ml, mL	milliliter (equivalent to cc)	tsp, t	teaspoon
mm	millimeter	U, u	unit
Na	sodium	vag	vaginal
NaCl	sodium chloride	Vit	vitamin
NEB	nebulizer	VO	verbal order

Important Note: Abbreviations should be written without periods.

*While subcutaneous can also have the abbreviations of SC, SQ, or subq, these abbreviations are noted on the ISMP's List of Error-Prone Abbreviations, Symbols, and Dose Designations. When handwritten they can be confused for other terms. Therefore we will be using "subcu" throughout the textbook. With the expected future universal implementation of electronic records and electronic charting, handwritten look-alike errors will hopefully become a thing of the past.

The **Institute for Safe Medication Practice (ISMP)** monitors medication administration and identifies practices that have contributed to medication errors. The ISMP has published a list of problematic abbreviations, **ISMP List of Error-Prone Abbreviations, Symbols, and Dose Designations** (Figure 5-1). Additionally, the **Joint Commission on Accreditation of Healthcare Organizations (JCAHO)** has approved a minimum list of "dangerous" abbreviations that have been prohibited effective January 1, 2004. Items required to be on an organization's DO NOT USE list are highlighted with a double asterisk (**) in the ISMP List (Figure 5-1).

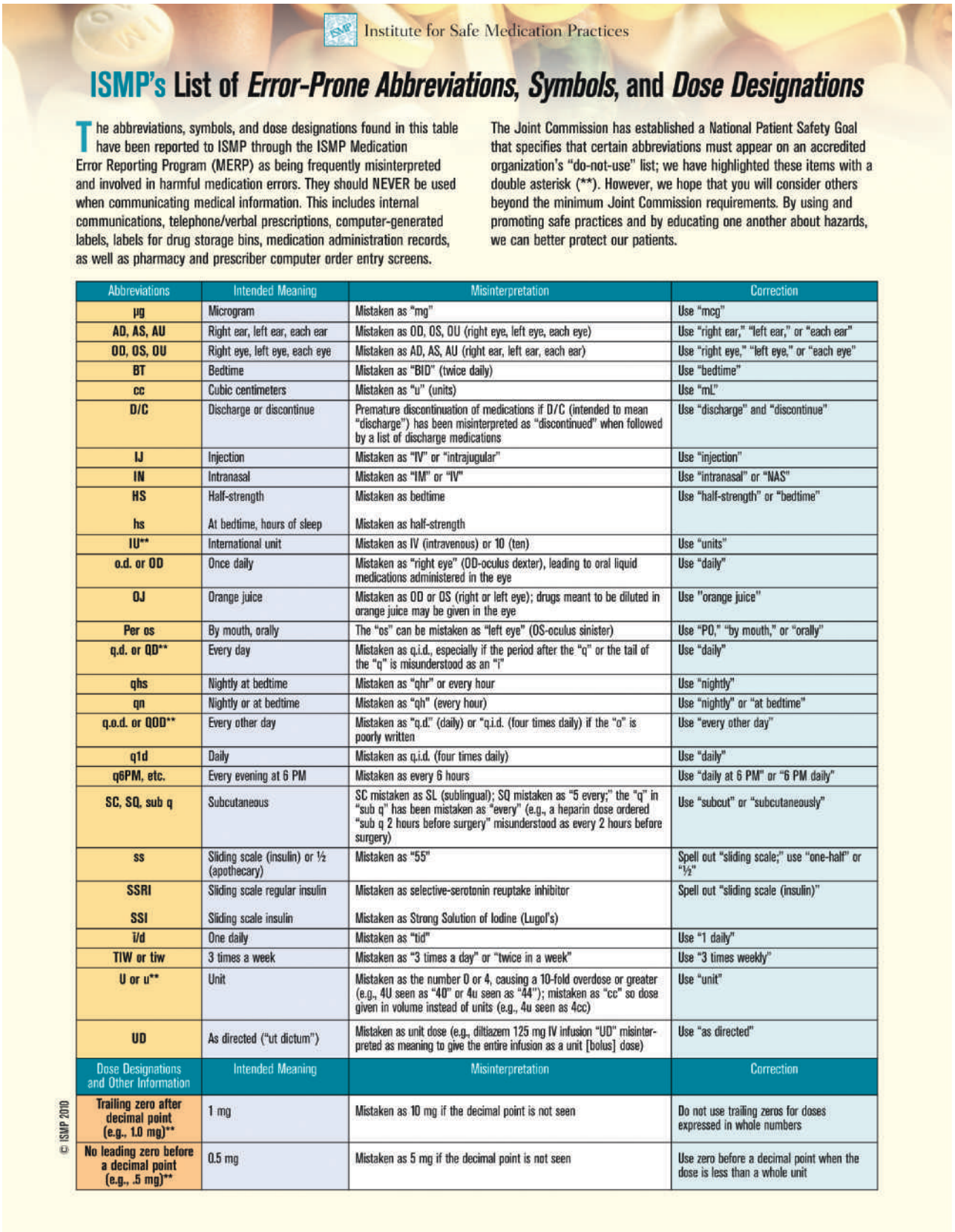
Another safety practice requires the avoidance of periods with all medical abbreviations. If poorly written the period could be mistaken as the number 1, and could cause an error in dosage.

Medication orders contain six parts.

1. Date
2. Patient's name
3. Medication name
4. Dosage or amount of medication
5. Route or manner of administration (if no route is specified, the oral route is usually the appropriate one). When in doubt, always check with the physician
6. Time to be administered, or frequency

Medication orders must always be written and signed by a physician. In an emergency the physician may give a verbal order (VO). It is the responsibility of the health care practitioner to *read back the order* (i.e., medication and amount) before administration and to write down medication, amount, and time of administration as soon as it is given. The physician will sign the medication order after the emergency.

Always determine the policy of the agency before taking a telephone order (TO). Some agencies require a registered nurse to take telephone orders. In other facilities, licensed practical (vocational) nurses are allowed to take telephone orders. When taking a telephone order, always obtain the name of the person calling in the order and write the name of that person and the time the call was made next to the medication ordered, for example, "To Dr. A. Smith, per Mary Jones, CMA @ 1300." Also repeat all of the details regarding the medication, dosage, frequency, and so on, as you write down the order. If you are the medical assistant, or nurse, calling in the prescription to the facility for the physician, be sure to *repeat the name of the drug, dosage, frequency, and route* to the physician as you write it on the patient's office record, adding the time the call was made and the name of the nurse receiving the call in the facility. This documentation is extremely important in preventing medication errors and legal complications. All phone orders must be followed by a read back statement; for example, "TO/RB" means it was a telephone order that was read back for accuracy. The physician must sign all verbal and telephone orders within 24 hours usually.



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ISMP's List of *Error-Prone Abbreviations, Symbols,* and *Dose Designations*

The abbreviations, symbols, and dose designations found in this table have been reported to ISMP through the ISMP Medication Error Reporting Program (MERP) as being frequently misinterpreted and involved in harmful medication errors. They should NEVER be used when communicating medical information. This includes internal communications, telephone/verbal prescriptions, computer-generated labels, labels for drug storage bins, medication administration records, as well as pharmacy and prescriber computer order entry screens.

The Joint Commission has established a National Patient Safety Goal that specifies that certain abbreviations must appear on an accredited organization's "do-not-use" list; we have highlighted these items with a double asterisk (**). However, we hope that you will consider others beyond the minimum Joint Commission requirements. By using and promoting safe practices and by educating one another about hazards, we can better protect our patients.

Abbreviations	Intended Meaning	Misinterpretation	Correction
µg	Microgram	Mistaken as "mg"	Use "mcg"
AD, AS, AU	Right ear, left ear, each ear	Mistaken as OD, OS, OU (right eye, left eye, each eye)	Use "right ear," "left ear," or "each ear"
OD, OS, OU	Right eye, left eye, each eye	Mistaken as AD, AS, AU (right ear, left ear, each ear)	Use "right eye," "left eye," or "each eye"
BT	Bedtime	Mistaken as "BID" (twice daily)	Use "bedtime"
cc	Cubic centimeters	Mistaken as "u" (units)	Use "mL"
D/C	Discharge or discontinue	Premature discontinuation of medications if D/C (intended to mean "discharge") has been misinterpreted as "discontinued" when followed by a list of discharge medications	Use "discharge" and "discontinue"
IJ	Injection	Mistaken as "IV" or "intrajugular"	Use "injection"
IN	Intranasal	Mistaken as "IM" or "IV"	Use "intranasal" or "NAS"
HS hs	Half-strength At bedtime, hours of sleep	Mistaken as bedtime Mistaken as half-strength	Use "half-strength" or "bedtime"
IU**	International unit	Mistaken as IV (intravenous) or 10 (ten)	Use "units"
o.d. or OD	Once daily	Mistaken as "right eye" (OD-oculus dexter), leading to oral liquid medications administered in the eye	Use "daily"
OJ	Orange juice	Mistaken as OD or OS (right or left eye); drugs meant to be diluted in orange juice may be given in the eye	Use "orange juice"
Per os	By mouth, orally	The "os" can be mistaken as "left eye" (OS-oculus sinister)	Use "PO," "by mouth," or "orally"
q.d. or QD**	Every day	Mistaken as q.i.d., especially if the period after the "q" or the tail of the "q" is misunderstood as an "i"	Use "daily"
qhs	Nightly at bedtime	Mistaken as "qhr" or every hour	Use "nightly"
qn	Nightly or at bedtime	Mistaken as "qh" (every hour)	Use "nightly" or "at bedtime"
q.o.d. or QOD**	Every other day	Mistaken as "q.d." (daily) or "q.i.d. (four times daily) if the "o" is poorly written	Use "every other day"
q1d	Daily	Mistaken as q.i.d. (four times daily)	Use "daily"
q6PM, etc.	Every evening at 6 PM	Mistaken as every 6 hours	Use "daily at 6 PM" or "6 PM daily"
SC, SQ, sub q	Subcutaneous	SC mistaken as SL (sublingual); SQ mistaken as "5 every;" the "q" in "sub q" has been mistaken as "every" (e.g., a heparin dose ordered "sub q 2 hours before surgery" misunderstood as every 2 hours before surgery)	Use "subcut" or "subcutaneously"
ss	Sliding scale (insulin) or ½ (apothecary)	Mistaken as "55"	Spell out "sliding scale;" use "one-half" or "½"
SSRI SSI	Sliding scale regular insulin Sliding scale insulin	Mistaken as selective-serotonin reuptake inhibitor Mistaken as Strong Solution of Iodine (Lugol's)	Spell out "sliding scale (insulin)"
i/d	One daily	Mistaken as "tid"	Use "1 daily"
TIW or tiw	3 times a week	Mistaken as "3 times a day" or "twice in a week"	Use "3 times weekly"
U or u**	Unit	Mistaken as the number 0 or 4, causing a 10-fold overdose or greater (e.g., 4U seen as "40" or 4u seen as "44"); mistaken as "cc" so dose given in volume instead of units (e.g., 4u seen as 4cc)	Use "unit"
UD	As directed ("ut dictum")	Mistaken as unit dose (e.g., diltiazem 125 mg IV infusion "UD" misinterpreted as meaning to give the entire infusion as a unit [bolus] dose)	Use "as directed"
Dose Designations and Other Information	**Intended Meaning**	**Misinterpretation**	**Correction**
Trailing zero after decimal point (e.g., 1.0 mg)**	1 mg	Mistaken as 10 mg if the decimal point is not seen	Do not use trailing zeros for doses expressed in whole numbers
No leading zero before a decimal point (e.g., .5 mg)**	0.5 mg	Mistaken as 5 mg if the decimal point is not seen	Use zero before a decimal point when the dose is less than a whole unit

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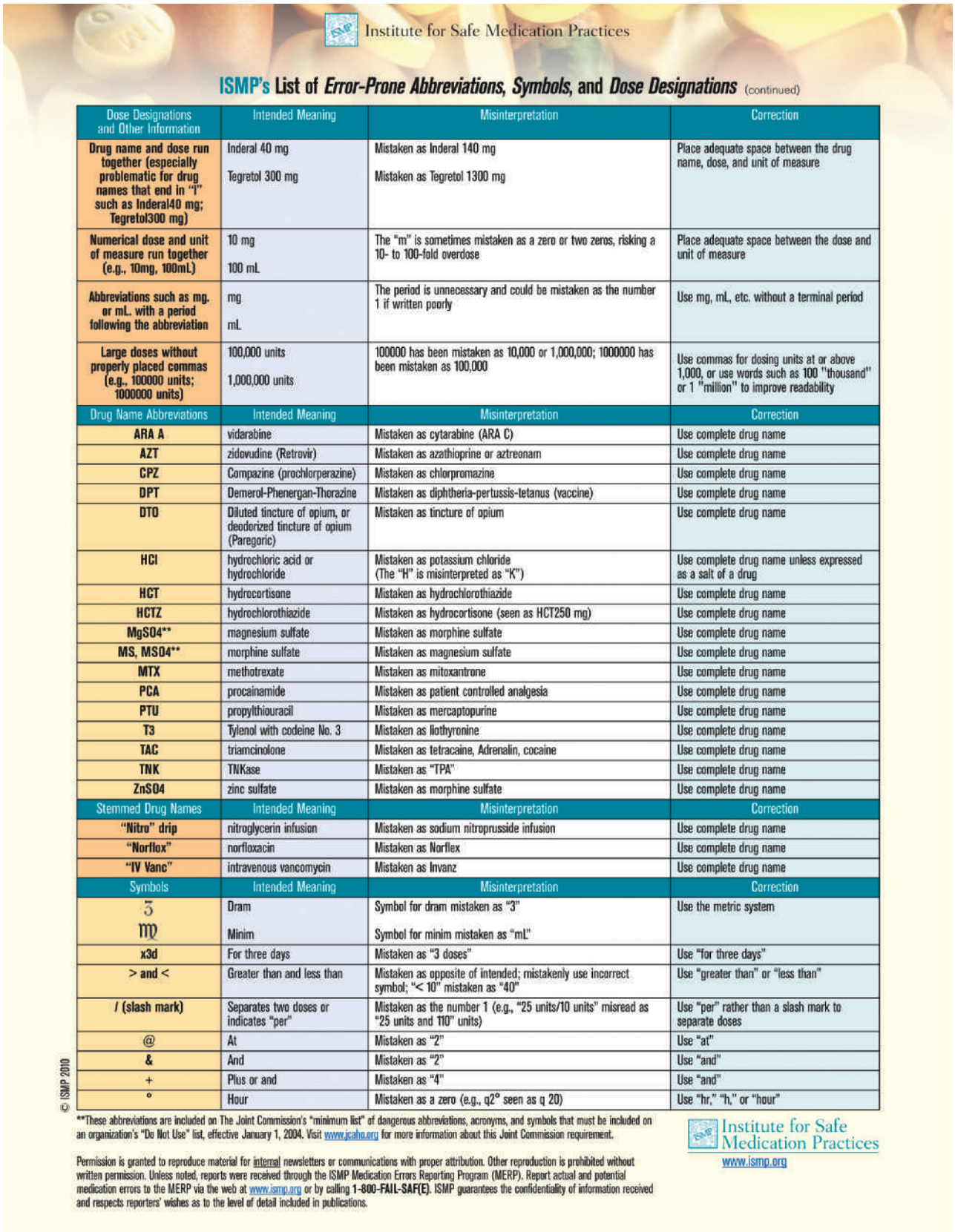
FIGURE 5-1 ISMP List of Error-Prone Abbreviations, Symbols, and Dose Designations.



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ISMP's List of *Error-Prone Abbreviations, Symbols,* and *Dose Designations* (continued)

Dose Designations and Other Information	Intended Meaning	Misinterpretation	Correction
Drug name and dose run together (especially problematic for drug names that end in "l" such as Inderal40 mg; Tegretol300 mg)	Inderal 40 mg Tegretol 300 mg	Mistaken as Inderal 140 mg Mistaken as Tegretol 1300 mg	Place adequate space between the drug name, dose, and unit of measure
Numerical dose and unit of measure run together (e.g., 10mg, 100mL)	10 mg 100 mL	The "m" is sometimes mistaken as a zero or two zeros, risking a 10- to 100-fold overdose	Place adequate space between the dose and unit of measure
Abbreviations such as mg. or mL. with a period following the abbreviation	mg mL	The period is unnecessary and could be mistaken as the number 1 if written poorly	Use mg, mL, etc. without a terminal period
Large doses without properly placed commas (e.g., 100000 units; 1000000 units)	100,000 units 1,000,000 units	100000 has been mistaken as 10,000 or 1,000,000; 1000000 has been mistaken as 100,000	Use commas for dosing units at or above 1,000, or use words such as 100 "thousand" or 1 "million" to improve readability
Drug Name Abbreviations	**Intended Meaning**	**Misinterpretation**	**Correction**
ARA A	vidarabine	Mistaken as cytarabine (ARA C)	Use complete drug name
AZT	zidovudine (Retrovir)	Mistaken as azathioprine or aztreonam	Use complete drug name
CPZ	Compazine (prochlorperazine)	Mistaken as chlorpromazine	Use complete drug name
DPT	Demerol-Phenergan-Thorazine	Mistaken as diphtheria-pertussis-tetanus (vaccine)	Use complete drug name
DTO	Diluted tincture of opium, or deodorized tincture of opium (Paregoric)	Mistaken as tincture of opium	Use complete drug name
HCl	hydrochloric acid or hydrochloride	Mistaken as potassium chloride (The "H" is misinterpreted as "K")	Use complete drug name unless expressed as a salt of a drug
HCT	hydrocortisone	Mistaken as hydrochlorothiazide	Use complete drug name
HCTZ	hydrochlorothiazide	Mistaken as hydrocortisone (seen as HCT250 mg)	Use complete drug name
MgSO4**	magnesium sulfate	Mistaken as morphine sulfate	Use complete drug name
MS, MSO4**	morphine sulfate	Mistaken as magnesium sulfate	Use complete drug name
MTX	methotrexate	Mistaken as mitoxantrone	Use complete drug name
PCA	procainamide	Mistaken as patient controlled analgesia	Use complete drug name
PTU	propylthiouracil	Mistaken as mercaptopurine	Use complete drug name
T3	Tylenol with codeine No. 3	Mistaken as liothyronine	Use complete drug name
TAC	triamcinolone	Mistaken as tetracaine, Adrenalin, cocaine	Use complete drug name
TNK	TNKase	Mistaken as "TPA"	Use complete drug name
ZnSO4	zinc sulfate	Mistaken as morphine sulfate	Use complete drug name
Stemmed Drug Names	**Intended Meaning**	**Misinterpretation**	**Correction**
"Nitro" drip	nitroglycerin infusion	Mistaken as sodium nitroprusside infusion	Use complete drug name
"Norflox"	norfloxacin	Mistaken as Norflex	Use complete drug name
"IV Vanc"	intravenous vancomycin	Mistaken as Invanz	Use complete drug name
Symbols	**Intended Meaning**	**Misinterpretation**	**Correction**
ʒ ♏	Dram Minim	Symbol for dram mistaken as "3" Symbol for minim mistaken as "mL"	Use the metric system
x3d	For three days	Mistaken as "3 doses"	Use "for three days"
> and <	Greater than and less than	Mistaken as opposite of intended; mistakenly use incorrect symbol; "< 10" mistaken as "40"	Use "greater than" or "less than"
/ (slash mark)	Separates two doses or indicates "per"	Mistaken as the number 1 (e.g., "25 units/10 units" misread as "25 units and 110" units)	Use "per" rather than a slash mark to separate doses
@	At	Mistaken as "2"	Use "at"
&	And	Mistaken as "2"	Use "and"
+	Plus or and	Mistaken as "4"	Use "and"
°	Hour	Mistaken as a zero (e.g., q2° seen as q 20)	Use "hr," "h," or "hour"

**These abbreviations are included on The Joint Commission's "minimum list" of dangerous abbreviations, acronyms, and symbols that must be included on an organization's "Do Not Use" list, effective January 1, 2004. Visit www.jcaho.org for more information about this Joint Commission requirement.

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FIGURE 5-1 continued

Note
Regulations vary from state to state regarding phone orders. Check the rules in your state regarding who can call in an order and who can receive a phone order and regarding time frame for physician's signature.

Medication orders can be written on the patient's record in the physician's office, clinic, or institution, or on a prescription blank (Figure 5-2). It is the responsibility of the health care practitioner to check the medication order for completeness by noting the six items—date, patient name, medication name, dosage, route, and frequency (plus additional items if using the prescription blank)—and to question any discrepancy, omission, or unusual order. The prescription blank contains two additional items: the physician's Drug Enforcement Administration registration number if the medication is a controlled substance and the number of times that the prescription can be refilled.

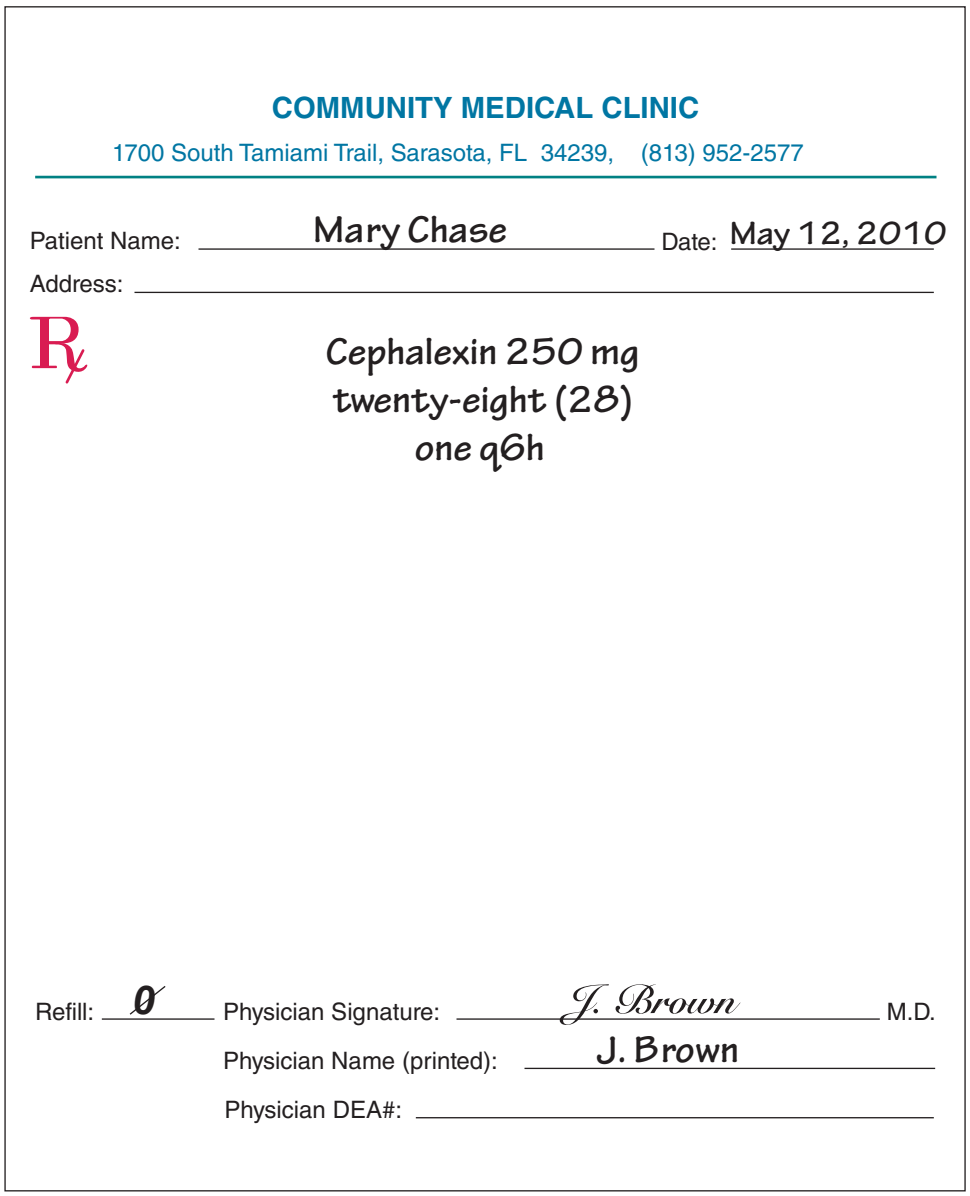

FIGURE 5-2 Prescription blank. Check for completeness, legibility and accuracy, including date, patient's name, medication name, dosage, route, frequency or time, number of refills, and DEA number for controlled substances. All prescriptions must be printed.

If there are to be no refills, write the word "NO," "NONE," or "Ø" after Refill. Never leave a blank space in that area on the prescription blank.

To reduce the incidence of medication errors due to misinterpretation of the prescription, some states have passed legislation* requiring the *name of the medication to be legibly printed or typed.* In addition, these regulations require the *quantity of the drug prescribed to be in both textual and numerical formats*, for example, "ten (10)." *The prescriber must also print his or her name under the signature* (Figure 5-2).

SYSTEMS OF MEASUREMENT

To carry out a medication order accurately, the person administering medications must have an understanding of the different systems of measurement. The original system of weights and measures for writing medication orders was the *apothecary system*. An apothecary is a pharmacist or druggist. A few drugs were still ordered by the apothecary system but this has now become obsolete. The **metric system** is the preferred system of measurement and is used at the present time. The third system of measurement is the *household system*, which is the least accurate. However, this system is more familiar to the layperson and is therefore used in prescribing medications for the patient at home. The health care practitioner must understand systems of measurement for accurate administration of medicines and for patient education as well. Medication orders are concerned with only two types of measurement: (1) measuring fluids, or liquid measure, and (2) measuring solids, or solid weight.

A brief discussion of the apothecary systems of measurement is given in case you come across these abbreviations. However, it is not recommend that you commit it to memory. The apothecary system of liquid measurement includes the minim, fluid dram, fluid ounce, pint, quart, and gallon. The apothecary system for measuring solid weights includes the grain, dram, ounce, and pound (Table 5-2).

The metric system was invented by the French in the late 18th century and is the international standard for weights and measures. The metric system of liquid measurement includes the liter and the milliliter, which is approximately equivalent to the cubic centimeter. The metric system for measuring solid weights includes the gram and the milligram as the measures most commonly used for medication prescriptions.

Table 5-2 Abbreviations for the Apothecary System

grain	gr
minim*	m, min
dram	dr

*A drop is approximately equivalent to 1 minim of water, but the type of solution may cause variation.

**An example of such legislation is the "Legible Prescription Law," Section 456.42, Florida Statutes, which became effective in Florida on July 1, 2003.*

At times you will find it necessary to convert a dosage from the metric or household system. It is important to memorize the few basic equivalents most commonly used. Table 5-3 lists commonly used approximate equivalents for liquid measurement. These figures are easily committed to memory. When **conversions** are necessary in the measurement of solids, you will find it useful to consult Table 5-4 for metric equivalents. If it is necessary to convert from the one system of measurement to another, always consult a conversion table or a pharmacist to avoid dangerous errors.

Equipment most commonly used for measuring medications includes the medicine cup and various syringes calibrated in milliliters and/or minims.

Table 5-3 Common Approximate Equivalents for Liquid Measurement

METRIC	HOUSEHOLD
5 mL	**1 tsp**
15 mL	1 tbsp
30 mL	2 tbsp
240 mL	1 measuring cup (240 mL)
500 mL	1 pt
1,000 mL	1 qt

Table 5-4 Metric Equivalents for Solid Measurement—Grams to Milligrams

METRIC (GRAMS)	METRIC (MILLIGRAMS)
1 g	**1,000 mg**
0.6 g	600 mg
0.5 g	**500 mg**
0.3 g	300 mg
0.2 g	200 mg
0.1 g	100 mg
0.06 g	**60 mg**
0.05 g	50 mg
0.03 g	**30 mg**

Note: Memorize all equivalents in boldface.

Pounds–Kilograms (kg) Conversion
1 pound = 0.453592 kg
1 kg = 2.2 pounds (lb)

To convert pounds to kilograms, divide number of pounds by 2.2.

Warning: Be very careful in calculating the weight in kilograms. The slightest error, especially in pediatric doses, could result in serious or fatal consequences.

PATIENT EDUCATION

When explaining dosage preparation, always speak directly to the patient and observe the patient for comprehension. Many older adult patients have difficulty hearing but are reluctant to admit lack of understanding. Ask them to repeat the directions.

Many older adult patients also have vision problems. Be sure the directions for dosage preparation are written clearly. If a family member will be assisting in preparation and administration of medications, include that person in the instruction. Be sure that any measuring equipment to be used is clearly marked.

Measuring spoons and clearly marked measuring cups should be used when available for household measurement. Such calibrated utensils are more accurate than tableware (Figure 5-3). Teaspoons, tablespoons, teacups, and drinking glasses vary in size and capacity, and therefore measurements are inaccurate with such utensils.

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FIGURE 5-3 For accurate household measurement, standard measuring spoons are used.

CHAPTER REVIEW QUIZ

Interpret the following orders.

1. Keflex 250-mg cap PO q6h

_____.

2. Neosporin ophth sol 2 gtt in each eye tid

_____.

3. Feosol 65 mg tab bid pc c̄ orange juice

_____.

4. Diuril 500 mg PO qAM

_____.

5. Dyazide 1 cap bid

_____.

6. Demerol 50 mg IM q4h prn for pain

_____.

7. Metamucil 1 tsp mixed c̄ 8 oz H_2O bid pc

_____.

8. Dulcolax supp R prn for constipation

_____.

9. Robitussin syr 1 tsp q4h prn for cough

_____.

10. Nitrostat 1 tab SL prn for angina attack, may repeat q5min 3 times

_____.

11. Phenergan supp 25 mg prn q6h for nausea

_____.

12. DC Phenergan 48h post-op

_____.

13. Glipizide 5 mg PO daily c̄ breakfast

_____.

14. Cefazolin 1 g IVPB q8h

_____.

15. Potassium chloride 20 mEq in NS 1L IV to run at 80 mL per hour

_____.

16. Insulin 20 units subcu daily ac breakfast

_____.

17. Tolinase 250 mg daily c̄ breakfast

_____.

18. Vasocidin ophth sol 1 gtt q3h in the right eye

_____.

19. Ceclor 20 mg/kg/daily in 2 equal doses q12h

_____.

20. Ambien 5 mg for sleep prn, may repeat once q noc

_____.

Fill in the blanks.

21. Which is the oldest system of measurement for medication?

_____.

22. Which system of drug measurement is used most frequently throughout the world?

_____.

23. Which is the least accurate system for measuring medicine?

_____.

24. Two different types of equipment used to measure drugs are _____ and _____.

Use Tables 5-3 and 5-4 to complete the following conversions and place the correct answer in the blank.

25. 1,000 mg = _____ g

26. 75 mg = _____ g

27. 1 kg = _____ pounds

28. 1 pound = _____ kg

29. 1 tsp = _____ mL

30. 1 tbl = _____ mL

31. 100 Kg = _____ lbs

32. 0.5 g = _____ mg

33. 1.0 g = _____ mg

34. 150 lbs = _____ Kg

Go to your StudyWARE™ CD-ROM and have fun learning as you play games and answer case study-related questions to help reinforce key concepts you learned in this chapter.

Go to your Study Guide and complete the review questions for this chapter.

Chapter 6

Safe Dosage Calculations

Objectives

Upon completion of this chapter, the learner should be able to

1. Identify the three steps for calculation of the dosage ordered when it differs from the dose on hand
2. Write the formula for each of the two methods of dosage calculation presented in this chapter
3. Convert from one system of measurement to another using the ratio and proportion method
4. Solve dosage problems using the basic calculation method
5. Solve dosage problems using the ratio and proportion method
6. List the cautions with the basic calculation method
7. List the cautions with the ratio and proportion method
8. Calculate safe dosages for infants and children
9. List the variables when assessing geriatric patients for safe dosage
10. List some steps to reduce medication errors
11. Define the Key Terms and Concepts

Key Terms and Concepts

Appropriate

Calculating dosage

Proportion

Ratio

Verify

"First, do no harm." Health care practitioners are dedicated to the principle of helping others, not harming them. Nowhere is this principle more important than in the calculation, preparation, and administration of safe dosages. One careless moment can lead to a catastrophe. It is the responsibility of the health care practitioner to be absolutely certain that the medication administered is exactly as prescribed by the physician *and* is also an **appropriate** dose for that particular patient. Doses for children and older adults can vary significantly from the average dose. Therefore, it may be necessary to compute a partial dose from the dose on hand for the average patient.

Many medications are dispensed by the pharmacist in unit-dose form, in which each individual dose of medicine is prepackaged in a separate packet,

vial, or prefilled syringe. Although much of the mixing and measuring of medications is now completed by the pharmacist, the person who is administering medications must understand the preparation of dosages in order to ensure accuracy. On occasion the dosage ordered differs from the dose on hand. Consequently, it may be necessary to calculate the correct dosage. Calculations can be a simple procedure if you follow the necessary steps in sequential order.

A working knowledge of basic arithmetic is required for accurate calculation of drug dosage. To understand the calculation of correct dosage, you must evaluate your basic arithmetic skills by completing the following mathematics pretest.

BASIC ARITHMETIC TEST

1. $6\frac{1}{4} + 3\frac{2}{3}$
2. $4\frac{2}{3} - 2\frac{1}{2}$
3. $2\frac{2}{3} \times 3\frac{2}{5}$
4. $\frac{2}{5} \div \frac{3}{4}$
5. $2\frac{2}{3} \div 5$
6. Write six and a third as a decimal.
7. $6.67 + 0.065 + 0.3$
8. $10.4 - 0.037$
9. 0.223×0.67
10. $46.72 \div 6.4$
11. Write 8% as a fraction and reduce.
12. Change $\frac{2}{5}$ to a decimal.
13. Write 0.023 as a percent.
14. Express 12% as a decimal.
15. Express 0.4 as a fraction and reduce.
16. Change $\frac{3}{5}$ to a percent.
17. Change $12\frac{1}{2}$ % to a decimal.
18. What is 75% of 160?
19. What is 9.2% of 250?
20. What is $37\frac{1}{2}$% of 192?
21. Which fraction is the largest: $\frac{1}{2}$, $\frac{2}{5}$, or $\frac{3}{10}$?
22. Which is the largest: $\frac{1}{3}$, 0.4, or 60%?
23. The label on the bottle reads 0.5 g per tablet. The doctor orders 0.25 g. How many tablets should you give?

After completing the quiz, check your answers (see end of chapter for answers). If there is an error, review mathematics for that area until all problems can be solved accurately and easily. A minimum score of 80% is

recommended as indicating readiness for dosage calculations. Those not meeting this criterion should seek remedial assistance in review of basics before beginning calculations.

CALCULATION GUIDELINES

Remember, there is no margin of error in administration of medications. It is possible for a small error in arithmetic to seriously harm a patient. A misplaced decimal point could cause a fatality. Safe dosage preparation requires (1) a working knowledge of basic arithmetic and (2) meticulous care with all calculations.

Calculations can be as simple as 1, 2, 3. When the dosage ordered differs from the dosage on hand, the problem can be solved simply by completing three basic steps:

1. Check whether all measures are in the same system. Convert if necessary by using Tables 5-3 and 5-4 or use the ratio and proportion method.
2. Write the problem in equation form using the *appropriate formula and labeling all parts*, and complete the necessary calculations.
3. *Check the accuracy* of your answer for reasonableness, and have someone else **verify** your calculations.

There are several different methods of **calculating dosage**. Either of the methods presented in this book may be used, or both methods may be used to verify accuracy. The two methods presented here are *basic calculation and ratio and proportion*. Basic calculation requires only simple arithmetic; ratio and proportion requires the ability to determine an unknown, *X*.

METHOD 1: BASIC CALCULATION

Use the following formula:

$$\frac{\text{desired dose}}{\text{on-hand dose}} \times \text{quantity of on-hand dose}$$

In short form

$$\frac{\text{D}}{\text{OH}} \times \text{Q}$$

EXAMPLE 1

The physician orders aspirin gr 10 q4h PRN for fever over 101°. On hand are aspirin gr 5 tabs.

Step 1. Check to see if all measures are in the same system. No conversion is necessary. Both measures are in grains.

Step 2. Use the formula $\frac{D}{OH} \times Q$ and label all parts:

$$\frac{10 \text{ gr}}{5 \text{ gr}} \times 1 \text{ tab} = 10 \div 5 = 2$$

$$2 \times 1 = 2 \text{ tabs}$$

Note: The labels of the desired and on-hand doses must be the same. The label of the answer must be the same as the quantity.

Step 3. Check for reasonableness. A dose of 2 tabs is within normal limits.

If the calculations resulted in an answer such as ¼ tablet or five tablets, the answer is not reasonable and the calculations should be rechecked. If calculations are correct after recheck, any unusual dosage should be checked with the person in charge: the pharmacist or the physician. *When in doubt, always question.*

EXAMPLE 2

The order reads Ampicillin 0.5 g. The unit dose packet reads 250 mg/cap.

Step 1. Check to see if all measures are in the same system. Convert grams to milligrams:

$$1 \text{ g} = 1{,}000 \text{ mg}$$

$$0.5 \text{ g} = 0.5 \times 1{,}000 = 500 \text{ mg}$$

Step 2. Use the formula $\frac{D}{OH} \times Q$ and label all parts:

$$\frac{500 \text{ mg}}{250 \text{ mg}} \times 1 \text{ cap} =$$

Reduce fractions to lowest terms:

$$\frac{500}{250} = 50 \div 25 = 2$$

$$2 \times 1 = 2 \text{ caps}$$

Step 3. Check for reasonableness. A dose of 2 caps is within normal limits.

EXAMPLE 3

The narcotics drawer contains vials of meperidine (Demerol) labeled 75 mg in 1 mL. The preoperative order reads Demerol 60 mg IM on call.

Step 1. Check to see if all measures are in the same system. No **conversion** is necessary.

Step 2. Use the formula $\frac{D}{OH} \times Q$ and label all parts:

$$\frac{60 \text{ mg}}{75 \text{ mg}} \times 1 \text{ mL} =$$

Reduce fractions to lowest terms:

$$\frac{60}{75} = \frac{12}{15} = \frac{4}{5}$$

Convert fractions to decimals:

$$\frac{4}{5} = 5\overline{)4.0}^{0.8}$$

Multiply by quantity.

$$0.8 \times 1 \text{ mL} = 0.8 \text{ mL}$$

Note: Fractions must be converted to decimals and rounded off to one decimal place to coincide with the markings on the syringe.

Step 3. Check for reasonableness. A dose of 0.8 mL is within normal limits.

EXAMPLE 4

The physician orders Versed 3 mg IM preoperatively. On hand are vials labeled 5 mg per mL.

Step 1. Check to see if all measures are in the same system. No conversion is necessary.

Step 2. Use the formula $\frac{D}{OH} \times Q$ and label all parts:

$$\frac{3 \text{ mg}}{5 \text{ mg}} \times 1 \text{ mL} = 3 \div 5 = 5\overline{)3.0}^{0.6}$$

$$0.6 \times 1 \text{ mL} = 0.6 \text{ mL}$$

Step 3. Check for reasonableness. A dose of 0.6 mL is within normal limits.

EXAMPLE 5

The order reads atropine sulfate 0.6 mg IM on call to surgery. Available ampules are labeled atropine sulfate 0.4 mg/mL.

Step 1. Check to see if all measures are in the same system. No conversion is necessary.

Step 2. Use the formula $\frac{D}{OH} \times Q$ and label all parts:

$$\frac{0.6 \text{ mg}}{0.4 \text{ mg}} \times 1 \text{ mL} = 0.6 \div 04 = 0.4\overline{)0.6}^{1.5}$$

$$1.5 \times 1 \text{ mL} = 1.5 \text{ mL}$$

Step 3. Check for reasonableness. A dose of 1.5 mL is within normal limits.

Cautions for the Basic Calculation Method

1. *Label* all parts of the formula.
2. Use the *same label* for desired and on-hand doses.
3. Use the *same label* for the quantity and the answer (the amount to be given).
4. *Reduce fractions* to lowest terms before dividing.
5. Multiply by the quantity after dividing.
6. Take extra care with decimals.
7. *Convert* fractions to decimals.
8. *Round off* decimals to one decimal place after computation is complete.
9. *Verify the accuracy* of calculations with an instructor.
10. Question the answer if not within normal limits (e.g., less than ½ tab, more than two tabs, or more than 2 mL for injection).

METHOD 2: RATIO AND PROPORTION

A **ratio** describes a relationship between two numbers. Example:

$$1 \text{ g} : 15 \text{ gr}$$

A **proportion** consists of two ratios that are equal. Example:

$$1 \text{ g} : 15 \text{ gr} = 2 \text{ g} : 30 \text{ gr}$$

Always label each term in the equation. The terms of each ratio must be in the same sequence. In the previous examples, the first term of each ratio is labeled g and the second term of each ratio is labeled gr.

To solve a problem with the ratio and proportion method, set up the formula with the known terms on the left and the desired and unknown terms on the right. Use *X* to represent the unknown. Label all terms.

For example, we know that 1,000 mg is equal to 1 g (known). We need to administer 500 mg (desired) and do not know how many grams are equivalent (unknown *X*). To convert a dosage from one system to another when a table of

metric and apothecary equivalents (such as Table 5-4) is unavailable, set up the problem as a proportion

$$\underset{\text{of measure}}{\textit{known}\ \text{unit}} : \underset{\text{equivalent}}{\textit{known}} = \underset{\text{of measure}}{\textit{desired}\ \text{unit}} : \underset{\text{equivalent}}{\textit{unknown}}$$

$$1{,}000\ \text{mg} : 1\ \text{g} = 500\ \text{mg} : X\text{g}$$

means

extremes

To solve the problem, multiply the two outer terms, or extremes, and then multiply the two inner terms, or means. Using our example

$$1{,}000X = 500 = 1{,}000\overline{)500.0}\ \ 0.5$$

$$X = 0.5\ \text{g}$$

We now know that our desired dose, 500 mg, is equal to 0.5 g.

When the dose ordered differs from the dose on hand, the problem can be solved simply by completing three basic steps:

1. Verify that all measures are in the same system. Convert if necessary by using a table of metric and apothecary equivalents if available or by using the ratio and proportion method if the equivalent is unknown.
2. Set up the problem as a proportion, *label all terms*, and complete the calculations. Use the following formula:

$$\underset{\text{on hand}}{\text{dose}} : \underset{\text{quantity}}{\text{known}} = \underset{\text{desired}}{\text{dose}} : \underset{\text{quantity}}{\text{unknown}}$$

   Note: The answer should be stated as a whole number or a decimal. Convert fractions to decimals and round off to one decimal place.
3. Check the accuracy of your answer for reasonableness and also have someone else verify your calculations.

EXAMPLE 1

The preoperative order reads Demerol 60 mg IM on call. The narcotics drawer contains vials labeled meperidine (Demerol) 100 mg/2 mL.

Step 1. Verify that all measures are in the same system. No conversion is necessary.

Step 2. Set up the problem as a proportion and label all terms:

$$\underset{\text{on hand}}{\text{dose}} : \underset{\text{quantity}}{\text{known}} = \underset{\text{desired}}{\text{dose}} : \underset{\text{quantity}}{\text{unknown}}$$

$$100\ \text{mg} : 2\ \text{mL} = 60\ \text{mg} : X\ \text{mL}$$

$$100X = 120 = 100\overline{)120.0}\ \ 1.2$$

$$X = 1.2 \text{ mL}$$

Step 3. Check for reasonableness. A dose of 1.2 mL is within normal limits.

EXAMPLE 2

The physician is treating a child weighing 44 pounds for epilepsy. The order reads phenobarbital elixir 3 mg/kg at bedtime. Phenobarbital elixir is labeled 15 mg/5 mL. How many mL will the child receive?

Step 1. Verify that all measures are in the same system. Pounds must be converted to kilograms (kg). To convert lbs to kg, divide the number of pounds by 2.2.

The child weighs 20 kg.

The order reads 3 mg/kg. Therefore, 3 mg/kg × 20 kg = 60 mg dose.

Step 2. Set up the problem as a proportion. Label all terms.

$$\frac{\text{dose on hand}}{\text{known quantity}} : = \frac{\text{dose desired}}{\text{unknown quantity}} :$$

$$15 \text{ mg} : 5 \text{ mL} = 60 \text{ mg} : X \text{ mL}$$

$$15X = 300 = 15\overline{)300}\ \ 20$$

$$X = 20 \text{ mL}$$

Step 3. Check for reasonableness. An oral dose of 20 mL is a large amount for a young child to take at one time. The physician might want to divide the daily dose. If so, the order would be written: phenobarbital 30 mg BID.

EXAMPLE 3

Meperidine Oral Solution is available as Demerol Syrup 50 mg/5 mL. The order reads Demerol liquid 150 mg PO q6h PRN.

Step 1. Verify that all measures are in the same system. No conversion is necessary.

Step 2. Set up the problem as a proportion. Label all terms.

$$\frac{\text{dose on hand}}{\text{known quantity}} : = \frac{\text{dose desired}}{\text{unknown quantity}} :$$

$$50 \text{ mg} : 5 \text{ mL} = 150 \text{ mg} : X \text{ mL}$$

$$50X = 750 = 50\overline{)750}^{\,15}$$

$$X = 15 \text{ mL}$$

Step 3. Check for reasonableness. An oral dose of 15 mL is appropriate for an adult.

EXAMPLE 4

An 88-lb child with cancer has an order for pain medication that reads morphine liquid PO 0.2 mg/kg q 4 h PRN. Available Morphine Solution is labeled 20 mg/5 mL.

Step 1. Verify that all measures are in the same system. Pounds must be converted to kilograms (kg). To convert lb to kg, divide number of pounds by 2.2. The child weighs 40 kg.

The order reads 0.2 mg/kg. Therefore, 0.2 mg/kg $\times$ 40 kg = 8-mg dose.

Step 2. Set up the problem as a proportion. Label all terms.

$$\begin{matrix}\text{dose}\\ \text{on hand}\end{matrix} : \begin{matrix}\text{known}\\ \text{quantity}\end{matrix} = \begin{matrix}\text{dose}\\ \text{desired}\end{matrix} : \begin{matrix}\text{unknown}\\ \text{quantity}\end{matrix}$$

$$20 \text{ mg} : 5 \text{ mL} = 8 \text{ mg} : X \text{ mL}$$

$$20X = 40 = 20\overline{)40}^{\,2}$$

$$X = 2 \text{ mL}$$

Step 3. Check for reasonableness. An oral dose of 2 mL is appropriate for a terminally ill child.

EXAMPLE 5

The physician orders Benadryl elixir 25 mg q12h. The bottle in the medicine cupboard is labeled 12.5 mg/5 mL.

Step 1. Verify that all measures are in the same system. No conversion is necessary.

Step 2. Write the problem as a proportion and label each term

$$\begin{matrix}\text{dose}\\ \text{on hand}\end{matrix} : \begin{matrix}\text{known}\\ \text{quantity}\end{matrix} = \begin{matrix}\text{dose}\\ \text{desired}\end{matrix} : \begin{matrix}\text{unknown}\\ \text{quantity}\end{matrix}$$

$$12.5 \text{ mg} : 5 \text{ mL} = 25 \text{ mg} : X \text{ mL}$$

$$12.5X = 125 = 12.5\overline{)125.00} = 125\overline{)125.00}^{\,10}$$

$$X = 10 \text{ mL}$$

Step 3. Check for reasonableness. The dose 10 mL is within normal limits for oral solution.

Cautions for the Ratio and Proportion Method

1. *Label* all parts of the equation.
2. The ratio on the *left* contains the *known* quantity, and the ratio on the *right* contains the *desired* and *unknown* quantities.
3. Terms of the second ratio must be in the same sequence as those in the first ratio.
4. *Multiply* the *extremes first* and then the means.
5. Take extra care with decimals.
6. *Convert* fractions to decimals. *Round off* decimals to one decimal place.
7. *Label* the answer.
8. *Verify the accuracy* of calculations with an instructor.
9. *Question* any unusual dosage not within normal limits (e.g., less than ½ tab, more than two tabs, or more than 2 mL for injection).

PEDIATRIC DOSAGE

Children are not miniature adults. You cannot merely take part of an adult dose and give it to a child. There are many other variables to consider. There are numerous formulas available for computing *approximate* child's dose based on either body surface area, weight, or age. However, other factors must be taken into consideration as well. In neonates, renal function and some enzyme systems needed for drug absorption and metabolism are not fully developed. The neonate's blood-brain barrier is more permeable and his total body water contributes a greater percentage of his body weight, also affecting drug absorption.

Appropriate dosage for children, as well as adults, must take into consideration variables such as age, weight, sex, and metabolic, pathological, or psychological conditions. Recommended pediatric drug dosages are derived from data obtained in clinical trials utilizing sick children. When preparing drug dosages for children, it is important to always refer to recommended dosages as listed in drug inserts, *Physicians' Desk Reference (PDR)*, or *AHFS Drug Information (AHFS DI)*.

Recommended dosages of drugs are often expressed in the references as a number of milligrams per unit of body weight, per unit of time. For example, the recommended dose for a drug might be 6 mg/kg/24 h. This information can then be used to

1. Calculate the dose for the individual patient
2. Check on the appropriateness of the prescribed dose, watching particularly for possible overdoses

EXAMPLE 1

The recommended dose of meperidine (Demerol) is 6 mg/kg/24 h for pain, in divided doses every four to six hours, as necessary. Demerol is available in ampules or cartridges labeled 50 mg/mL. How much Demerol would be appropriate for a 33-pound child as a single dose every six hours?

Step 1. Convert pounds to kilograms (divide number of pounds by 2.2).

$$33 \text{ pounds} = 15 \text{ kg}$$

6 mg per kg in 24 hr is recommended.

$$6 \text{ mg} \times 15 \text{ kg} = 90 \text{ mg in 24 hr}$$

Step 2. Calculate the number of *milliliters needed in 24 h.* Write the problem as a proportion and label each term.

$$\begin{matrix}\text{dose}\\ \text{on hand}\end{matrix} : \begin{matrix}\text{known}\\ \text{quantity}\end{matrix} = \begin{matrix}\text{dose}\\ \text{desired}\end{matrix} : \begin{matrix}\text{unknown}\\ \text{quantity}\end{matrix}$$

$$50 \text{ mg} : 1 \text{ mL} = 90 \text{ mg} : X \text{ mL}$$

$$50X = 90 = 50\overline{)90.0}^{\,1.8}$$

$$X = 1.8 \text{ mL in 24 hours}$$

Then, calculate the number of *milliliters* needed in six hours. Remember, the unknown quantity is always the last term in the equation.

$$24 \text{ h} : 1.8 \text{ mL} = \text{six hours} : X \text{ mL}$$

$$24X = 10.8 = 24\overline{)10.80}^{\,0.45}$$

$$X = 0.45 \text{ mL dose every six hours}$$

Step 3. The appropriateness of this dose can be checked by applying *Clark's Rule:*

$$\frac{\text{child's wt in lb}}{\text{average adult wt}} \times \text{adult dose} = \text{child's } \textit{approximate} \text{ dose}$$

$$\frac{33}{150} \times 100 \text{ mg} = 22 \text{ mg approximate child's dose}$$

Note: The average adult weight is 150 pounds.

Demerol is available in ampules labeled 100 mg/2 mL

$$100 \text{ mg} : 2 \text{ mL} = 22 \text{ mg} : X \text{ mL}$$

$$100X = 44 = 100\overline{)44.00}\quad 0.44$$
$$\underline{400}$$
$$400$$

$X = 0.44$ mL dose to be administered

Remember, this is a *general* rule and other variables must be considered when assessing for appropriateness of dosage.

GERIATRIC DOSAGE

Special consideration must be given to preparation and administration of safe dosage to older adults. As with children, the dose frequently needs to be reduced. Factors leading to possible dangerous cumulative effects can include slower metabolism, poor circulation, or impairment of liver, kidneys, lungs, or central nervous system. Any chronic disease, debility, dehydration, or electrolyte imbalance can affect assimilation of drugs and interfere with therapeutic effect. Many drugs can impair mental status of older adults, leading to confusion. Any older adult taking many drugs is also at risk for potentially lethal interactions. There is no formula to guide you in safe geriatric dosage. Careful assessment on an *individual* basis, constant monitoring, and reduction of dosage, whenever possible, are the rules to follow. Each individual reacts differently to drugs, and changes occur over time. You have the responsibility to question the appropriateness of any drug, and especially as the patient's condition changes. See also Chapter 27, Drugs and Older Adults.

PREVENTION OF MEDICATION ERRORS

Medication errors can occur for a number of reasons: administering the wrong drug, the wrong amount, at the wrong time, by the wrong route, or to the wrong patient. The Rights of Medication Administration will be discussed in the next chapter. However, we will consider here errors that can occur when the drug order is misinterpreted.

- Never leave the decimal point naked. Writing .2 instead of 0.2 could cause the decimal point to be missed and could result in an overdose. Always place a zero *before* a decimal point; for example, 0.2, 0.5.
- Never place a decimal point and zero after a whole number. The decimal point could be missed and the zero could be misinterpreted, for example, 5.0 mg could be read as 50 mg. The correct way is to write 5 mg.
- Avoid using decimals whenever whole numbers can be used as alternatives; for example, 0.5 g can be expressed as 500 mg.
- Have a second qualified person double-check any calculations for accuracy.

- If you have difficulty interpreting the spelling of a drug name or the number used for the dosage, or the dosage seems inappropriate, *always question* the order. This is not only your duty, but you have an ethical and legal responsibility to be sure that the drugs you administer are safe. If a medication error results in legal action, you could be held accountable, even though the order was written incorrectly. You are expected to recognize inappropriate dosage, to check reference books with unfamiliar drugs, and to ask the physician or pharmacist about any questionable dosage.

CHAPTER REVIEW QUIZ

Section A

The available dosages are listed with each drug. Choose the most appropriate available form to deliver the dosage ordered. Use only *one* form of each drug. Indicate the *amount* and *which drug form* you should give for the following orders. *Use the smallest number of tablets possible.*

Drug and Dose Ordered	Amount to Administer
1. atenolol (Tenormin) 75 mg Available 50 mg and 100 mg tablets of Tenormin	_____ of _____ mg tab
2. buspirone (Buspar) 25 mg Available 5 mg and 10 mg tablets of Buspar	_____ of _____ mg tab
3. alprazolam (Xanax) 0.75 mg Available 0.25 mg, 0.5 mg, and 1 mg tablets of Xanax	_____ of _____ mg tab
4. bumetanide (Bumex) 2 mg Available 0.5 mg and 1 mg tablets of Bumex	_____ of _____ mg tab
5. cimetidine (Tagamet) 200 mg Available 300 mg and 400 mg tablets of Tagamet	_____ of _____ mg tab
6. furosemide (Lasix) 60 mg Available 20 mg and 40 mg tablets of Lasix	_____ of _____ mg tab
7. levothyroxine (Synthroid) 0.3 mg Available 0.05 mg, 0.1 mg, and 0.15 mg tablets of Synthroid	_____ of _____ mg tab
8. propranolol (Inderal) 15 mg Available 10 mg, 20 mg, and 40 mg tablets of Inderal	_____ of _____ mg tab
9. prednisone 15 mg Available 5 mg, 10 mg, and 20 mg tablets of prednisone	_____ of _____ mg tab
10. sertraline (Zoloft) 75 mg Available 50 mg and 100 mg tablets of Zoloft	_____ of _____ mg tab

Section B

Show your work. Label and circle your answers.

1. The physician orders Lovenox 1 mg/kg subcu q12h. The patient weighs 176 lb. Lovenox is available 100 mg in 1 mL.

a. What is the patient's weight in kilograms? _____

b. What is the dose of Lovenox to be administered? _____ mg in _____ mL

2. The medication order reads Demerol 60 mg IM. The narcotic drawer contains syringes labeled meperidine (Demerol) 75 mg/mL.

a. How many mL would you administer? _____

b. How many mL would you discard and mark as "wasted" on the narcotic record?

_____

3. Lasix is available in 40 mg tablets. The order reads Lasix 60 mg PO qAM. How many tablets should you give?

4. Phenergan 12.5 mg IV is ordered. Available vials of phenergan are labeled 25 mg/mL. How many mL would you administer?

5. Acetaminophen elixir 650 mg PO is ordered. The container is labeled 325 mg/5 mL.

a. How many mL would you administer? _____

b. How many teaspoons per dose? _____

6. Morphine sulfate PO 30 mg liquid is ordered. Morphine oral solution is labeled 20 mg/mL. How many mL would you administer?

7. The medication order reads heparin 5,000 units. Vials available in the medication cupboard are labeled heparin 10,000 units/mL. How many milliliters should you draw into the syringe?

8. Digoxin elixir is available in 50 mcg/mL. The physician orders 125 mcg PO daily. How many milliliters should you give?

9. The physician orders prednisone PO 7.5 mg daily. Prednisone is available in 5-mg and 10-mg scored tablets, which can be broken in half. Which strength tablet and how many tablets should you give?

10. Amoxicillin suspension 750 mg PO q8h is ordered. Liquid medication available is labeled 250 mg/5 mL. How many milliliters should you give?

11. Calcium carbonate 1,000 mg PO daily is prescribed, to be given in divided doses bid. Available tablets contain calcium 250 mg/tab. How many tablets should be taken each time?

12. Cheratussin AC contains 10 mg of codeine in each teaspoon (5 mL). If 2 tsp Cheratussin AC PO is prescribed q4h, how much codeine would be contained in each dose?

13. The physician orders Ivermectin tablets for a 200-lb adult with scabies. The recommended dose is 0.2 mg/kg. Ivermectin tablets are labeled 6 mg. How many tablets should be given for the dose?

14. The physician orders Ceclor Suspension 200 mg PO q8h for a 44-lb child. Ceclor Suspension is available 250 mg/5 mL.

a. How many mL should be administered each time? _____

b. Recommended dosage of Ceclor is 30 mg/kg/daily. How many mg would be appropriate for this child daily? _____

15. List five variables to consider in determining a child's dose:

_____, _____, _____, _____,

and _____

16. List five factors that could lead to serious cumulative effects with medicines in the elderly:

_____, _____, _____, _____,

and _____

Go to your StudyWARE™ CD-ROM and have fun learning as you play games and answer case study-related questions to help reinforce key concepts you learned in this chapter.

Go to your Study Guide and complete the review questions for this chapter.

Answers to Basic Arithmetic Test

1.	$9\frac{11}{12}$	**7.**	7.035	**13.**	2.3%	**19.**	23
2.	$2\frac{1}{6}$	**8.**	10.363	**14.**	0.12	**20.**	72
3.	$9\frac{1}{15}$	**9.**	0.14941	**15.**	$\frac{2}{5}$	**21.**	½
4.	$\frac{8}{15}$	**10.**	7.3	**16.**	60%	**22.**	60%
5.	$\frac{8}{15}$	**11.**	$\frac{2}{25}$	**17.**	0.125	**23.**	½
6.	6.333	**12.**	0.4	**18.**	120		

Chapter 7

Responsibilities and Principles of Drug Administration

Objectives

Upon completion of this chapter, the learner should be able to

1. Describe four responsibilities of the health care provider in safe administration of medications
2. List the six Rights of Medication Administration
3. Explain moral, ethical, and legal responsibilities regarding medication errors
4. Cite three instances of medication administration that require documentation
5. Explain the rights of the health care practitioner to question or refuse to administer medications
6. Define the Key Terms and Concepts

Key Terms and Concepts

Documentation of drug administration

Reporting of medication errors

Responsibilities of drug administration

Six Rights of Medication Administration

MedWatch

RESPONSIBLE DRUG ADMINISTRATION

The safe and accurate administration of medications requires knowledge, judgment, and skill. The **responsibilities** of the health care provider in this vital area include:

1. Adequate, up-to-date *information* about all medications to be administered, including purpose, potential side effects, cautions, and contraindications, and possible interactions.
2. *Wisdom* and judgment to accurately *assess* the patient's needs for medications, to *evaluate* the response to medications, and to *plan* appropriate interventions as indicated.
3. *Skill in delivery* of the medication accurately, in the best interests of the patient, and with adequate documentation.
4. *Patient education* to provide the necessary information to the patient and family about why, how, and when medications are to be administered and potential side effects and precautions with administration by the layperson.

Responsibility for safe administration of medications requires that the health care practitioner be familiar with every medication before administration. Knowledge of the typical and most frequently used drugs of the systems (as described in Part II of this text) is imperative. However, this is only a framework upon which to build and add other knowledge of new drugs or new effects as changes in medicine become known. Unfamiliar drugs should never be administered. Resources such as the *PDR*, the *AHFS Drug Information*, the *USP/DI*, package inserts, and pharmacists must be consulted *before* administration in order to become familiar with the desired effect, potential side effects, precautions and contraindications, and possible interactions with other drugs or with foods.

Responsibility for safe administration of medications requires *complete planning* for patient care, including prior *assessment*, *interventions*, and *evaluations* of the results of drug therapy. Assessment involves taking a complete history, including all medical conditions (e.g., pregnancy or illness), allergies, and all other medications in use, including over-the-counter drugs, vitamins, and herbal remedies. Assessment also involves careful observation of the patient's vital signs, posture, skin temperature and color, and facial expression before and after drug administration. Appropriate interventions require judgment in timing, discontinuing medicine if required, and taking steps to counteract adverse reactions, as well as knowing what and when to report to the physician. Evaluation and documentation of results also play a vital role for all health care providers, including the physician, in planning effective drug therapy.

The safe administration of medications necessitates training to develop skills in delivery of medications. The goal is to maximize the effectiveness of the drug with the least discomfort to the patient. Sensitivity to the unique needs of each patient is encouraged (e.g., awareness of difficulty swallowing or impaired movement that could affect administration of medications).

Patient education is an essential part of the safe administration of medicines. If patients are to benefit from drug therapy, they must understand the importance of taking the medicine in the proper dosage, on time, and in the proper way. Information for patients should be in language they understand, with instruction both verbal and written, as well as demonstrations of techniques when indicated. If the medication administration requires extra equipment or has multiple steps, a return demonstration should be required.

Administration of medication carries moral, ethical, and legal responsibilities. Some rules and regulations vary with the institution, agency, or office. When in doubt, consult those in authority—supervisors or administrators—and/or policy and procedure books. However, documentation on the patient's record is always required for all medicines given, as well as for patient education provided. In addition, controlled substances given must also be recorded in a narcotics record as explained in Chapter 1.

MEDICATION ERRORS

Medication errors can and do occur in all health care settings. More errors are reported from acute care settings, where the risk is greatest. However, outpatient facilities, ambulatory care sites, home health care, and long-term

care facility practitioners have challenges unique to their practice as well. Patients in these settings often are older adults and likely to have several chronic conditions requiring multiple medications (see Chapter 27, Drugs and Older Adults). Increasing the number of medications an individual receives not only increases the risk of interactions and adverse side effects, but also increases the risk of error.

Medication errors can occur in the following situations:

1. Administering a drug to the wrong patient
2. Administering an incorrect drug
3. Administering a drug via an incorrect route or at the wrong time.
4. Administering an incorrect dosage.
5. Improperly documenting drug administration information on a patient's medical record.

Meticulous care in preparation and administration of medications reduces the chances of error. However, if a mistake is made, it is of the utmost importance to **report it** immediately to the one in charge so that corrective action can be taken for the patient's welfare. The patient's record should reflect the corrective action taken for justification in case of legal proceedings. An incident report must also be completed as a legal requirement. Failure to report errors appropriately can jeopardize the patient's welfare, as well as increase the possibility of civil suits against the health care provider and/or the risk of loss of professional license or certificate. Honesty is not only the best policy, it is the *only* policy for moral, ethical, and legal reasons.

Health care practitioners have a responsibility to provide quality care and provide for patient safety at all times. Remember, *"First, do no harm."* This challenge includes prevention of medication errors and also **reporting** errors so that corrective steps can be taken. As part of this goal, the U.S. Pharmacopeia (USP) has established a Medication Errors Reporting (MER) program. Confusion over the similarity of drug names, either written or spoken, accounts for approximately one-quarter of all reports to this agency. Therefore, the MER has published a USP Quality Review report, *Look-Alike and/or Sound-Alike Product Errors*, listing many similar drug names that have led to medication errors.

StudyWARE™ CONNECTION

The *USP Quality Review No. 82 report* is included on the StudyWARE™ CD-ROM for your reference.

In addition, the Agency for Healthcare Research and Quality (AHRQ) has federally certified the Institute for Safe Medication Practices (ISMP) as a Patient Safety Organization (PSO). Health care practitioners and the public should be encouraged to report errors to ISMP since a PSO confers both privilege and confidentiality to the information reported. Error reporting by health care professionals and hospitals is necessary to develop safety alerts and quality improvement programs.

PRINCIPLES OF ADMINISTRATION

When preparing to administer medications, several basic principles should always be kept in mind

1. *Cleanliness.* Essential to safe administration of medicines. Always wash hands before handling medicines, and be sure preparation area is clean and neat.

2. *Organization.* Necessary for safe administration of medicines. Always be sure medications and supplies are in the appropriate area and in adequate supply. When stock drugs are used, they should be reordered immediately.
3. *Preparation area.* Should be well lighted and away from distracting influences.

Guidelines to review before giving medicines are called the **Six Rights of Medication Administration** (Figure 7-1):

1. Right medication
2. Right amount
3. Right time
4. Right route
5. Right patient
6. Right documentation

Right Medication

You can confirm that you have the right medication by carefully comparing the name of the drug prescribed (on the physician's order sheet, prescription blank, medication record, or medicine card) with the label on the package, bottle, or

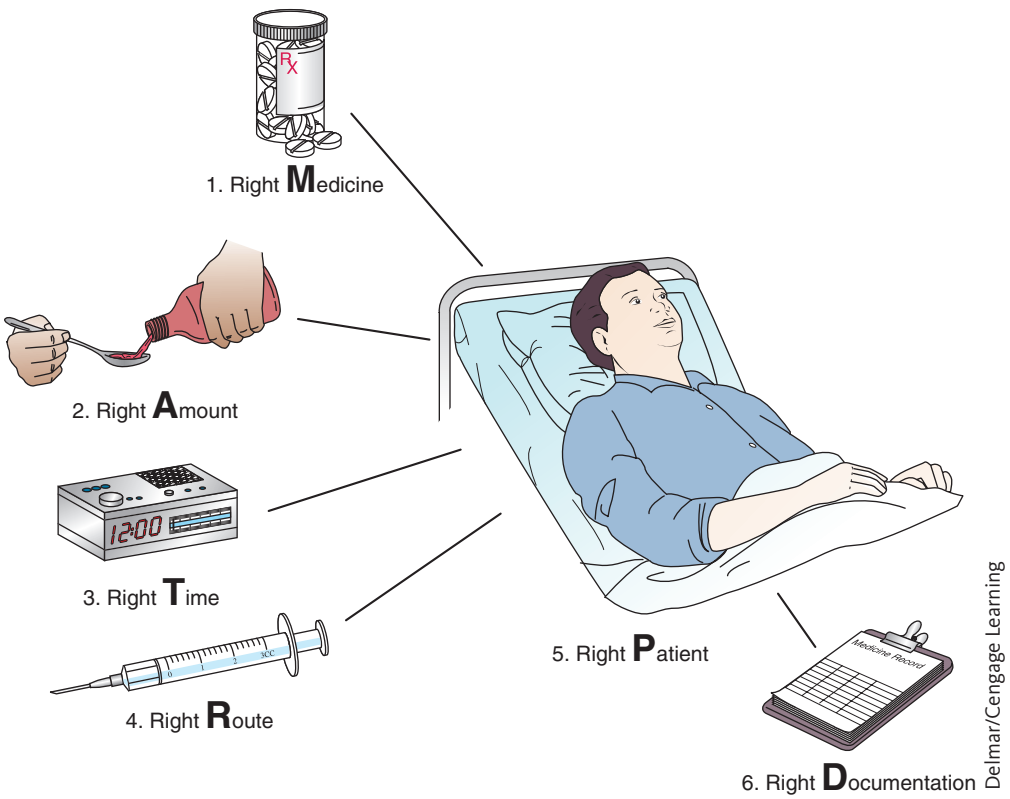

FIGURE 7-1 The Six Rights of Medication Administration.

unit-dose packet (medications with each dose separately sealed in an individual paper, foil, plastic, or glass container). *Never* give medication when the name of the medication is obscured in any way. Some drugs have names that sound or look similar (e.g., Novolin 70/30 and Novolog Mix 70/30), and therefore it is essential to scrutinize every letter in the name when comparing the medicine ordered with the medicine on hand. Accuracy can be facilitated by placing the unit-dose packet next to the name of the drug ordered on the patient's record, while comparing the drug ordered with the drug on hand. (See Figure 8-2 in Chapter 8.)

If there is any question about the drug order because of handwriting, misspelling, inappropriateness, allergies, or interactions, you have the *right* and *responsibility to question* the physician and/or the pharmacist.

Never give medications that someone else has prepared. *Never* leave medications at the bedside unless specifically ordered by the doctor (e.g., nitroglycerin tablets and contraceptives are frequently ordered to be left with the patient for self-administration). If the patient is unable to take a medication when you present it, the medication must be returned (in an unopened packet) to the patient's drawer in the medicine cart or medicine room. Never open the unit-dose packet until the patient is prepared to take the medicine.

Right Amount

Administering the right amount of drug is extremely important. The drug dosage ordered must be compared *very carefully* with the dose listed on the label of the package, bottle, or unit-dose packet. Here again, accuracy can be facilitated by placing the unit-dose packet next to the written order on the patient's record while comparing the dose ordered with the dose on hand.

The three different systems of measurement (household, apothecary, and metric) were discussed in Chapter 5. It is important to consult a table of equivalents (Table 5-4), if necessary, to convert from one system to another. Directions for calculation of different drug doses were presented in Chapter 6. Drug calculations are infrequent with unit-dose packaging. However, if it is necessary to compute calculations, such calculations must be checked by another trained health care practitioner, pharmacist, or doctor to verify accuracy. Be especially careful when the dose is expressed in decimals or fractions. Always recheck the dose if less than ½ tablet or more than 2 tablets is required, or more than 2 mL for injection. An unusual dosage should alert you to the possibility of error. Those who administer medications have the right, as well as the responsibility, to question any dosage that is unusual or seems inappropriate for the individual patient. Remember that drug action is influenced by the condition of the patient, metabolism, age, weight, sex, and psychological state (see Chapter 3). The health care practitioner has the responsibility of reporting the results of careful assessment and observations in order to assist the physician in prescribing the right dosage for each patient.

Directions for measurement and preparation of the right dose are described in Chapters 8 and 9. An important part of the patient education includes complete instructions about the importance of preparing and taking the right amount of medicine prescribed by the physician.

Right Time

The time for administration of medications is an important part of the drug *dosage*, which includes the amount, frequency, and number of doses of medication to be administered. For maximum effectiveness, drugs must be given on a prescribed schedule. The physician's order specifies the number of times per day the medicine is to be administered (e.g., bid, or twice a day). Some medications need to be maintained at a specific level in the blood (therapeutic level) and are therefore prescribed at regular intervals around the clock (e.g., q4h, or every 4 hours). Some medications, such as some antibiotics, are more effective on an empty stomach and are therefore prescribed ac (before meals). Medications that are irritating to the stomach are ordered pc (after meals). Drugs that cause sedation are more frequently prescribed at hour of sleep. If the physician does not prescribe a specific time for administration of a drug, the health care practitioner arranges an appropriate schedule, taking into consideration the purpose, action, and side effects of the medication. Patient education includes instruction about the right time to take specific medicines and why.

Right Route

The route of administration is important because of its effect on degree of absorption, speed of drug action, and side effects. Many drugs can be administered in a variety of ways (see Chapter 4). The physician's order specifies the route of administration. If no route is specified, the oral route is used unless conditions warrant otherwise (e.g., nausea, vomiting, or difficulty swallowing). Those administering medications have the right and responsibility to question the appropriateness of a route based on assessment and observation of the patient. Change of route may be indicated because of the patient's condition. However, the route of administration may not be changed without the physician's order.

Right Patient

The patient who is to receive the medication must be identified by use of certain techniques to reduce the chance of error. In health care facilities, the patient's wrist identification band should be checked *first*, and then the patient should be called by name or asked to state her name, *before* administering the medication. In the ambulatory care setting, the patient can be asked to give name and date of birth; this can be verified with the chart before administering medications. If the patient questions the medication or the dosage, recheck the order and the medicine before giving it.

Right Documentation

Another essential duty is **documentation**. Every medication given must be recorded on the patient's record, along with *dose*, *time*, *route*, and *location* of injections. In addition, any unusual or adverse patient reactions must be noted. If the medication is given on a PRN (as necessary) basis (e.g., for pain),

notation should also be made on the patient's record of the effectiveness of the medication. The person administering the medication must also sign or initial the record after administration (the policy of each facility determines the exact procedure to be followed). The accuracy of medication documentation is a very important legal responsibility. At times, patients' records are examined in court, and the accuracy of medication documentation can be a critical factor in some legal judgments.

Documentation also includes the recording of narcotics administered on the special controlled substances record kept with the narcotics. If narcotics are destroyed because of partial dosage, cancellation, or error, two health care practitioners must sign as witnesses of the disposal of the drug (the policy about documentation of narcotics may vary with the agency).

In summary, safe and effective administration of medications involves current drug information; technical and evaluation skills; and moral, ethical, and legal responsibilities. Guidelines include the six Rights of Medication Administration. In addition, the health care practitioner has the right and responsibility to question any medication order that is confusing or illegible or that seems inappropriate, and the right to refuse to administer any medication that is not in the best interests of the patient. The welfare of the patient is the primary concern in administration of medications.

MedWatch

The Food and Drug Administration (FDA) issued a form in 1993 to assist health care professionals in reporting serious, adverse events or product quality problems associated with medications, medical devices, or nutritional products regulated by the FDA, for example, dietary supplements or infant formulas. Even the large, well-designed clinical trials that precede FDA approval cannot uncover every problem that can come to light once a product is widely used. For example, a drug could interact with other drugs in ways not revealed during clinical trials. Reports by health care professionals can help ensure the safety of drugs and other products regulated by the FDA.

In response to these voluntary reports from the health care community, the FDA has issued warnings, made labeling changes, required manufacturers to do postmarketing studies, and ordered the withdrawal of certain products from the market. Such actions can prevent injuries, suffering, disabilities, congenital deformities, and even deaths.

You are not expected to establish a connection or even wait until the evidence seems overwhelming. The agency's regulations will protect your identity and the identities of your patient and your facility. With your cooperation, MedWatch can help the FDA better monitor product safety and, when necessary, take swift action to protect your patients and you. MedWatch encourages you to regard voluntary reporting as part of your professional responsibility. See Figure 7-2 for a MedWatchform, which can be reproduced, and for instructions for completing and submitting this form to the FDA. In addition, you can complete a MedWatch online voluntary reporting form (3500) by visiting www.fda.gov/medwatch/.

StudyWARE™ CONNECTION

See It In Action! Go to the StudyWARE™ CD-ROM to view a video on *Medication Errors, Documentation, and Administration.*

U.S. Department of Health and Human Services

MEDWATCH

The FDA Safety Information and Adverse Event Reporting Program

For VOLUNTARY reporting of adverse events, product problems and product use errors

Page 1 of ___

Form Approved: OMB No. 0910-0291, Expires: 12/31/2011
See OMB statement on reverse.

FDA USE ONLY
Triage unit sequence #

PLEASE TYPE OR USE BLACK INK

A. PATIENT INFORMATION

1. **Patient Identifier** — In confidence
2. **Age at Time of Event or Date of Birth:**
3. **Sex** ☐ Female ☐ Male
4. **Weight** ____ lb or ____ kgs

B. ADVERSE EVENT, PRODUCT PROBLEM OR ERROR

Check all that apply:

1. ☐ **Adverse Event** ☐ **Product Problem** *(e.g., defects/malfunctions)*
☐ **Product Use Error** ☐ **Problem with Different Manufacturer of Same Medicine**

2. **Outcomes Attributed to Adverse Event** *(Check all that apply)*
☐ Death: _____ *(mm/dd/yyyy)*
☐ Life-threatening
☐ Hospitalization - initial or prolonged
☐ Required Intervention to Prevent Permanent Impairment/Damage (Devices)
☐ Disability or Permanent Damage
☐ Congenital Anomaly/Birth Defect
☐ Other Serious (Important Medical Events)

3. **Date of Event** *(mm/dd/yyyy)*
4. **Date of this Report** *(mm/dd/yyyy)*

5. **Describe Event, Problem or Product Use Error**

6. **Relevant Tests/Laboratory Data, Including Dates**

7. **Other Relevant History, Including Preexisting Medical Conditions** *(e.g., allergies, race, pregnancy, smoking and alcohol use, liver/kidney problems, etc.)*

C. PRODUCT AVAILABILITY

Product Available for Evaluation? *(Do not send product to FDA)*
☐ Yes ☐ No ☐ Returned to Manufacturer on: _____ *(mm/dd/yyyy)*

D. SUSPECT PRODUCT(S)

1. Name, Strength, Manufacturer *(from product label)*

#1 Name:
Strength:
Manufacturer:

#2 Name:
Strength:
Manufacturer:

2. **Dose or Amount** / **Frequency** / **Route**

#1
#2

3. **Dates of Use** *(If unknown, give duration) from/to (or best estimate)*
#1
#2

4. **Diagnosis or Reason for use** *(Indication)*
#1
#2

5. **Event Abated After Use Stopped or Dose Reduced?**
#1 ☐ Yes ☐ No ☐ Doesn't Apply
#2 ☐ Yes ☐ No ☐ Doesn't Apply

8. **Event Reappeared After Reintroduction?**
#1 ☐ Yes ☐ No ☐ Doesn't Apply
#2 ☐ Yes ☐ No ☐ Doesn't Apply

6. **Lot #**
#1
#2

7. **Expiration Date**
#1
#2

9. **NDC # or Unique ID**

E. SUSPECT MEDICAL DEVICE

1. **Brand Name**
2. **Common Device Name**
3. **Manufacturer Name, City and State**

4. **Model #** / **Lot #**
Catalog # / **Expiration Date** *(mm/dd/yyyy)*
Serial # / **Other #**

5. **Operator of Device**
☐ Health Professional
☐ Lay User/Patient
☐ Other: _____

6. **If Implanted, Give Date** *(mm/dd/yyyy)*
7. **If Explanted, Give Date** *(mm/dd/yyyy)*

8. **Is this a Single-use Device that was Reprocessed and Reused on a Patient?**
☐ Yes ☐ No

9. **If Yes to Item No. 8, Enter Name and Address of Reprocessor**

F. OTHER (CONCOMITANT) MEDICAL PRODUCTS

Product names and therapy dates *(exclude treatment of event)*

G. REPORTER *(See confidentiality section on back)*

1. **Name and Address**
Name:
Address:
City: State: ZIP:

Phone # / **E-mail**

2. **Health Professional?** ☐ Yes ☐ No
3. **Occupation**
4. **Also Reported to**
☐ Manufacturer
☐ User Facility
☐ Distributor/Importer

5. **If you do NOT want your identity disclosed to the manufacturer, place an " X " in this box:** ☐

FORM FDA 3500 (1/09) Submission of a report does not constitute an admission that medical personnel or the product caused or contributed to the event.

Source: Partial MED WATCH form. The FDA Medical Products Reporting Program for voluntary reporting by health professionals of adverse events and product problems. Visit www.fda.gov for the complete, interactive MED WATCH form and instructions for completing.

FIGURE 7-2A MedWatch form. The FDA Medical Products Reporting Program for voluntary reporting by health professionals of adverse events and product problems.

ADVICE ABOUT VOLUNTARY REPORTING

Detailed instructions available at: http://www.fda.gov/medwatch/report/consumer/instruct.htm

Report adverse events, product problems or product use errors with:

- Medications *(drugs or biologics)*
- Medical devices *(including in-vitro diagnostics)*
- Combination products *(medication & medical devices)*
- Human cells, tissues, and celluar and tissue-based products
- Special nutritional products *(dietary supplements, medical foods, infant formulas)*
- Cosmetics

Report product problems - quality, performance or safety concerns such as:

- Suspected counterfeit product
- Suspected contamination
- Questionable stability
- Defective components
- Poor packaging or labeling
- Therapeutic failures (product didn't work)

-Fold Here-

Report SERIOUS adverse events. An event is serious when the patient outcome is:

- Death
- Life-threatening
- Hospitalization - initial or prolonged
- Disability or permanent damage
- Congenital anomaly/birth defect
- Required intervention to prevent permanent impairment or damage (devices)
- Other serious (important medical events)

Report even if:

- You're not certain the product caused the event
- You don't have all the details

How to report:

- Just fill in the sections that apply to your report
- Use section D for all products except medical devices
- Attach additional pages if needed
- Use a separate form for each patient
- Report either to FDA or the manufacturer *(or both)*

Other methods of reporting:

- 1-800-FDA-0178 - To FAX report
- 1-800-FDA-1088 - To report by phone
- www.fda.gov/medwatch/report.htm - To report online

If your report involves a serious adverse event with a device and it occurred in a facility outside a doctor's office, that facility may be legally required to report to FDA and/or the manufacturer. Please notify the person in that facility who would handle such reporting.

-Fold Here-

If your report involves a serious adverse event with a vaccine call 1-800-822-7967 to report.

Confidentiality: The patient's identity is held in strict confidence by FDA and protected to the fullest extent of the law. FDA will not disclose the reporter's identity in response to a request from the public, pursuant to the Freedom of Information Act. The reporter's identity, including the identity of a self-reporter, may be shared with the manufacturer unless requested otherwise.

The public reporting burden for this collection of information has been estimated to average 36 minutes per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing the collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden to:

Department of Health and Human Services
Food and Drug Administration
Office of Chief Information Officer (HFA-710)
5600 Fishers Lane
Rockville, MD 20857

Please DO NOT RETURN this form to this address.

OMB statement:
"An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB control number."

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

FORM FDA 3500 (1/09) (Back) **Please Use Address Provided Below – Fold in Thirds, Tape and Mail**

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service
Food and Drug Administration
Rockville, MD 20857

Official Business
Penalty for Private Use $300

BUSINESS REPLY MAIL
FIRST CLASS MAIL PERMIT NO. 946 ROCKVILLE MD

POSTAGE WILL BE PAID BY FOOD AND DRUG ADMINISTRATION

NO POSTAGE NECESSARY IF MAILED IN THE UNITED STATES OR APO/FPO

MEDWATCH
The FDA Safety Information and Adverse Event Reporting Program
Food and Drug Administration
5600 Fishers Lane
Rockville, MD 20852-9787

Source: Partial MED WATCH form. The FDA Medical Products Reporting Program for voluntary reporting by health professionals of adverse events and product problems. Visit www.fda.gov for the complete, interactive MED WATCH form and instructions for completing.

FIGURE 7-2B continued

CHAPTER REVIEW QUIZ

Complete the statements by filling in the blanks.

1. Before administering any medication, you should have the following information about the drug:

_____

_____

_____

_____

2. Before administering any medication, you should have the following three pieces of information about the patient:

_____ _____

other _____

3. Assessment of the patient's need for pain medication and reactions to drugs includes observation of the following four signs:

_____

_____

_____

_____

4. Patient education about medication should include the following four pieces of information:

_____

_____

_____

_____

5. When administering a controlled substance, documentation is necessary in what two places:

_____

_____

6. Documentation of an injection given for pain should include the following five pieces of information:

7. Name the Six Rights of Drug Administration:

8. Medication errors must be reported immediately, and documentation includes recording the information in the following two areas:

Go to your StudyWARE™ CD-ROM and have fun learning as you play games and answer case study-related questions to help reinforce key concepts you learned in this chapter.

Go to your Study Guide and complete the review questions for this chapter.

Chapter 8

Administration by the Gastrointestinal Route

Objectives

Upon completion of this chapter, the learner should be able to

1. Describe the advantages and disadvantages of administering medications orally, by nasogastric or gastrostomy tube, and rectally
2. Explain appropriate action when patient is NPO, has dysphagia, refuses medication, vomits medication, or has allergies
3. List special precautions in preparation of timed-release capsules, enteric-coated tablets, and oral suspensions
4. Demonstrate measurement of liquid medications with medicine cup and syringe
5. Demonstrate proficiency in administering medications orally, by nasogastric or gastric tube, and rectally
6. Satisfactorily complete all of the activities listed on the checklists
7. Define the Key Terms and Concepts

Key Terms and Concepts

Dysphagia

Gastric tube administration

Nasogastric tube administration

Oral medication administration

Rectal medication

Medications are administered by the gastrointestinal route more often than any other way. Gastrointestinal administration includes four categories: oral, nasogastric tube, gastric tube, and rectal.

*Advantages of the **oral route*** include:

- Convenience and patient comfort
- Safety, because medication can be retrieved in case of error or intentional overdose
- Economy, because there are few equipment costs

Disadvantages of the oral route include:

- Slower onset of absorption and action
- Rate and degree of absorption that vary with gastrointestinal contents and motility
- Some drugs (e.g., insulin and heparin) destroyed by digestive fluids and must be administered by injection
- Cannot be used with nausea or vomiting
- Dangerous to use if patient has difficulty swallowing (**dysphagia**), because of possible aspiration; aspiration is the inhalation of a foreign substance or regurgitated gastric contents, which can cause severe lung damage.
- Cannot be used for unconscious patients
- Cannot be used if patient is NPO (e.g., before surgery or while fasting for a laboratory test or X-ray examination)

Administration of medications by nasogastric tube is sometimes ordered when the patient is unable to swallow for prolonged periods of time because of illness, trauma, surgery, or unconsciousness. Medications are usually administered intravenously when these conditions exist for short periods of time.

Advantages of the ***nasogastric tube*** include:

- Ability to bypass the mouth and pharynx when necessary
- Elimination of numerous injections

The *disadvantage of the nasogastric tube* with a conscious patient is the discomfort of the tube in the nose and throat for prolonged periods of time.

When a patient is unable to take nourishment by mouth for a very extended period of time, the surgeon will sometimes insert a *gastric tube* through the skin of the abdomen, directly into the stomach. This G-tube, or peg tube, as it is sometimes called, is secured in place and can remain there for feeding purposes indefinitely. Medication can be administered via the G-tube, directly into the stomach.

Medications are sometimes administered by the rectal route when nausea or vomiting is present, or the patient is unconscious or unable to swallow. *Advantages of the* ***rectal route*** include:

- Bypassing the action of digestive enzymes
- Avoidance of irritation to the upper GI tract
- Usefulness with dysphagia

Disadvantages of the rectal route include:

- Many medications are unavailable in suppository form
- Some patients have difficulty retaining suppositories (e.g., older adults and children)
- Prolonged use of some rectal suppositories can cause rectal irritation (e.g., bisacodyl)
- Absorption may be irregular or incomplete if feces are present

See It In Action! Go to the StudyWARE™ CD-ROM to view a video on *rectal administration of drugs*. Note: While this video emphasizes the five rights of medication administration, keep in mind the recently added sixth right of "proper documentation".

ADMINISTRATION OF MEDICATIONS ORALLY

Guidelines for Oral Medications Administration

1. Wash your hands (Figure 8-1).
2. Locate appropriate medication sheet and check for completeness of the order (i.e., date, patient's name, medication name, dosage, route, and time).
3. Check for special circumstances (e.g., allergies or NPO).
4. Be sure that you know the purpose of the drug, possible side effects, contraindications, cautions, interactions, and normal dosage range. If unfamiliar with the drug, consult a reference book for this information.
5. Select appropriate receptacle in which to place medication (i.e., paper medicine cup for tablets or capsules and plastic medicine cup for liquids).
6. Locate medication in medication cupboard or medication cart drawer and compare the label against the medication sheet for the Six Rights of Medication Administration: right medicine, right amount, right time, right route, right patient, and right documentation (Figure 8-2). Also be sure to check the drug's expiration date.

Delmar/Cengage Learning

FIGURE 8-1 Medical asepsis handwash.

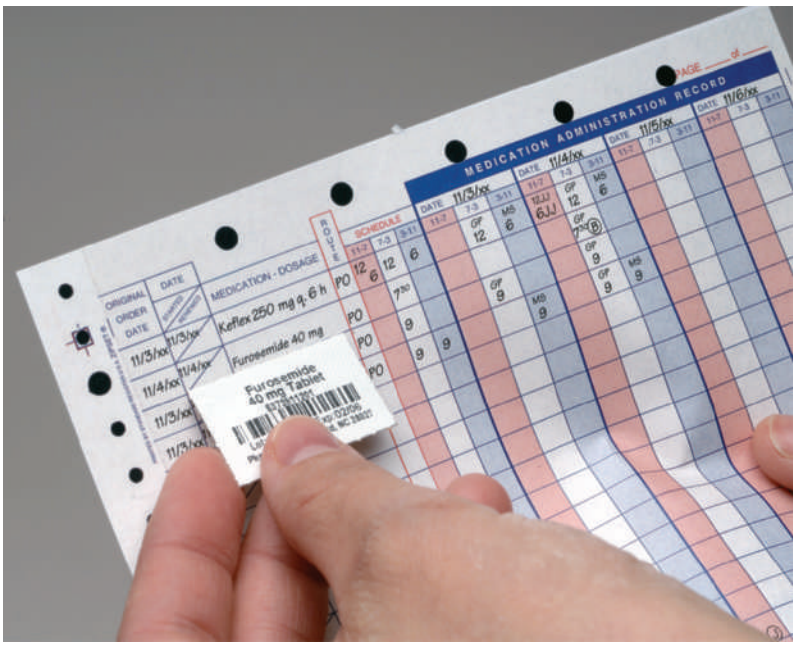

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FIGURE 8-2 Compare name and dosage on medication package with the Medication Administration Record.

Delmar/Cengage Learning

FIGURE 8-3 Keep the unit-dose packet intact until you are with the patient.

7. If the dose ordered differs from the dose on hand, complete calculations on paper and check for accuracy with instructor or coworker in clinical setting.
8. Prepare the dosage as ordered. Do not open unit-dose packages until you are with the patient (Figure 8-3). If medication is liquid, see "Preparation of Liquid Medications" later in this section.
9. Take medication in cup to patient and place it on table nearby.
10. Check patient's identification bracelet (Figure 8-4). Ask the patient to *tell you* his or her name and date of birth (DOB). Compare this information with the medication administration record to verify that you have the right patient.
11. Call patient by name and explain what you are doing. Answer any questions. Recheck medication order if patient expresses any doubts. Use this opportunity for patient education about the medication.
12. Monitor patient's vital signs if required for specific medication (e.g., blood pressure, apical pulse, or respiration). Blood pressure should always be taken and recorded *before* administering antihypertensives.
13. Open unit-dose package and place container in the patient's hand. Avoid touching the medication (Figure 8-5).
14. Provide full glass of water and assist the patient as necessary (e.g., raise the head of the bed and provide drinking straw if required).
15. Stay with the patient until the medication has been swallowed. Make the patient comfortable before you leave the room.

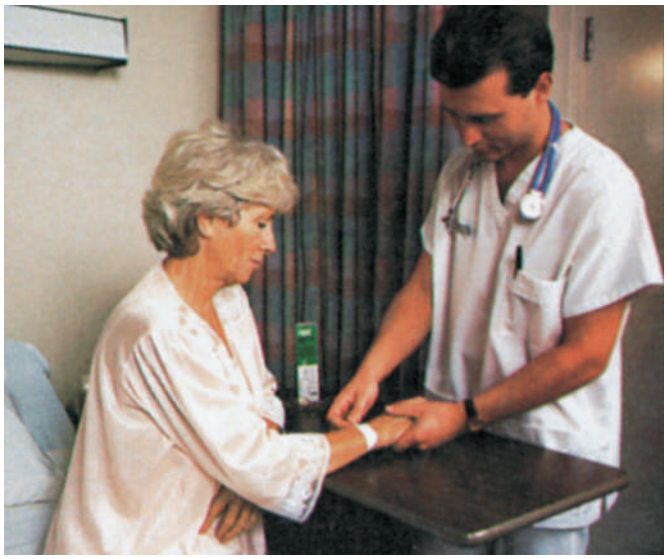

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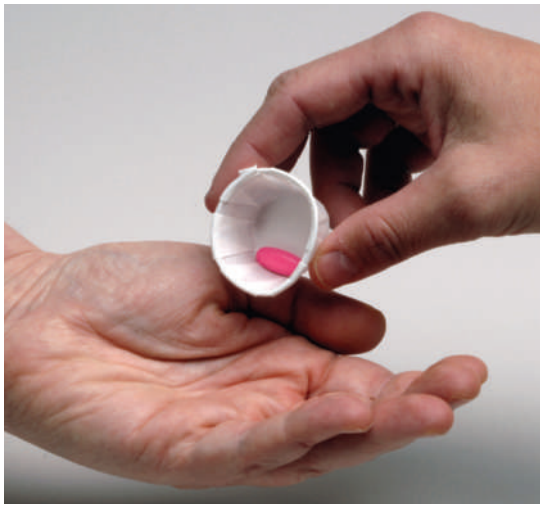
FIGURE 8-4 Check identification to be sure it is the right patient. Also ask the patient for name and date of birth and verify with the Medication Record. Always check for allergies.

Delmar/Cengage Learning



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(A) (B)

FIGURE 8-5 Do not touch medicine. (A) Open the unit-dose packet and drop the tablet in a cup. (B) Place the cup containing the medicine in the patient's hand.

16. Discard used medicine cup and wrappers in wastebasket.
17. Record the medication, dosage, time, and your signature or initials in the correct place on patient's record according to rules of the facility.
18. Document on patient's record and report if a medication is withheld or refused and the reason. Record and *report* any unusual circumstances associated with administration or any adverse side effects.

Special Considerations for Oral Administration

1. If patient is NPO, check with the person in charge regarding appropriate procedure, based on reason for NPO. If patient is fasting for laboratory X-ray tests, medication can usually be given at a later time with possible modification of time schedule. If patient is NPO for surgery, nausea, or dysphagia, it may be necessary to consult the doctor regarding a change of route. Do not omit the medications completely without specific instructions to that effect. Abrupt withdrawal of some medications, for example, phenytoin (Dilantin) or diazepam (Valium), may lead to seizures.
2. *Always check the patient's record carefully for allergies* and be aware of the components of combination products. Patients with a history of allergy should be watched carefully for possible drug reactions when any new medication is administered.
3. Give the most important medicine first, e.g., cardiac medicine before vitamin.
4. Elevate the patient's head, if not contraindicated by the patient's condition, to aid in swallowing.
5. Stay with the patient until the medication is swallowed. *Do not* leave the medication at the bedside or in the patient's possession unless ordered by physician.
6. Administer oral medications with water, unless ordered otherwise. *Do not* give medicine with fruit juice, milk, or any other liquid unless indicated by specific directions. The absorption of many medicines (e.g., antibiotics) is inhibited by interaction with acid or alkaline products.
7. Medications whose action depends on contact with the mucous membranes of the mouth or throat (e.g., topical anesthetics or fungicides) *should not* be administered with any fluid or food.
8. *Do not* open or crush timed-release capsules or enteric-coated tablets.
9. If tablets must be divided, *do not* break by hand. If available, a pill-cutter may be used. In home care setting, cut with a knife on score marks only.
10. When removing tablets or capsules from a stock bottle, pour into lid and from there into medicine cup. *Do not* touch tablets or capsules.
11. *Do not* administer any medication that is discolored, has precipitated, is contaminated, or is outdated.
12. If a patient is NPO, refuses the medication, or vomits within 20–30 minutes of taking the medication, always report this to the person in charge. A written order from the physician is required to change either the medication or the route of administration. Document on the patient's record the time of emesis and appearance of the emesis, for example, medication remained intact.

13. If the patient refuses a medication, determine the reason. Report the refusal and reason to the person in charge and record all information on patient's record.
14. Tablets (unless enteric coated) may be crushed with mortar and pestle or pill-crusher. Capsules (except timed-release capsules) may be opened and the contents mixed with applesauce, pudding or ice cream to facilitate administration for patients with difficulty swallowing (e.g., children and the elderly). Check diet to be sure these foods are allowed. Be sure that any equipment used to crush medication is wiped clean.

Note In some areas a physician's order is required for pill crushing. If available, ask for the medication to be ordered in liquid or powdered form.

Preparation of Liquid Medications

Follow the "Guidelines for Administration of Oral Medications," at the beginning of this section. Preparation of *liquid medications* requires these additional steps:

1. Shake bottle if indicated. Remove cap and place cap upside down on table.
2. Hold medicine bottle with label side upward to prevent smearing of label while pouring (Figure 8-6).
3. In other hand, hold medicine cup at eye level and place thumbnail on level to which medication will be poured (Figure 8-6).

Delmar/Cengage Learning

FIGURE 8-6 Hold the medicine bottle with label side up and medicine cup at eye level, with thumbnail marking measurement.

4. While holding the medicine cup straight at eye level, pour the prescribed amount of medication.
5. Replace cap on bottle.
6. Compare the information on the medication sheet against the label on the stock bottle and the quantity of drug in the cup.
7. Replace medication bottle in cupboard or medicine cart.
8. Recheck the Six Rights of Medication Administration.
9. Proceed with the "Guidelines for Administration of Oral Medications."

When administering liquid medication to someone who is unable to drink from a cup (e.g., infants and persons with wired jaws), a syringe may be used. Follow the "Guidelines for Administration of Oral Medications." Administration of *liquid medications orally via syringe* requires these additional steps:

1. Pour prescribed medication into medicine cup.
2. Withdraw prescribed amount with syringe.
3. Check medication and order using the six Rights of Medication Administration.
4. Identify the patient, verify name and date of birth (DOB), and elevate the patient's head.
5. Be sure the patient is alert and able to swallow.
6. Place the syringe tip in the pocket between the cheek and the gums. (When administering large amounts of liquid via syringe, it helps to fit a 2-inch length of latex tubing on the syringe tip to facilitate instillation of the medication into the cheek pocket.)
7. Instill the medication slowly to lessen chances of aspiration.
8. Be sure all medication is swallowed before leaving the patient.
9. Proceed with "Guidelines for the Administration of Oral Medications."
10. Remember the "sixth right" and document appropriately.

StudyWARE™ CONNECTION

See It In Action! Go to the StudyWARE™ CD-ROM to view a video on *oral medications.*

Administration of liquid oral medications is the preferred form for children less than 5 years old. In addition, flavored medications are often preferred and better tolerated by young children.

ADMINISTRATION OF MEDICATIONS BY NASOGASTRIC TUBE

A nasogastric tube is not inserted solely for the purpose of administering medication. However, medications are sometimes ordered by this route when a nasogastric tube is in place for tube feeding or for suction. When medications are ordered by nasogastric tube, follow the "Guidelines for Administration of Oral Medications" and "Preparation of Liquid Medications."

Nasogastric tube administration of medication requires these additional steps:

1. Check the medication order using the six Rights of Medication Administration.
2. Wash hands (Figure 8-1). Wear gloves when handling tubes.
3. Prepare the medication as ordered and take to the patient's room. Be sure the medication is at room temperature.
4. Check identification bracelet, ask the patient his or her name and verify, and explain the procedure. Elevate head of bed, if not contraindicated.
5. Hold the end of the tube up and remove the clamp, plug, or adapter.
6. Make sure that the tube is properly placed in the stomach by using at least two tests (Figure 8-7).
   a. Aspirate with bulb or piston syringe for stomach contents and check the pH of the aspirated fluids. The pH of gastric juice is acid (0.9–1.5). If the aspirate does not meet these parameters or if there is any question, do *not* instill any liquids. Instead, report to the person in charge. If the criteria are met, flush the tube with normal saline solution or with water.
   b. Place a stethoscope over the patient's stomach, attach the syringe to the tube, and inject about 30 mL of air. If you hear a swooshing or rumbling sound, air has entered the stomach, verifying correct placement.

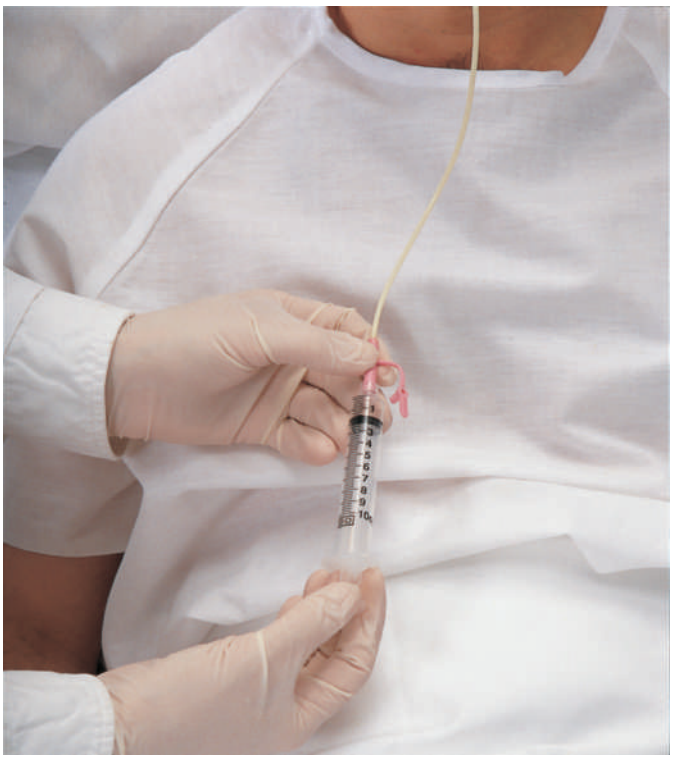

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FIGURE 8-7 Test for correct placement of nasogastric tube. Aspirate with syringe and check the pH of aspirated fluids.

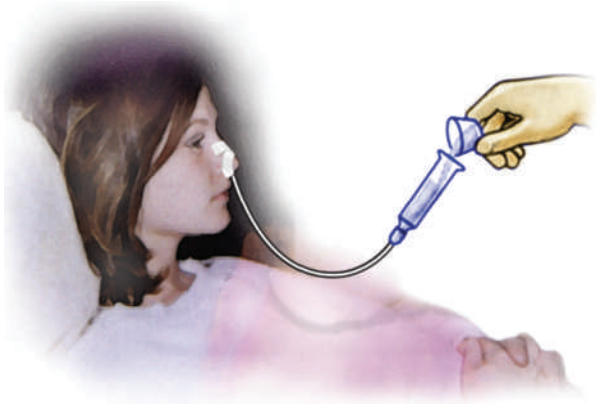

FIGURE 8-8 Pinch tube shut before filling syringe. Let fluid flow in by gravity. Hold syringe at level of patient's shoulder. Flush tube with water.

7. Clamp the tube with your fingers by bending it over upon itself or by pinching it. While tube is closed, remove plunger or bulb from syringe, leaving syringe attached firmly to tubing (Figure 8-8).
8. Pour medication into syringe. Release or unclamp the tubing and let medication flow through by gravity. Never force fluids down a nasogastric tube (Figure 8-8). Watch the patient during the procedure and stop immediately at any sign of discomfort, coughing, or shortness of breath by pinching the tube. Holding the syringe too high causes fluid to run in too quickly, possibly causing nausea and vomiting. Syringe should be at level of patient's shoulder.
9. Before the syringe empties completely, flush the tube by adding 60–100 mL of water, to the syringe or amount ordered. If the patient's input and output are being monitored, be sure to add this amount to the patient's record.
10. After the water has run in, pinch the tube, remove the syringe, and clamp or plug the tube. If the patient is on suction, be sure to leave suction turned *off* for at least 30 min until medication is absorbed, then restart suction as ordered.
11. Position patient on right side and/or elevate head of bed to encourage the stomach to empty. Make the patient comfortable.
12. Proceed with "Guidelines for the Administration of Oral Medications" for documentation.

ADMINISTRATION OF MEDICATIONS BY GASTRIC TUBE

Gastric tube administration of medications is a simple matter. If a patient has a gastric tube in place in the abdomen, medications can be administered per order in this way. Directions for "Administration of Medications by Nasogastric Tube" can be followed, only omitting number 6. No test for placement of tube is necessary. The rest of the directions regarding flushing the tube afterward and positioning the patient, and so on, should be followed carefully. Remember to document appropriately.

ADMINISTRATION OF MEDICATIONS RECTALLY

Medications are sometimes ordered to be administered by rectal route. The **rectal medication** may be in suppository form or in liquid form to be administered as a retention enema. This treatment is more effective with the patient's cooperation. Tact and consideration are required for successful administration of rectal medications. Remember to respect the patient's dignity and privacy by closing the door and curtains completely. Do not expose the patient unnecessarily.

The retention enema is administered in the same way as a cleansing enema. However, the retention enema must be retained approximately 30 min or more for absorption of the medication. Therefore, the patient is instructed to lie quietly on either side to aid in retention. If the patient is uncooperative, unconscious, or has poor sphincter control, the buttocks can be taped together with 2-inch paper adhesive for 30 min. Do not use this method unless absolutely necessary. Remember to treat the patient with dignity. Always explain everything you are doing and why. Even if patients are unconscious or unable to speak, they may be able to hear and cooperate in some way if they understand.

Administration of Rectal Suppository

1. Wash hands.
2. Check the medication order using the Six Rights of Medication Administration.
3. Identify medication (purpose, side effects, contraindications, cautions, and normal dose range). Research information if necessary.
4. Assemble supplies: disposable glove and water-soluble lubricant.
5. Select the medication as ordered, checking medication name and dosage again. Some suppositories are stored in a refrigerator, and some may be stored at room temperature, according to manufacturer's instructions.
6. Check patient's identification bracelet, ask patient for name and DOB and explain the procedure. Answer any questions.
7. Close door and curtain completely.
8. Lower the head of the bed if necessary and position the patient on left side with upper knee bent. Keep patient covered, exposing only the rectal area (Figure 8-9).
9. Put on disposable gloves.
10. Remove suppository from wrapper and lubricate the tapered end with water-soluble lubricant.
11. With nondominant hand, separate the patient's buttocks gently so you can see the anus.
12. Ask patient to take a deep breath. Insert the lubricated suppository gently into the rectum and push gently with gloved index finger until the suppository has passed the internal sphincter (Figure 8-10). With infants, use gloved *little* finger.

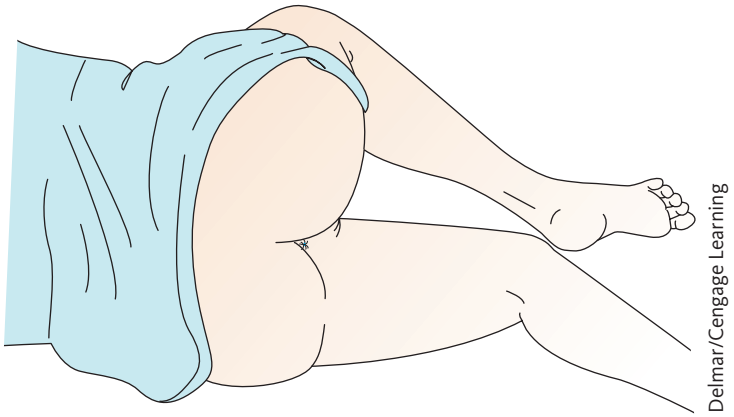

FIGURE 8-9 Drape and position patient on side with upper knee bent.

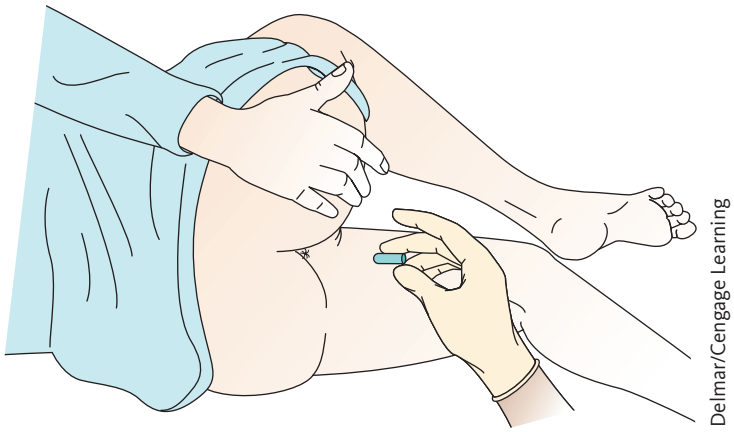

FIGURE 8-10 Lubricate the tip of suppository and insert it with covered index finger. Push the suppository past the sphincter.

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See It In Action! Go to the StudyWARE™ CD-ROM to view a video on *administering rectal medications.*

13. Urge the patient to retain the suppository for at least 20 min. If patient is unable to cooperate, hold the buttocks together as required.
14. Remove and dispose of gloves, turning them inside out as you remove them.
15. Be sure the patient is comfortable, with covers and bed adjusted appropriately.
16. Wash hands.
17. Record the medication in the appropriate place.

CHAPTER REVIEW QUIZ

1. Name six disadvantages of oral administration compared with administration by injection.

_____

_____

_____

_____

_____

_____

Match the column on left with the appropriate action on the right. Actions may be used more than once.

2. _____	To facilitate swallowing	**a.**	Watch closely for drug reactions
3. _____	If NPO for laboratory tests	**b.**	Crush tablet, mix with applesauce
4. _____	Patient vomits 15 min after	**c.**	Administer first
5. _____	Most medications	**d.**	Cannot be opened
6. _____	Patient is allergic to penicillin	**e.**	Elevate patient's head
7. _____	Most important medicine	**f.**	Notify person in charge
8. _____	Tablet cannot be swallowed	**g.**	Modify schedule, give medicine later
9. _____	Timed-release capsules	**h.**	Administer with water
10. _____	Dilantin ordered PO, patient NPO for surgery	**i.**	Leave medication at bedside

Complete the following statements by filling in the blanks.

When pouring liquid medicine:

11. The bottle should be held _____.
12. The medicine cup should be held _____.
13. The bottle cap should be placed _____.
14. If medication is in suspension, the bottle should first be _____.

When administering medication by nasogastric tube:

15. Check tube placement first with two tests:

_____

_____

Check the appropriate answer.

16. _____ **a.** Medication should be pushed through the nasogastric tube by pressure on barrel of syringe.

_____ **b.** Medication should flow through the nasogastric tube by gravity.

17. _____ **a.** Medication should be cold.

_____ **b.** Medication should be at room temperature.

18. _____ **a.** Patient's head should be elevated.

_____ **b.** Patient should be placed in Trendelenburg position.

19. Name four steps in administration of a rectal suppository that are different from PO administration.

_____

_____

_____

_____

20. Medication documentation should include:

_____

_____

_____

_____

Checklist for Administration of Oral Medications

Activity	Rating S	Rating U
1. Washed hands	_____	_____
2. Checked medication sheet for date, dosage, time, route, and allergies	_____	_____
3. Identified medication: purpose, side effects, contraindications, cautions, interaction, and normal dosage range	_____	_____
4. Selected appropriate medicine cup	_____	_____
5. Selected correct medication and checked label against medication sheet for six Rights of Medication Administration	_____	_____
6. Calculated correct dosage on paper if necessary and verified calculations with instructor	_____	_____
7. Placed medication as ordered in cup without opening packet or touching medication; prepared liquid medication by shaking if necessary, pouring away from label and measuring at eye level	_____	_____
8. Identified patient by checking bracelet and asking patient for name and DOB. To prevent aspiration, make sure head of bed is elevated unless otherwise ordered	_____	_____
9. Explained procedure to patient and answered any questions about medication	_____	_____
10. Checked patient's vital signs if necessary for specific medicine	_____	_____
11. Opened unit-dose packages and offered medication in container to patient	_____	_____
12. Provided drinking water and assisted patient as necessary	_____	_____
13. Made patient comfortable and left unit in order	_____	_____
14. Recorded medication, dosage, time, and signature or initials on patient's record (the sixth right)	_____	_____

Note: S, satisfactory; U, unsatisfactory.

Checklist for Administration of Rectal Suppository

Activity	Rating S	Rating U
1. Washed hands	_____	_____
2. Checked the medication order for date, dosage, time, route, and allergies	_____	_____
3. Identified medication: purpose, side effects, contraindications, cautions, and normal dosage range	_____	_____
4. Assembled supplies: gloves and lubricant	_____	_____
5. Selected correct medication and checked label with medication order for six Rights of Medication Administration	_____	_____
6. Identified patient by checking bracelet and asking patient for name and DOB	_____	_____
7. Explained procedure to patient and answered any questions about medication	_____	_____
8. Closed door and curtain	_____	_____
9. Positioned patient on left side with upper knee bent and only rectal area exposed	_____	_____
10. Put on disposable gloves	_____	_____
11. Removed wrapping from suppository and lubricated tapered end	_____	_____
12. With nondominant hand, separated buttocks gently	_____	_____
13. Instructed patient to take a deep breath and inserted suppository gently, pushing it past the sphincter	_____	_____
14. Instructed patient about retaining the suppository	_____	_____
15. Removed gloves correctly and disposed of them appropriately	_____	_____
16. Made patient comfortable and left unit in order	_____	_____
17. Washed hands	_____	_____
18. Recorded medication, dosage, time, and signature or initials on patient's record	_____	_____

Note: S, satisfactory; U, unsatisfactory.

Go to your StudyWARE™ CD-ROM and have fun learning as you play games and answer case study-related questions to help reinforce key concepts you learned in this chapter.

Go to your Study Guide and complete the review questions for this chapter.

Chapter 9

Administration by the Parenteral Route

Objectives

Upon completion of this chapter, the learner should be able to

1. Name four parenteral routes with systemic effects
2. Explain administration via the sublingual and buccal routes, including instructions to the patient
3. Demonstrate application of nitroglycerin ointment and the transdermal patch
4. Identify three conditions treated with transcutaneous delivery systems
5. Compare and contrast advantages and disadvantages of inhalation therapy
6. Describe patient education for those receiving inhalation therapy with hand-held nebulizers
7. List cautions when administering IPPB therapy
8. Identify the three parts of the syringe and the three parts of the needle
9. Select appropriate-length and correct-gauge needles for various types of injections
10. List three types of syringes and a purpose for each
11. Demonstrate drawing up medications from a vial and an ampule
12. Describe and demonstrate an intradermal injection
13. Describe and demonstrate a subcutaneous injection
14. Describe five sites for intramuscular injection and demonstrate intramuscular injection
15. Give purpose and demonstration of Z-track injection
16. List four types of administration for local effects
17. Define the Key Terms and Concepts

Key Terms and Concepts

Inhalation therapy
Intradermal
Intramuscular
Local effects
Parenteral
Subcutaneous
Systemic effects
Topical
Transcutaneous

Parenteral routes include any route other than the gastrointestinal tract. The most common form of parenteral administration is injection. However, other routes must be considered as well: the skin, mucous membranes, eyes, ears, and respiratory tract.

Parenteral administration can be understood more easily if the *purpose* of administration or the effects desired are considered as two categories: systemic and local. **Systemic effects** are those affecting the body as a whole, the entire system. The goal of administering drugs for systemic effects is to distribute the medication through the circulatory system to the area requiring treatment. Parenteral routes with systemic effects include (1) sublingual or buccal, (2) transcutaneous (transdermal), (3) inhalations, and (4) injections.

Local effects are those limited to one particular part (location) of the body, with very little, if any, effect on the rest of the body. Medications in this category include:

1. Medications applied to the skin for skin conditions, sometimes called **topical** medications
2. Drugs applied to the mucous membranes to treat that specific tissue
3. Medications instilled in the eyes for eye conditions
4. Medications instilled in the ears for ear conditions

SUBLINGUAL AND BUCCAL ADMINISTRATION

With sublingual administration, the medication is placed under the tongue. The drug is absorbed directly into the circulation through the numerous blood vessels located in the mucosa of this area. With buccal administration, the medication is placed in the pouch between the cheek and the gum at the back of the mouth. The sublingual route is used more commonly than buccal. Medications absorbed in this way are unaffected by the stomach, intestines, or liver. Absorption via this route is quite rapid, and therefore this method is used frequently when quick response is required (e.g., with nitroglycerin to treat acute angina pectoris). The constricted coronary blood vessels are usually dilated within a few minutes, bringing quick relief from pain.

For the sublingual or buccal route, include the following instructions:

1. Hold the tablet in place with mouth closed until medication is absorbed.
2. Do not swallow the medication.
3. Do not drink or take food until medication is completely absorbed.

TRANSCUTANEOUS DRUG DELIVERY SYSTEM

Transcutaneous, or transdermal, systems deliver the medication to the body by absorption through the skin. Nitroglycerin ointment, for example, is applied to the skin in prescribed amounts every few hours for prevention of

angina pectoris. The absorption is slower, and therefore this method is not effective in the treatment of acute angina attacks. Other transcutaneous delivery systems utilize a patch impregnated with a particular medication, applied to the skin, and left in place for continuous absorption. Examples of transcutaneous drug delivery systems include nitroglycerin (Nitro-Dur), in which the patch is sometimes left in place for 12 h daily (e.g., on in the morning and removed at night) for treatment of chronic angina; scopolamine (Transderm-Scop), in which the patch is placed behind the ear and left in place up to 72 h, as necessary, to prevent motion sickness; and fentanyl (Duragesic), applied on the skin and changed every 72 h in the management of chronic pain in patients requiring opiate analgesia. (See Analgesics, Chapter 19.) Other medications delivered transdermally include Estrogen (Estraderm). Absorption by this method is slower, but the action is more prolonged than with other methods of administration.

Note To reduce the occurrence of headaches, sometimes the physician will order the nitroglycerin ointment or patch to be applied at bedtime and removed the next day at noon.

PATIENT EDUCATION

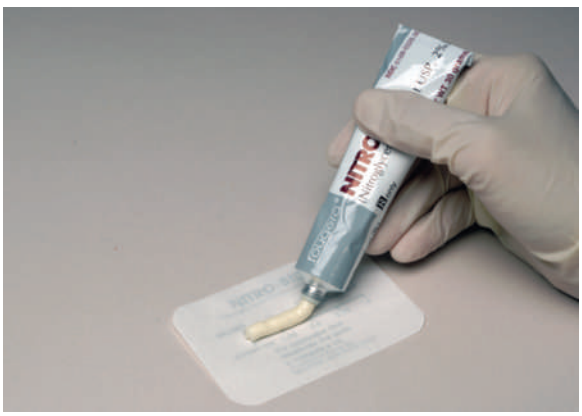
For those applying transcutaneous systems of administration, include the following instructions. With nitroglycerin ointment (Figure 9-1):

1. Squeeze the prescribed amount of ointment onto Appli-Ruler paper. When the ointment reaches the correct marking, give the tube a slight twist to cut off the ointment and recap the tube.
2. *Do not* touch the ointment! Absorption of ointment through the skin of the fingers can cause a severe headache. Wearing gloves eliminates this risk.
3. Carefully fold the Appli-Ruler paper lengthwise with the ointment inside.
4. Flatten the folded paper carefully to spread the ointment inside. *Do not* allow the ointment to reach the edges of the paper. Keep paper folded.
5. Rotate sites for application. Appropriate areas include chest, back, upper arms, and upper legs. *Do not* shave the area. Be sure the area is clean, dry, and free of irritation, rash, and abrasion.
6. After the area for application is exposed, open the paper carefully and apply paper to the skin, ointment side down. *Do not* touch the ointment. Fasten paper in place with paper tape. Write the date, time and initials on the tape.
7. Remove previous paper carefully, without touching the inside, and discard in trash container. Cleanse area and inspect skin for any sign of irritation. Report and record any skin changes.

8. Wash hands immediately.
9. Report and record any skin changes or complaints of headache.

With transdermal sealed drug delivery systems (Figure 9-2):

1. Remove previous patch carefully, without touching the inside, and discard in designated container. Cleanse area and inspect skin for irritation.
2. Select site for new administration, rotating areas. Be sure the skin is clean, dry, and free of irritation.
3. Open the packet carefully, pulling the two sides apart *without touching the inside.*
4. Apply the side containing the medication to the skin. Press the adhesive edges down firmly all around. If for any reason the adhesive edges do not stick, fasten in place with paper tape. This is usually unnecessary. Write date, time, and initials on patch.
5. Wash hands immediately.



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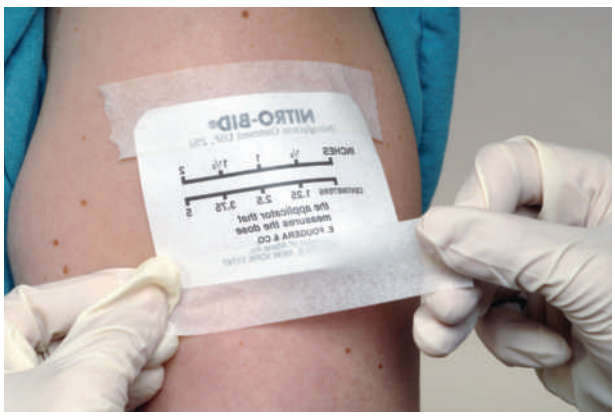
(A)



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(B)

FIGURE 9-1 Transdermal administration of nitroglycerin ointment. (A) Ointment is measured on Appli-Ruler paper. (B) Paper containing ointment is applied to the skin and fastened with paper tape. Write date and time on tape.

INHALATION THERAPY

Medications are frequently administered by inhalation method, especially to those with chronic pulmonary conditions, such as asthma. Patients may self-administer the medication with a metered dose inhaler (MDI) or small-volume nebulizer (SVN) (Figure 9-3), or the physician may prescribe intermittent positive pressure breathing (IPPB) therapy, to be administered by trained personnel.

Advantages of **inhalation therapy** include:

1. Rapid action of the drug, with local effects within the respiratory tract

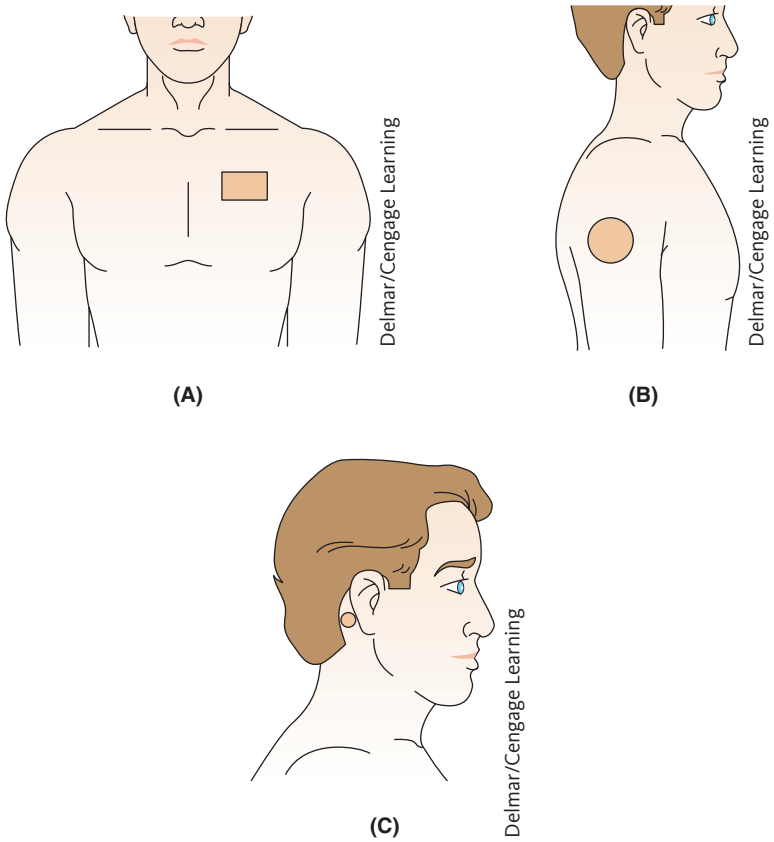


FIGURE 9-2 Transdermal drug delivery. Dermal patches vary in size and shape. (A,B) For prevention of angina pectoris. (C) For prevention of motion sickness. Other patches are also available for analgesia, estrogen replacement, and smoking cessation.

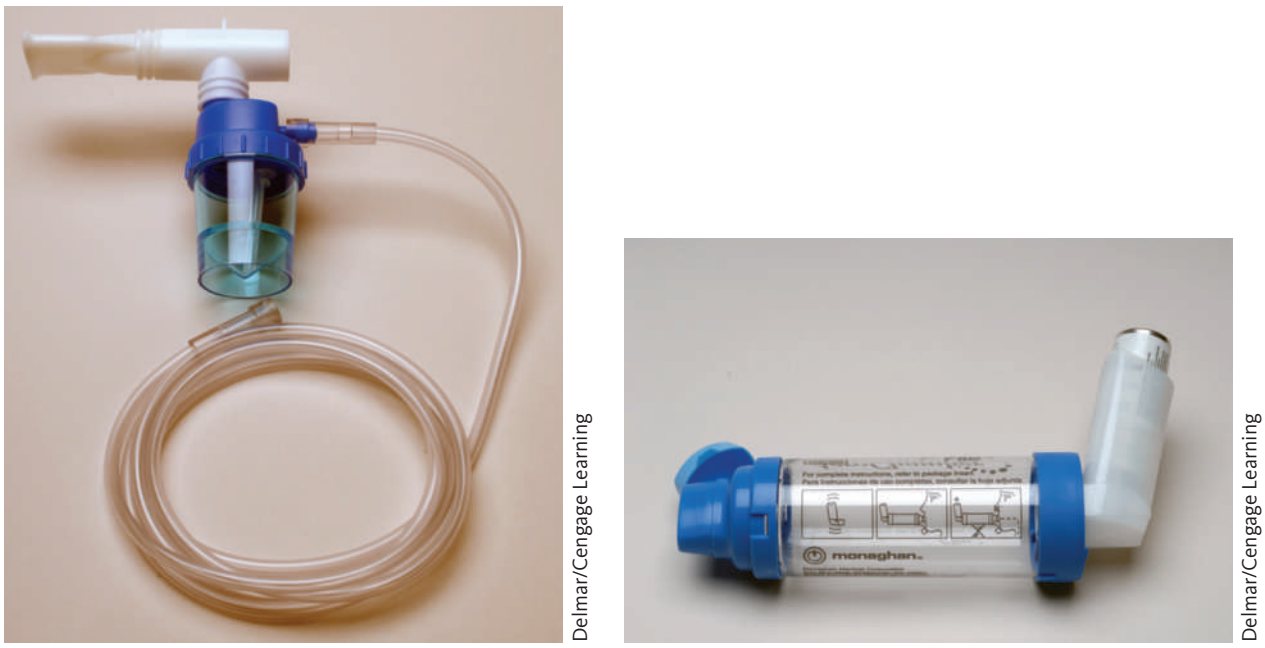


FIGURE 9-3 (A) Small-volume aerosol nebulizer. (B) Metered-dose inhaler (MDI) with spacer.

2. Potent drugs may be given in small amounts, minimizing the side effects
3. Convenience and comfort of the patient

Disadvantages of inhalation therapy include:

1. Requires cooperation of the patient in proper breathing techniques for effectiveness.
2. Adverse systemic side effects may result rapidly because of extensive absorption capacity of the lungs.
3. Improperly administered, or too frequently administered, inhalations can lead to irritation of the trachea or bronchi, or bronchospasm.
4. Asthmatic and COPD (chronic obstructive pulmonary disease) patients sometimes become dependent on a small-volume nebulizer or MDI.
5. If not cleaned properly, the small-volume nebulizer can be a source of infection.

Metered Dose Inhaler (MDI)

Metered dose inhalers (see Figure 9-3B) have become more popular in recent years. These devices deliver a measured (metered) dose via a propellant within a canister. MDIs are portable and easy to use, and recently more drugs have become available in the inhaler form. Proper administration by the patient is essential for drug effectiveness. Older adult patients may have difficulty coordinating the depression of the canister and inhaling at the same time. A *spacer* may be added to act as a reservoir for the aerosol, allowing the patient to first depress the canister and then inhale. Many spacers have an audible horn or whistle to signal the patient if inspiration is too rapid. MDIs may be used in pediatric patients with a mouthpiece or a mask. A full MDI canister provides approximately 200 puffs of medication.

See Chapter 26 for more information on respiratory medications and for variations of the MDI.

How to Use a Metered Dose Inhaler (MDI)

1. Sit upright or stand.
2. Assemble inhaler and shake for 10 seconds. (For consistent dosing, it is recommended to discharge a waste dose if it has been 24 hours since you last used your inhaler.)
3. Place the mouthpiece between the lips, forming a seal, or use a spacer prescribed by your physician.
4. Exhale slowly and completely.
5. Push down on the inhaler while breathing in slowly and deeply to full capacity.
6. Hold your breath for at least 5–10 seconds.
7. Exhale slowly through pursed lips.

If your prescription is for more than 1 puff, rest for 1 or 2 minutes before the second dose.

Note: If a bronchodilator and an inhaled steroid medication are to be given at the same time, administer the bronchodilator first and then the steroid.

Important: If using an inhaled steroid (such as Asmanex, Aerobid, Flovent, or QVAR), rinse your mouth out with mouth wash or water after using the inhaler to reduce risk of developing an oral fungal infection such as thrush.

Small-Volume Nebulizers (SVNs, MINI-NEBs, MED-NEBs)

Many drugs for the respiratory system may be delivered in aerosol form via a small-volume nebulizer (SVN) (see Figure 9-3A). The nebulizer is powered by a gas source, usually a small air compressor in the home care setting. For optimal drug deposition in the lung, proper breathing techniques must be used by the patient. The patient should be instructed to inhale slowly and deeply, perform a short breath hold, and exhale slowly. In addition to the side effects of the drugs themselves (see Chapter 26), patients should be cautioned that dizziness may occur if they hyperventilate (breathing too rapidly). Proper cleaning of equipment on a daily basis is essential to avoid infection.

PATIENT EDUCATION

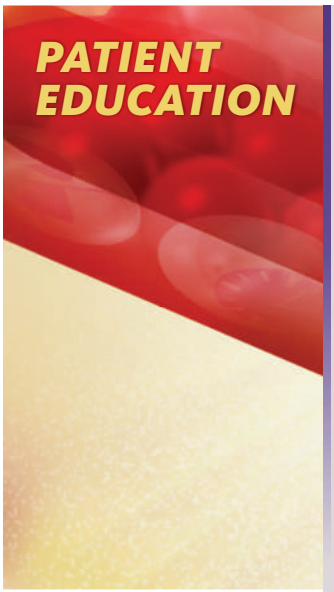
Proper Home Cleaning of Small-Volume Nebulizer

1. Disassemble the pieces of the nebulizer. Wash in mild soapy water and rinse thoroughly.
2. Place in a solution of one part vinegar to two parts water. Soak for 20–30 minutes.
3. Wash your hands with soap and water.
4. Remove the nebulizer parts from vinegar solution and rinse with warm tap water.
5. Allow to dry completely.
6. Reassemble pieces for next use.

Dry Powdered Inhalers (DPIs)

In recent years, dry-powder inhalers (DPIs) have become popular to use especially with children. DPIs are devices that deliver a drug in powdered form into the lung with no propellant or external power source. The patient must generate a sufficient inspiratory flow rate for the powder to aerosolize properly and therefore it is used for prophylactic treatment and not for acute breathing problems. The advantages of a DPI are that it is small and relatively easy to use and eliminates any timing technique problems with an MDI. It also can be used in very cold environments such as ski slopes where propellants may not work as effectively. The disadvantages are fewer drugs are available in powder

form and the patient must be able to generate a significant inspiratory effort for proper drug delivery.



With use of an inhaler or nebulizer, include the following instructions:

1. Name of the medication, dosage, and how often it is to be administered.
2. Desired effects and possible adverse side effects (e.g., palpitations, tremor, nervousness, dizziness, headache, nausea, dry mouth, irritated throat, hoarseness, or coughing).
3. Notify the physician if any adverse side effects occur or if the medication seems ineffective. The doctor may want to change the dosage or the medication.
4. Caution *not* to take any other medication, including over-the-counter drugs, without doctor's permission. Many drugs and alcohol can interact with these drugs, causing serious side effects.
5. Rising slowly from a reclining position will help prevent dizziness.
6. Rinsing the mouth after inhalation will counteract dry mouth or unpleasant taste.
7. Perform a step-by-step demonstration with the patient, answering all questions.
8. Rinsing equipment after use and storage of medication as indicated on the package.
9. Importance of not smoking.
10. Importance of handwashing before treatments.

See It In Action! Go to the StudyWARE™ CD-ROM to view videos on showing a patient how to use an inhaler and administering nebulized medications.

Intermittent Positive Pressure Breathing (IPPB)

Intermittent positive pressure breathing treatments may be ordered by the physician. IPPB combines administration of an aerosol with a mechanical breather to assist patients who are unable to take a deep breath on their own. Health care personnel, such as respiratory therapists or nurses, are specifically trained in the use of this equipment.

Cautions with IPPB therapy include:

1. Monitor vital signs closely, watching for a sudden drop in blood pressure, tachycardia, and decreased or shallow respirations.
2. Observe for nausea or distended abdomen.
3. Watch for tremors or dizziness.
4. Assure the patient that coughing after the treatment is to be expected. The goal of the treatment is to aid in coughing up the loosened secretions.
5. Record effectiveness of therapy and any side effects observed or reported by the patient.

INJECTIONS

To administer **injections,** you must be familiar with the equipment.

Syringes

The syringe has three parts (Figure 9-4):

1. ***Barrel.*** The outer, hollow cylinder that holds the medication. It contains the calibrations for measuring the quantity of medication.
2. ***Plunger.*** The inner, solid rod that fits snugly into the cylinder. Pulling back on the plunger allows solution to be drawn into the syringe. Pushing forward on the plunger ejects solution or air from the syringe.
3. ***Tip.*** The portion that holds the needle. Most tips are plain. Some larger syringes contain a metal attachment at the tip, called a Luer-Lok, which locks the needle in place.

Most syringes are plastic and disposable after one use. Some syringes for special procedures are glass and must be resterilized after use.

Needles

The needle has three parts:

1. ***Hub.*** The flared end that fits on the tip of the syringe.
2. ***Shaft.*** The long, hollow tube embedded in the hub. Needles have shafts with different lengths. Shorter needles (½, ⅜, and ⅝ inches) are used for **intradermal** (into the skin) or **subcutaneous** (into the tissue just below the skin) injections. Longer needles (1½ and 2 inches) are used for **intramuscular** (into the muscle) injections. The length of the needle depends on the type of injection and the size of the patient (i.e., shorter needles for children and thin adults and longer needles for larger adults). The gauge is the size of the lumen, or hole, through the needle, or the diameter of the shaft. The gauge is numbered in reverse order (i.e., the thinner needle with the smaller

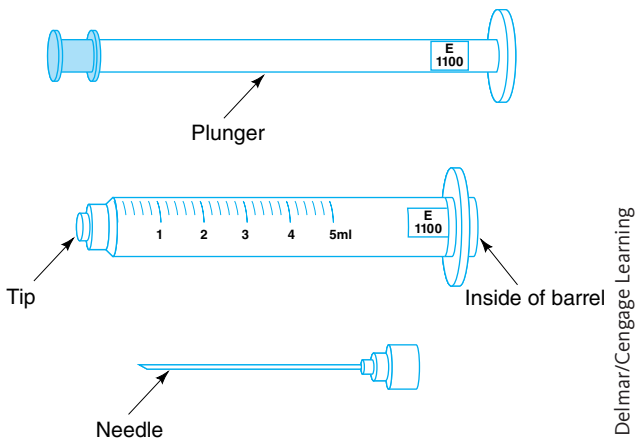


FIGURE 9-4 Parts of a syringe and needle that must remain sterile during preparation and administration of medication.

diameter has the larger number, e.g., 25 gauge for subcutaneous injections, and 19–21 gauge, a thicker needle with a larger opening, for IM or IV injections. The size of the gauge is determined by the site of the injection and the viscosity of the solution (e.g., blood and oil require a thicker-gauge needle, e.g., 15–18).

3. ***Tip.*** The tip is the pointed end with a beveled edge.

Three main types of syringes are used for injections. The type used is determined by the medication and the dosage. The three types are:

1. ***Standard syringe.*** Used most frequently for subcutaneous or intramuscular injections, calibrated or marked in cubic centimeters (cc) or milliliters (mL) and minims (m) (Figure 9-5). The most commonly used size is 3 mL or 2½ mL. Larger sizes of 5–50 mL are available for other purposes (e.g., irrigations, withdrawing fluids from the body, and intravenous injections).
2. ***Tuberculin (TB) syringe.*** Used for intradermal injections of very small amounts of a substance (e.g., testing for tuberculosis or for allergies). The TB syringe is also used for subcutaneous injections when a small amount of medication, less than 1 mL, is ordered (e.g., in pediatrics). The TB syringe is calibrated in tenths of a milliliter and in minims and holds only a total of 1 cc, or 1 mL (Figure 9-6).
3. ***Insulin syringe.*** Used only for injection of insulin and is calibrated in units. The size in common use today is U-100, in which 100 units of insulin is equal to 1 mL. The standard U-100 syringe has a dual scale: even numbers on one side and odd numbers on the other side. Look carefully at the calibrations on each side. Count each calibration (on one side only) as two units (Figure 9-7A).

   There are also smaller insulin syringes to more accurately measure small amounts of insulin, such as for children (Figure 9-7B for Lo-Dose Insulin Syringes 50 Units and 30 Units). Look carefully at the calibrations. In these Lo-Dose syringes, each calibration counts *only one* unit. It is extremely important that you study the calibrations carefully each time you prepare for an insulin injection, to prevent a medication error from negligent misinterpretation. **All insulin dosages should be double-checked by two caregivers before administration.**

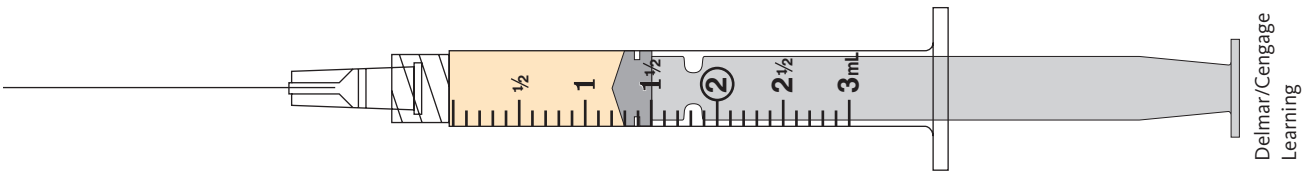


FIGURE 9-5 3-mL syringe.

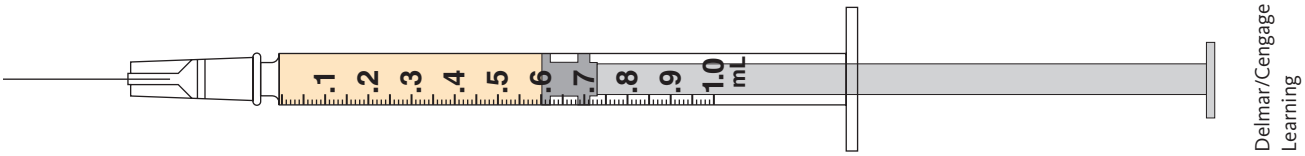
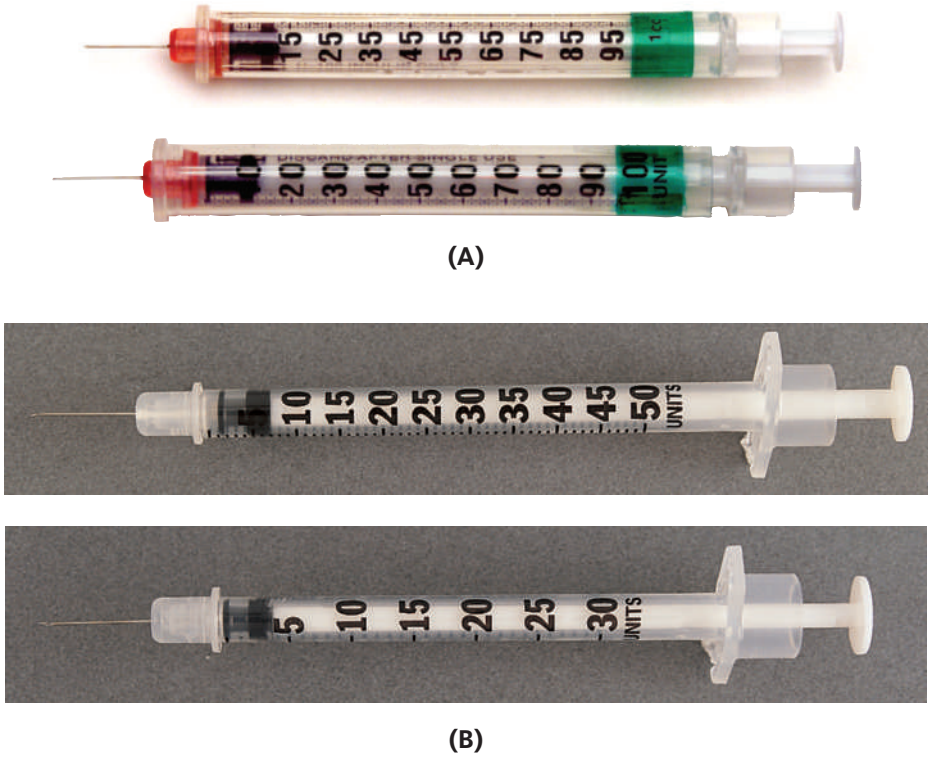


FIGURE 9-6 Tuberculin syringe with 1-mL capacity.

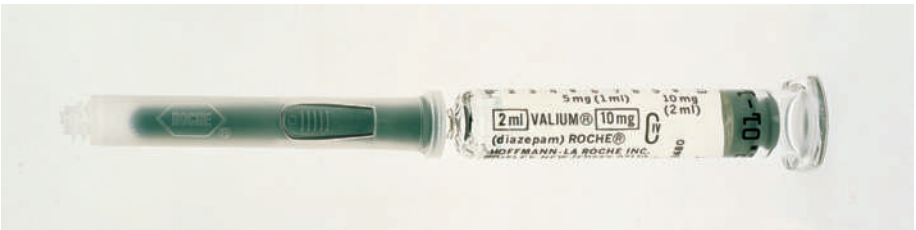


(A)

(B)

Source: Courtesy of Becton Dickinson and Company.

FIGURE 9-7 Insulin syringes. (A) Opposite sides of the same standard U-100 insulin syringe; note the numbers. (B) Lo-dose insulin syringes, 50 units and 30 units.



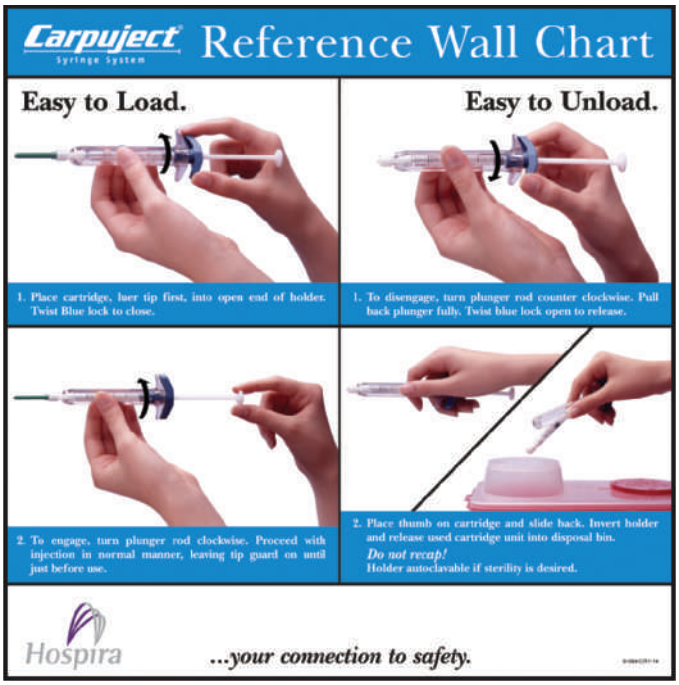
Source: Courtesy of Roche Laboratories, Inc.

FIGURE 9-8 Prefilled, single-dose syringe.

When instructing new diabetics in self-administration or administration by a family member, be sure that they can see and understand the calibrations and what they represent.

Prefilled syringes are available for certain medications (Figure 9-8). A premeasured amount of the drug is contained in the syringe. Check the dose ordered, compare with the dose in the syringe, and adjust if necessary. After injection, discard the syringe with needle attached and uncapped in the disposal bin.

Prefilled cartridges are also available, in which a premeasured amount of a medication is contained in a disposable cartridge. These prefilled units are made ready for injection by placing the cartridge in a holder. This unit can then be used to access a needleless IV system, or a needle can be attached to administer intramuscular or subcutaneous injections. After administration, the used cartridge is released from the holder and dropped into the disposal bin.



Source: Carpuject Syringe System reprinted with permission from Hospira, Inc., Lake Forest, IL.

FIGURE 9-9 Carpuject prefilled cartridge.

StudyWARE™ CONNECTION

See It In Action! Go to the StudyWARE™ CD-ROM to view a video on the *cartridge injection system*.

If a needle is attached, it is released *uncapped* along with the cartridge into the bin. An example of such a unit is the *Carpuject*, produced by Hospira (Figure 9-9). Other units are also available. Follow the manufacturer's direction regarding assembly of the cartridge unit.

Drawing Up Medications

1. Wash hands.
2. Assemble equipment (i.e., syringe, needle, packaged alcohol wipes, and medication ampule or vial).
3. Check the order using the Six Rights of Medication Administration.
4. If medication is contained in a vial, first remove the protective cap. Wipe the rubber diaphragm on top with an alcohol wipe. Check vial for date and discoloration of contents (Figure 9-10).
5. Seat the needle securely on the syringe by pressing firmly downward on the top of the needle cover. Pull the needle cover straight off. *Note:* Luer-Loks require a half-turn to lock the needle in place.
6. Draw air into the syringe equal to the amount of solution you will be withdrawing from the vial. Insert needle into center of rubber diaphragm and inject air into vial (Figure 9-11). Invert vial and withdraw prescribed dosage (Figure 9-12). Be sure syringe is filled to proper level with solution and no bubbles are present. Withdraw needle from vial. For intramuscular injections, a small bubble (0.2 mL) of air may now be added to the correct dose of medicine already in the syringe.

Delmar/Cengage Learning

FIGURE 9-10 Preparing to withdraw medication from a vial. Cleanse the top with alcohol wipe.

Delmar/Cengage Learning

FIGURE 9-11 Injection of air into vial. Vial is upright so air is not injected into fluid.

Delmar/Cengage Learning

FIGURE 9-12 Withdrawal of prescribed amount of medication. Invert the vial. Be sure needle point is in fluid, not in the air.

7. The needle must now be recapped *carefully* to maintain sterility and prevent needle sticks. After withdrawing solution from an ampule or vial, the needle cap is laid horizontally on a flat surface. The syringe is held in the dominant hand, and the sterile needle is inserted carefully into the cap. The syringe with needle attached is then used to scoop up the cap without touching it. *Do not contaminate the needle* by touching it to the outside of the cap. Remember, *only sterile needles are to be recapped* (Figure 9-13). An alternative method would be to remove the needle from the syringe carefully and discard the needle in the sharps container, replacing it with a sterile, capped needle.

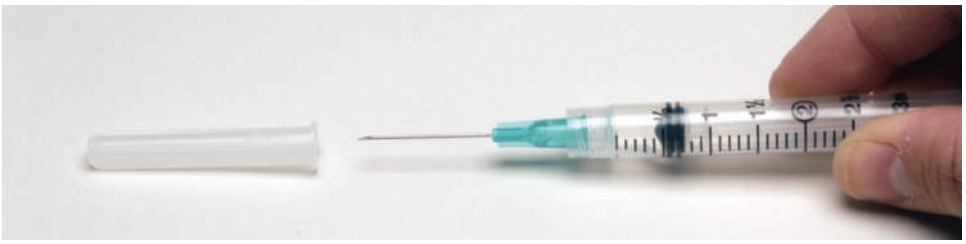


FIGURE 9-13 Recapping sterile needle. After withdrawing solution from an ampule or a vial, the needle cap is laid horizontally on a flat surface. The syringe is held in the dominant hand, and the sterile needle is inserted *carefully* into the cap. The syringe with needle attached is then used to scoop up the cap without touching it. Contaminated needles are never recapped but are discarded uncapped in sharps container.

8. If medication is contained in an ampule, hold tip with alcohol wipe to protect your fingers and break open along the scored marking at the neck. Tip vial and withdraw prescribed amount of medication. Recap needle carefully according to previous directions (Figure 9-13). Some facilities require the use of a filter needle to withdraw fluid from an ampule. Check the regulations in your area.

PATIENT EDUCATION

If two drugs are to be combined in a syringe, you must first check for compatibility of the drugs.

See It In Action! Go to the StudyWARE™ CD-ROM to view videos on *filling a syringe from a vial and drawing meds from two vials*.

Administration by Injection

Intradermal injections are usually administered into the skin on the inner surface of the lower arm. For allergy testing, the upper chest and upper back areas may also be used. A small amount (0.1–0.2 mL) is injected so close to the surface that a wheal, or bubble, is formed by the skin expanding (Figure 9-14).

Technique for intradermal injection is as follows:

1. Wash hands.
2. Assemble equipment (i.e., TB syringe, 26 or 27 gauge, $\frac{3}{8}$-inch needle, alcohol wipes, 2 × 2 gauze square and medication).
3. Check the order using the Six Rights of Medication Administration and draw up medication.
4. Identify patient and explain procedure. Arm should be supported on flat surface.
5. Put on gloves.
6. Cleanse skin with alcohol wipe on inner surface of the forearm (or other area if ordered by the physician). Allow the skin to dry thoroughly. Do *not* blow or fan the skin to assist drying as this can foster

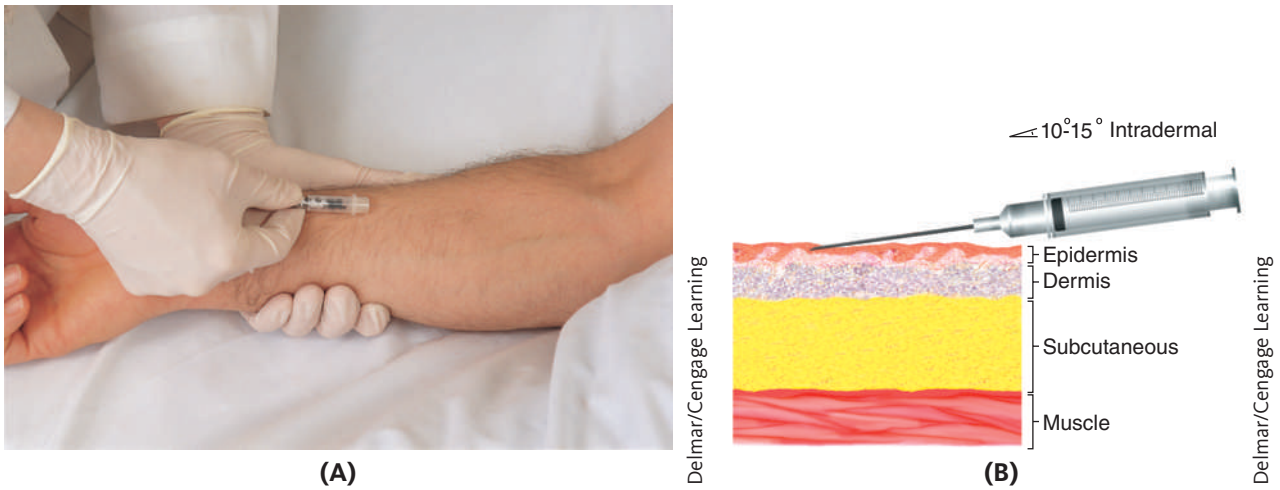


FIGURE 9-14 Intradermal injection. Hold the arm in nondominant hand and stretch the skin taut. ***The needle bevel is up***. The needle is almost flat against the arm. Inject slowly just under the skin so that a bubble forms.

infection. (If you inject before the skin is dry, you might introduce alcohol into the skin and interfere with test results.) Avoid areas with hair or blemishes.

7. Hold the patient's arm in your nondominant hand and *stretch the skin taut*.
8. Hold the syringe so that *the bevel* is *up* and the needle is almost flat against the patient's arm. Slowly insert the needle only far enough to cover the lumen or opening in the needle. The point of the needle should be visible through the skin.
9. Inject the medication *very slowly*. You should see a small, white bubble in the skin forming immediately. If no bubble forms, withdraw the needle slightly; it may be too deep. If solution leaks out as you inject, the needle is not deep enough.
10. After correct amount of medication is injected, withdraw needle and apply gentle pressure with 2 × 2 gauze. *Do not* massage the area or you may interfere with test results.
11. Discard syringe with needle *uncapped* into sharps container immediately without touching needle. Remove gloves. Wash hands.
12. Note drug name, dosage, time, date, and site of injection on patient's record.
13. Instruct the patient not to scrub, scratch, or rub the area. Provide written instructions regarding time to return for reading. Tell the patient to contact the physician immediately or report to an emergency facility if breathing difficulty, hives, or a rash appears.

CAUTION Do not start allergy testing unless emergency equipment is available nearby and personnel are trained in emergency care in case of anaphylactic response. Patients receiving allergy testing should remain in office or clinical facility for 30 minutes after injection to be observed for possible anaphylactic reaction.

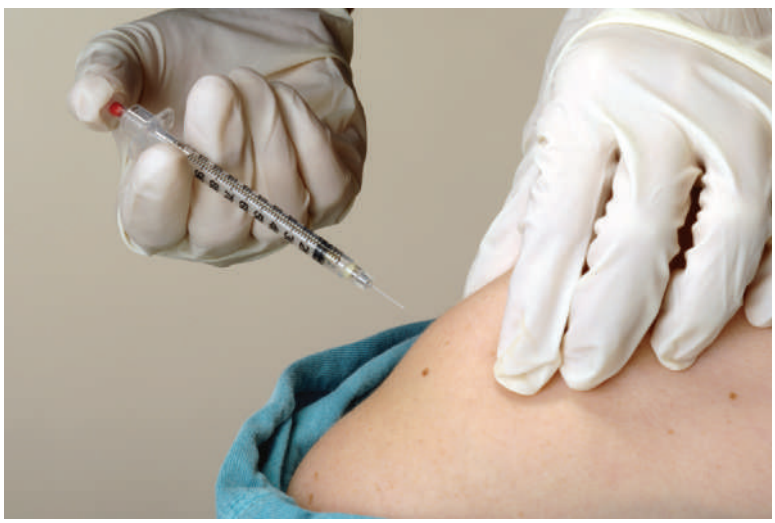
StudyWARE™ CONNECTION

See It In Action! Go to the StudyWARE™ CD-ROM to view a video on Intradermal Injection. *Note:* While this video emphasizes the five Rights of Medication Administration, keep in mind the recently added sixth right of "proper documentation."

Subcutaneous injections are administered into the fatty tissues on the upper outer arm, front of the thigh, abdomen, or upper back (Figure 9-15). A 2½–3-mL syringe is usually used with a 24–26-gauge, ⅜–⅝-inch needle. No more than 2 mL of medication may be administered subcutaneously.

Technique for subcutaneous injection is as follows:

1. Wash hands.
2. Assemble equipment (correct-size syringe and needle, alcohol wipes, 2 × 2 gauze square, and medication).
3. Check the order with the Six Rights of Medication Administration and draw up medication.
4. Identify patient, ask the patient's name, check armband, and explain procedure.
5. If patient is receiving frequent injections, be sure to rotate injection sites.
6. Put on gloves.
7. Cleanse skin with alcohol wipe.
8. Pinch the skin into a fat fold of at least 1 inch (Figure 9-15).
9. Insert the needle at a 45-degree angle. A 90-degree angle may be used with a ⅜ needle, if there is sufficient subcutaneous tissue, and also for insulin and heparin injections.
10. Pull back on the plunger (aspirate). If any blood appears in the syringe, withdraw the needle. Place pressure with dry 2 × 2 gauze over injection site until bleeding stops. Discard the syringe with needle *uncapped* into sharps container immediately. You will then have to draw up fresh solution with another sterile syringe and needle. (Do not aspirate with heparin injection.) It is also not necessary to aspirate with an insulin syringe as the needle is shorter. Therefore, there is not a danger of contacting larger blood vessels.



Delmar/Cengage Learning

FIGURE 9-15 Subcutaneous injection. The tissue is pinched, and the needle is held at a 45-degree angle.

11. Inject the medication *slowly*, pushing the plunger all the way. Too rapid injection may cause pain.
12. Place dry 2 × 2 gauze over the entry site, applying pressure with it, as you withdraw the needle rapidly. Do not push down on the needle while withdrawing it.
13. Massage the site gently with the dry 2 × 2 gauze to speed absorption. (*Do not* massage with heparin or insulin injection.) Be sure there is no bleeding.
14. Discard syringe with needle *uncapped* into sharps container immediately.
15. Remove gloves and discard.
16. Wash hands.
17. Note the medication, dosage, time, date, site of injection, and your signature on the patient's record.
18. Observe the patient for effects and record observations.

Subcutaneous injection of heparin includes:

1. Administer the heparin subcutaneously in the fat pad along the lower abdomen, at least two inches (approximately three fingers) below the umbilicus. Use ⅝- or ⅞-inch needle. Grasp the skin to form a fat pad, but do not pinch the tissues. Insert the needle with a dart-like motion at 90-degree angle. *Do not aspirate.* Release fingers holding the fat pad and inject *slowly*.
2. Rotate injection sites and document site of injection.
3. Do not rub the site with an alcohol sponge. Merely hold the sponge on the site gently for approximately 10 seconds.
4. Be sure there is no bleeding from the site.

StudyWARE™ CONNECTION

See It In Action! Go to the StudyWARE™ CD-ROM to view a video on *subcutaneous injections*.

Intramuscular injections are administered deep into large muscles (Figure 9-16). There are five recommended sites.

1. ***Dorsogluteal.*** Upper outer quadrant of the buttock (preferred site for adults)
2. ***Ventrogluteal.*** Above and to the outside of the buttock area, on the hip
3. ***Deltoid.*** Upper outer arm above the axilla
4. ***Vastus lateralis.*** Front of the thigh toward the outside of the leg
5. ***Rectus femoris.*** Front of the thigh toward the midline of the leg

The intramuscular route has two advantages over the subcutaneous route:

1. A larger amount of solution can be administered (up to 3 mL, or a maximum of 1 mL in children).
2. Absorption is more rapid because the muscle tissue is more vascular (i.e., contains many blood vessels).

The needle must be long enough to go through the subcutaneous tissue into the muscle. The length of the needle varies with the size of the patient.

With a child or very thin, emaciated adult, a 1-inch needle is usually adequate. For most adults, a 1½-inch needle is appropriate. However, for an obese person, a 2-inch needle might be required. The needle is inserted at a 90-degree angle with the skin spread taut (Figure 9-16).

Because there are more large blood vessels and nerves in this deeper tissue, the site for injection must be chosen more precisely. Using the illustrations as a guide, follow these steps in selecting the site:

1. ***Dorsogluteal site.*** Most commonly used for adults, but not for children under 3 years old (Figure 9-17). Position the patient flat on the stomach (prone) with the toes pointed inward or on the side with the upper leg flexed. Identify the site by drawing an imaginary line from the posterior superior iliac spine to the greater trochanter

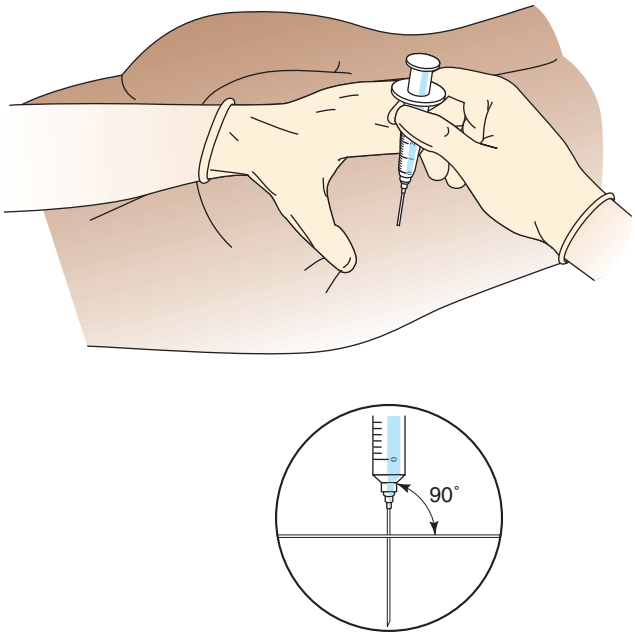


FIGURE 9-16 Intramuscular injection. The skin is held taut. The needle is at a 90-degree angle.

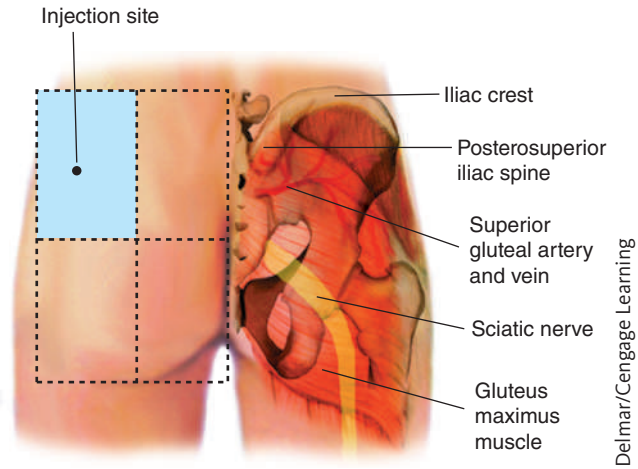


FIGURE 9-17 Dorsogluteal site for IM injection. Most common site for adults.

of the femur. These two bony prominences can be palpated with the thumb and forefinger. The injection is given above and to the outside of this line. Note that this site is high enough to avoid the sciatic nerve and the major blood vessels.

2. ***Ventrogluteal site.*** Can be used for all patients. Position the patient on the back or side (Figure 9-18). Identify the site by placing the palm of your hand on the patient's greater trochanter. Place the index finger on the anterior superior iliac spine and the middle finger on the iliac crest. The injection is made into the center of the V formed between the index and middle fingers.
3. ***Deltoid site.*** Seldom used because the muscle is smaller and is close to the radial nerve (Figure 9-19). The maximum solution that can be used

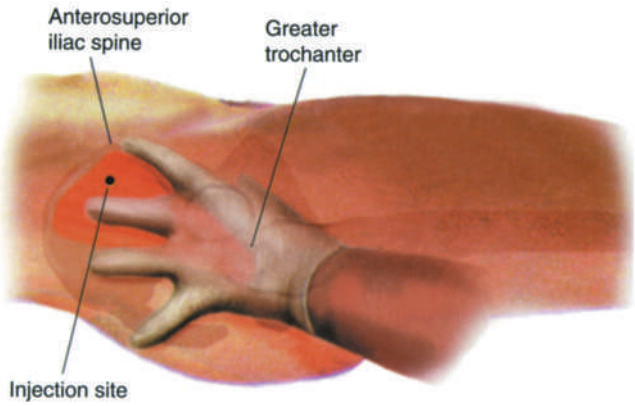


FIGURE 9-18 Ventrogluteal site for IM injection. Can be administered with patient on back or side.

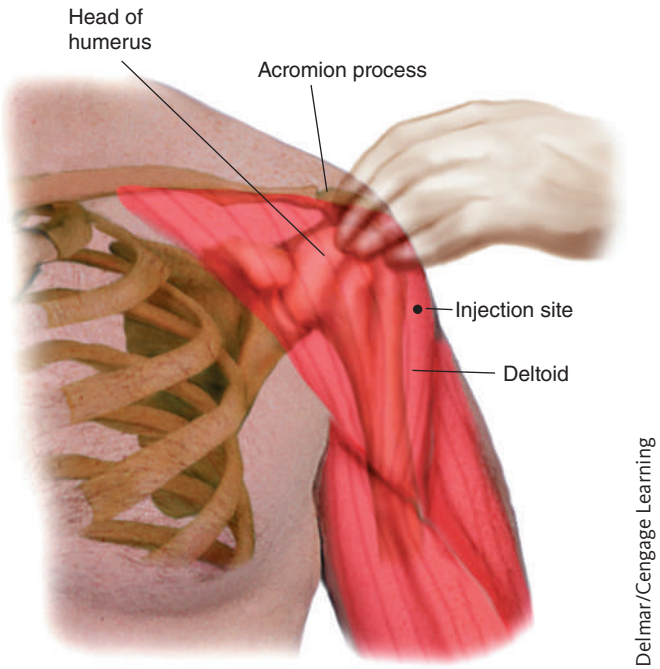


FIGURE 9-19 Deltoid site for IM injection. Maximum of 1-mL of medication and 1-inch needle is used. Injected above the level of the armpit.

is 1 mL; and a shorter needle, 1 inch, is used. Caution must be exercised to avoid the clavicle, humerus, acromium, brachial vein and artery, and radial nerve. Identify the site by drawing an imaginary line across the arm at the level of the armpit. The injection is made above this line and below the acromium on the outer aspect of the arm.

4. ***Vastus lateralis.*** Located on the anterior lateral thigh, the preferred site for infants, since these muscles are the most developed for children under the age of three years (Figure 9-20). In the older, nonambulatory, and emaciated adult, this muscle may be wasted and insufficient for injection. Identify the mid-portion on the side of the thigh by measuring one hand breadth above the knee and one hand breadth below the great trochanter. The area between is the site for injection.
5. ***Rectus femoris.*** Located just medial to the vastus lateralis, but does not cross the midline (Figure 9-21). It is the preferred site for self-injection because of its accessibility. It is located in the same way as the vastus lateralis. Caution: Do not get too close to the midline,

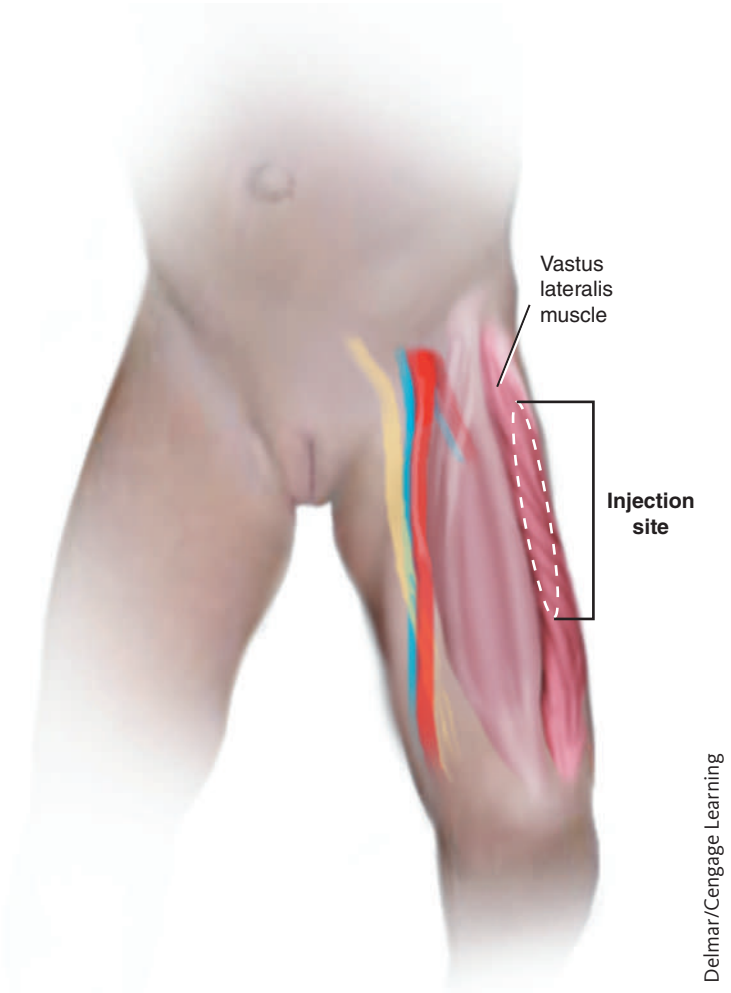


FIGURE 9-20 Vastus lateralis site for IM injection, preferred for infants. Injected on the anterior lateral thigh.

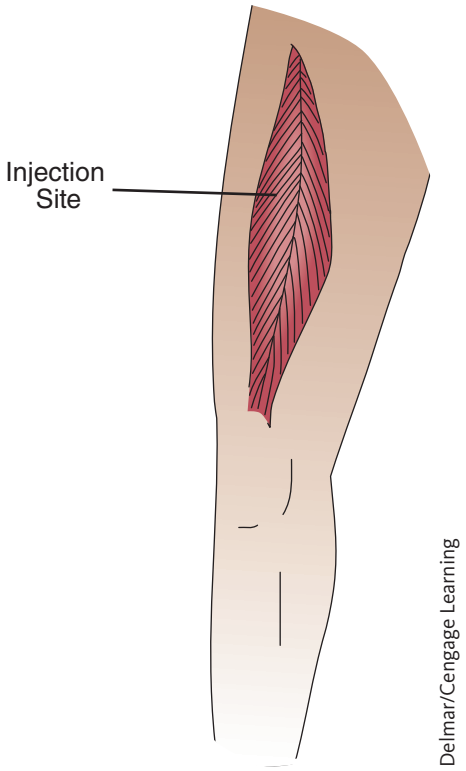


FIGURE 9-21 Rectus femoris site for IM injection. Preferred for self-injection. Injected medial to the vastus lateralis, but not too close to midline.

which is adjacent to the sciatic nerve and major blood vessels. If the muscle is not well developed, injections in this site may be painful.

Technique for intramuscular injection is as follows:

1. Wash hands.
2. Assemble equipment (i.e., correct-size syringe, needle, alcohol wipes, 2 × 2 gauze square, and medication).
3. Check the order with the Six Rights of Medication Administration and draw up the medication, or insert appropriate prefilled cartridge into Tubex or Carpuject holder.
4. After measuring correct amount of medication in syringe, draw 0.2 mL of air into the syringe to clear the needle. Recap carefully using the method illustrated in Figure 9-13.
5. Identify the patient, ask the patient's name and check armband, and explain procedure.
6. If patient is receiving frequent injections, be sure to rotate sites.
7. Put on gloves.
8. Position the patient and expose area to be used for injection.
9. Cleanse skin with alcohol wipe.
10. With your nondominant hand, stretch the skin taut at the injection site.
11. Insert the needle at a 90-degree angle with a quick, dart-like motion of your dominant hand.

12. Pull back on the plunger (aspirate), and follow previous guidelines if blood appears.
13. Inject the medication at a slow, even rate.
14. Withdraw the needle rapidly, holding dry 2 × 2 gauze over the site.
15. Apply pressure and massage area gently with alcohol wipe.
16. Discard syringe with needle *uncapped* into sharps container immediately.
17. Discard gloves and wash hands.
18. Note the medication, dosage, time, date, site of injection, and your signature on the patient's record.
19. Observe the patient for effects and record observations.

The *Z-track method* (Figure 9-22) is used for injections that are irritating to the tissue, such as iron dextran, hydroxyzine, or cefazolin. The dorsogluteal is the site for this type of intramuscular injection.

Technique for the Z-track method is as follows:

1. Draw up the medication and then add 0.3–0.5 mL of air to the syringe. Then replace the needle with a sterile one two to three inches long.
2. Stretch the skin as far as you can to the outer side and hold it there.
3. After cleansing the site, insert the needle with a dart-like motion, aspirate, and then inject the medication *slowly*. Wait ten seconds before withdrawing the needle.
4. Withdraw the needle and allow the skin to return to normal position. This seals off the needle track.
5. Press firmly on injection site with 2 × 2 gauze square. Do not massage the site, as this could spread the medication to the subcutaneous tissue, causing irritation.
6. Advise the patient that walking will aid absorption and to avoid tight garments, such as girdles, that cause pressure on the site.

StudyWARE™ CONNECTION

See It In Action! Go to the StudyWARE™ CD-ROM to view videos on *intramuscular injections and the Z-track method.*

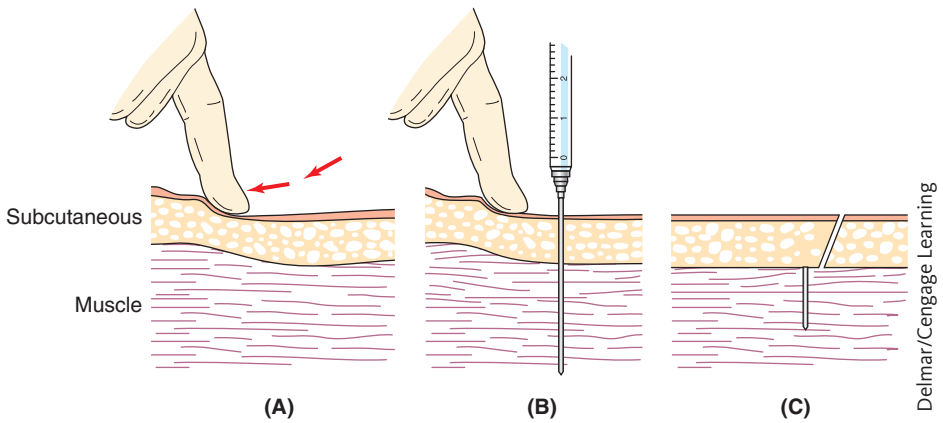


FIGURE 9-22 Z-track method of IM injection of iron preparations. (A) Skin and subcutaneous tissue pulled to one side and held there. (B) Needle is placed in muscle. (C) Z-track sealed when tissue released.

SKIN MEDICATIONS

Topical medications for the skin are prescribed for a great variety of conditions and are available in a variety of forms: ointments, lotions, creams, solutions, soaks, and baths. Administration of topical medications requires knowledge of the condition being treated and the purpose of the treatment, and strict adherence to directions as prescribed by the doctor or provided by the pharmacist, or to instructions on the medication container or in a package insert. *When in doubt regarding administration techniques, always ask* a qualified person for advice. Some specific principles for skin medications are outlined in Chapter 12. In addition, good judgment is also required.

Several suggestions for applying topical medications include:

1. For burns, use sterile gloves to apply, and cover with sterile dressings because of the danger of infection. Use gentle, light touch because of pain.
2. For skin conditions in which there is irritation or itching, use cotton-ball or snug-fitting gloves to apply. *Never* use gauze, which can cause additional irritation and discomfort.
3. Follow physician's order regarding covering or leaving open to the air.
4. Wash old medication off before applying new, unless specifically directed to do otherwise.

APPLICATION TO THE MUCOUS MEMBRANES

Medications applied to the mucous membranes also come in a variety of forms: suppositories, ointments, solutions, sprays, gargles, and so on. Always follow the specific directions that accompany the individual medication, unless directed to do otherwise by the physician. When in doubt, always ask questions.

EYE MEDICATIONS

Technique for instillation of eye medications is as follows:

1. Wash hands.
2. Assemble eye medication (ophthalmic solution or ointment).
3. Check the order with the Six Rights of Medication Administration. Pay particular attention to *percentage* on medication label and to *which eye* is to be treated (right eye, left eye, or both eyes).
4. Identify patient, ask the patient's name and explain procedure.
5. Put on gloves.
6. Position patient flat on back or upright with head back. Ask the patient to look up.
7. Carefully instill the ophthalmic solution, correct number of drops, or ointment into the lower conjunctival sac, using caution

to avoid contamination of the tip of the dropper or ointment tube (Figure 9-23). Do not let solution run from one eye to the other.

8. Tell the patient to close the eye gently so as not to squeeze out the solution.
9. Press gently on the inner canthus following administration of eyedrops (Figure 9-24). Systemic absorption is thus minimized with medications such as corticosteroids, miotics, and mydriatics.
10. Remove gloves.

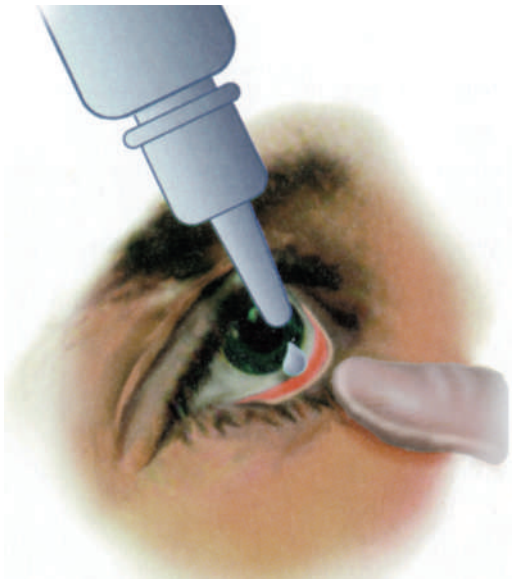


FIGURE 9-23 Instilling eye medication. Gently press the lower lid down and have the patient look upward. Ophthalmic solution is dropped inside lower eyelid.

FIGURE 9-24 Gentle pressure on the inner canthus following administration of ophthalmic medications. Systemic absorption is thus minimized with medications such as corticosteriods, miotics, and mydriatics.

See It In Action! Go to the StudyWARE™ CD-ROM to view a video on *administering eye and ear medications*.

11. Wash hands. Replace medication in appropriate place.
12. Record the medication, dosage, time, date, and which eye was treated, on the patient's record.
13. When more than one eye medication is ordered, wait at least five minutes before instilling the second medication.
14. If eyedrops and ointment are ordered for the same time, instill eyedrops first, wait five minutes, then apply ointment.

When in doubt about administration of any medication, always ask a qualified person for advice. Never guess! Remember that the patient who is receiving the medication could be you or your loved one. By thinking of yourself in the patient's place you will have the proper attitude to administer medications with competence, good judgment, and compassion.

Checklist for Intradermal Injection

Activity	Rating S	Rating U
1. Washed hands	_____	_____
2. Checked medication order for date, dosage, time, route, and allergies	_____	_____
3. Identified medication: purpose, side effects, cautions, and normal dosage range	_____	_____
4. Assembled supplies: TB syringe, 27-gauge, ⅜-inch needle, alcohol wipes, and medication	_____	_____
5. Checked medication vial against medication sheet using the Six Rights of Medication Administration	_____	_____
6. Withdrew correct dose from vial *after* cleansing top with alcohol and injecting equivalent amount of air into vial	_____	_____
7. Recapped needle using sterile technique (see Figure 9-13 for technique)	_____	_____
8. Identified patient by checking bracelet and asking the patient's name and DOB	_____	_____
9. Explained procedure to patient and answered any questions regarding procedure	_____	_____
10. Positioned patient with inner forearm exposed and supported on a flat surface	_____	_____
11. Put on gloves	_____	_____
12. Selected area without hair or blemish, cleansed skin with alcohol wipe, and allowed skin to dry	_____	_____
13. Held patient's arm with nondominant hand, stretching the skin taut	_____	_____
14. Expelled any air bubbles from syringe	_____	_____
15. Inserted needle point slowly, bevel side up, only enough to cover needle opening; point of needle visible through skin	_____	_____
16. Injected medication very slowly, with immediate formation of small bubble	_____	_____
17. Withdrew needle and applied gentle pressure to injection site with dry gauze (no massage)	_____	_____
18. Discarded syringe with needle *uncapped* into sharps container	_____	_____
19. Removed gloves	_____	_____
20. Washed hands	_____	_____
21. Recorded drug name, dosage, time, date, and site of injection on patient's record and signed or initialed entry	_____	_____
22. Observed patient for 30 min. for possible anaphylactic reaction; identified location of emergency equipment and medication if required	_____	_____
23. Provided written instructions regarding time to return for reading; instructed patient to avoid scrubbing, scratching, or rubbing the area and to report to emergency facility with dyspnea, hives, or rash	_____	_____

Note: S, satisfactory; U, unsatisfactory.

Checklist for Subcutaneous Injection

Activity	Rating S	Rating U
1. Washed hands	_____	_____
2. Checked medication order for date, dosage, time, route, and allergies	_____	_____
3. Identified medication: purpose, side effects, contraindications, interactions, and normal dosage range	_____	_____
4. Assembled supplies: 2½–3-mL, TB or insulin syringe; 24–26-gauge, ⅜–⅝ inch needle; alcohol wipes; and medication vial or ampule	_____	_____
5. Checked medication against medication sheet using the Six Rights of Medication Administration; also checked drug for date and discoloration	_____	_____
6. Calculated correct dosage on paper if necessary and checked calculations with instructor	_____	_____
7. If drug is contained in *vial*, withdrew correct amount after cleansing top with alcohol wipe and injecting equivalent amount of air into vial. If drug is contained in *ampule*, held tip with alcohol wipe while breaking it at neck. Withdrew correct amount of drug without bubbles in syringe	_____	_____
8. Recapped needle using proper sterile technique	_____	_____
9. Identified patient by checking identification bracelet and asking the patients' name and DOB	_____	_____
10. Explained procedure to patient and answered any questions	_____	_____
11. Selected appropriate site, using rotation if frequent injections	_____	_____
12. Put on gloves	_____	_____
13. Cleansed skin with alcohol wipe	_____	_____
14. Pinched skin into fold with nondominant hand	_____	_____
15. Expelled any air bubbles from syringe	_____	_____
16. Inserted needle at a 45-degree angle and released skin fold	_____	_____
17. While holding needle hub with nondominant hand, aspirated for blood (used new site if necessary)	_____	_____
18. Injected medication slowly	_____	_____
19. Placed alcohol wipe over entry site, and applied pressure as needle was withdrawn; massaged site gently (with heparin, pressure only, no massage)	_____	_____
20. Disposed of syringe and needle uncapped in sharps container	_____	_____
21. Removed and discarded gloves	_____	_____
22. Washed hands	_____	_____
23. Recorded drug name, dosage, time, date, site of injection, and signature on patient's record; also recorded effects after appropriate time	_____	_____

Note: S, satisfactory; U, unsatisfactory.

Checklist for Intramuscular Injection

Activity	Rating S	Rating U
1. Washed hands	_____	_____
2. Checked medication order for date, dosage, time, route, and allergies	_____	_____
3. Identified medication: purpose, side effects, cautions, and normal dosage range	_____	_____
4. Assembled supplies: 2½, 3-mL syringe; 1½–2 inch needle, usually 21 gauge; alcohol wipes; and medication	_____	_____
5. Checked medication against medication sheet using the Six Rights of Medication Administration; if PRN medication, checked time of last dose	_____	_____
6. If narcotic, signed and checked time of last dose on controlled substance sheet; calculated correct dosage on paper if necessary	_____	_____
7. If drug is contained in *vial*, withdrew correct amount after cleansing top with alcohol wipe and injecting equivalent amount of air into vial. If drug is contained in *ampule*, held tip with alcohol wipe while breaking it at neck. Withdrew correct amount of drug without bubbles in syringe. Used filtered needle to administer dose drawn from ampule.	_____	_____
8. *After* drug measured accurately in syringe, drew 0.2 mL air into syringe	_____	_____
9. Recapped needle using sterile technique (see Figure 9-13 for techniques)	_____	_____
10. Identified patient by checking bracelet and asking their name and DOB	_____	_____
11. Explained procedure to patient and answered any questions	_____	_____
12. Closed door to room and/or curtain around bed	_____	_____
13. Selected appropriate site, using rotation if frequent injections	_____	_____
14. Put on gloves	_____	_____
15. Positioned patient appropriately, exposing only the area for injection	_____	_____
16. Cleansed skin with alcohol wipe	_____	_____
17. With forefinger and thumb of nondominant hand, spread the skin *taut* at injection site	_____	_____
18. Inserted needle at a 90-degree angle with a quick, dart-like motion of dominant hand	_____	_____
19. Aspirated for blood (used new site if necessary)	_____	_____
20. Injected medication at a slow, even rate	_____	_____
21. Applied pressure with alcohol wipe over entry site as needle was withdrawn rapidly; massaged site gently with alcohol wipe unless medication irritating (with cefazolin, hydroxyzine, or iron dextran, pressure only, no massage)	_____	_____
22. Made sure there was no bleeding before covering patient and making patient comfortable	_____	_____
23. Disposed of syringe and needle *uncapped* in sharps container	_____	_____
24. Discarded gloves appropriately; washed hands	_____	_____
25. Recorded drug, name, dosage, time, date, site of injection, and signature on patient's record	_____	_____

Note: S, satisfactory; U, unsatisfactory.

Checklist for Instillation of Eye Medication

Activity	Rating S	Rating U
1. Washed hands	_____	_____
2. Checked the order with the Six Rights of Medication Administration; noted percent of strength of drug, which eye, and allergies	_____	_____
3. Identified medication: purpose, side effects, and cautions	_____	_____
4. Identified patient by checking bracelet and asking the patient's name and DOB	_____	_____
5. Explained procedure to patient and answered any questions regarding procedure	_____	_____
6. Positioned patient on back or upright with head back	_____	_____
7. Asked the patient to look up	_____	_____
8. Used aseptic technique to instill correct number of drops or ointment dosage into lower conjunctival sac	_____	_____
9. Gently closed the eyelid and applied pressure to the inner canthus (eye drops only)	_____	_____
10. Washed hands and replaced medication in appropriate place	_____	_____
11. Recorded medication, dosage, time, date, and which eye was treated, on patient's record	_____	_____

Note: S, satisfactory; U, unsatisfactory.

CHAPTER REVIEW QUIZ

Fill in the blanks.

1. Parenteral includes any routes other than the _____.
2. Systemic effects are those affecting _____.
3. The four parenteral routes with systemic effects include:

_____ _____

_____ _____

Label the routes according to their action. Use R for rapid and S for slow. Match each route with the appropriate definition:

	Action		Definition
4. _____	Sublingual	_____	**a.** Given with a needle
5. _____	Transcutaneous	_____	**b.** Nebulizer or IPPB
6. _____	Inhalation	_____	**c.** Under the tongue
7. _____	Injection	_____	**d.** Skin patch

8. What precautions should be observed when applying transcutaneous systems?

_____

9. DPI refers to _____.

Select the correct needle for the purpose. Needle size may be used for more than one purpose.

	Purpose	Needle
10. _____	Subcutaneous injection	**a.** 21 gauge, 1½ inch
11. _____	Intravenous injection	**b.** 25 gauge, ⅝ inch
12. _____	Allergy testing	**c.** 18 gauge
13. _____	Intramuscular injection	**d.** 27 gauge, ⅜ inch

14. What are the two purposes of the tuberculin syringe?

_____

_____

15. The insulin syringe is calibrated in _____, and 1 mL is equal to _____ in an insulin syringe.

16. On a standard insulin syringe, each calibration represents _____ unit/s.

On a Lo-Dose insulin syringe, each calibration represents _____ unit/s.

Match the injection with the proper technique:

	Injection	Technique
17. _____	Intramuscular	**a.** Needle 45-degree angle, skin pinched up
18. _____	Subcutaneous	**b.** Needle flat, bevel up, skin taut
19. _____	Intradermal	**c.** Needle 90-degree angle, skin taut

20. List the five sites for intramuscular injections and when each is used.

_____

_____

_____

_____

_____

21. Why is the Z-track method used? _____

Describe Z-track administration. _____

_____

_____

22. Define local effects. _____

_____

List four areas to administer medication for local effects.

_____ _____

_____ _____

Go to your StudyWARE™ CD-ROM and have fun learning as you play games and answer case study-related questions to help reinforce key concepts you learned in this chapter.

Go to your Study Guide and complete the review questions for this chapter.

Chapter 10

Poison Control

Objectives

Upon completion of this chapter, the learner should be able to

1. Identify four routes by which poisons may be taken into the body
2. List five conditions in which vomiting, after the ingestion of poisons, could be injurious to the patient
3. Describe the first step to take in the event of any poisoning and the procedure to follow
4. Explain the purpose of activated charcoal and when it is given
5. Name three clinical procedures required when caring for patients who have been poisoned
6. Describe appropriate therapy for poisoning by inhalation, external poison, and insect sting
7. Identify two groups of people at risk for poisoning
8. List 10 recommendations for patient education to help prevent poisoning
9. Define the Key Terms and Concepts

Key Terms and Concepts

Antidotes

Emetic

Ingestion

Poison

A **poison** is a substance taken into the body by ingestion, inhalation, injection, or absorption that interferes with normal physiological functions. In some cases, only a small amount of a substance can cause severe tissue damage directly (e.g., corrosives). In other cases, the substance can be beneficial in small amounts, but lethal in excessive amounts (e.g., overdose of medication).

In a case of suspected poisoning, the best policy is to contact a Poison Control Center directly, or through an emergency care facility. Instructions can then be given by phone for appropriate emergency treatment based on the type of poison and the patient's condition, age, and size.

POISONING BY INGESTION

The most common type of poisoning is by **ingestion**, or swallowing. Children between the ages of one and five are most at risk for poisoning. Before 2004 it was recommended that children who had ingested poisons be given the **emetic** ipecac syrup to induce vomiting. However, extensive research conducted through The American Association of Poison Control Centers, Toxic Exposure Surveillance System, identified several concerns regarding ipecac.

1. Outcomes failed to justify its effectiveness.
2. Adverse effects, such as persistent vomiting could interfere with other treatment.
3. There has been evidence of widespread abuse of ipecac by people with anorexia and bulimia.

Therefore, in early 2004, The American Academy of Pediatrics (AAP) issued a policy statement on poison treatment in the home. The AAP recommended against keeping ipecac in the home and further recommended that ipecac presently in the home be disposed of safely.

The first step to take in any poisoning is to contact your local Poison Control Center. This number can be obtained by calling the national toll-free Poison Control number: **1-800-222-1222**. Callers should be prepared to give details regarding the poison and the age, weight, and health status of the individual who took the poison. Mention allergies and asthma if present.

Under the following conditions vomiting could be injurious to the patient and should be avoided if possible:

1. Ingestion of corrosive substances such as mineral acids or caustic alkalis (e.g., carbolic acid, ammonia, drain cleaners, oven cleaners, dishwasher detergent, and lye). Check also for burns around or in the mouth. If the ingested substance burned tissue on the "way down," it is likely it will also burn and damage tissue on the "way back up" and therefore vomiting can cause additional tissue damage.
2. Ingestion of volatile petroleum products (e.g., gasoline, kerosene, lighter fluid, and benzene). Vomiting can cause aspiration and/or asphyxiation (suffocation).
3. Ingestion of convulsants (e.g., strychnine or iodine). Vomiting can precipitate seizures.
4. If patient is semiconscious, severely inebriated, in shock, convulsing, or has no gag reflex. Vomiting could cause choking, aspiration, and/or asphyxiation.
5. If patient is less than one year old.
6. In patients with cardiac or vascular disease, vomiting can increase blood pressure and precipitate a stroke, cardiac arrhythmias, or atrioventricular block.

If any of the above-mentioned conditions exist, the patient should be transported *immediately* to an emergency care facility. Trained personnel can remove the stomach contents by gastric lavage, if appropriate, and administer appropriate antidotes as indicated.

Antidotes, such as flumazenil or naloxone and/or CPR (cardiopulmonary resuscitation), may be required in poisoning with CNS depressants. The routine use of gastric lavage is no longer recommended by the American Academy of Clinical Toxicology and is *not* used in patients who have ingested corrosives, because of the danger of perforating the damaged tissue of the esophagus. If perforation exists, surgery is required. Observation is required in an acute care facility.

Sometimes a substance such as activated charcoal is administered by mouth to minimize systemic absorption of the ingested poison. If indicated, gastric lavage followed by or preceded and followed by activated charcoal may be more effective than activated charcoal alone. However, if activated charcoal is given it may interfere with antidotes given via the gastric route as well (e.g., n-acetylcysteine for Tylenol poisoning) but the clinical significance of this is unknown.

Personnel caring for poisoning victims should observe the following cautions:

- *Be sure to save emesis.* It may be necessary to send it to a laboratory to determine the type of poison. In addition, save any evidence of what may have caused the poisoning such as plant parts, mushroom, pills, etc. If there is doubt about the poison, the doctor may also order urine and blood tests for toxicology.
- Closely monitor the vital signs of patients who have taken poison of any kind.
- Observe closely for possible confusion, tremors, convulsions, visual disturbances, loss of consciousness, respiratory distress, or cardiac arrhythmias.

POISONING BY INHALATION

Poisoning by inhalation requires symptomatic treatment: fresh air, oxygen, and CPR if indicated. Incomplete combustion and fires can produce carbon monoxide. Carbon monoxide poisoning can quickly rob the tissues of vital oxygen and high percentage oxygen therapy or even oxygen under pressure (hyperbaric oxygen) in severe cases may be needed. Inhaling insect spray may require administration of an antidote.

EXTERNAL POISONING OF SKIN OR EYES

External poisons should be flushed from the skin for 20 minutes or eyes for 30 minutes with a continuous stream of water. The patient should then be transported to an emergency care facility for further treatment as required. Systemic absorption of poisons through the skin may require administration of an antidote.

POISONING BY STING AND SNAKEBITE

See It In Action! Go to the StudyWARE™ CD-ROM to view a video on *how to manage an obstructed airway*.

Poisoning by insect sting (e.g., bee, wasp, scorpion, or fire ant) should be treated by cleansing the area, immediately removing the stinger, and applying an icepack to the site of the sting. If the patient is allergic, watch closely for possible anaphylactic reaction. CPR and administration of epinephrine and corticosteroids may be required. Transport the patient to an emergency care facility immediately if indicated. Some allergic persons carry a kit with medication prescribed by their doctor (e.g., an epinephrine auto-injector for self-injection or injection by someone else).

After emergency care is completed, aftercare to lessen the pain, discomfort, and redness associated with stings can include application of topical corticosteroid ointment. (See Topical Corticosteroids in Table 12-1.)

Do not apply ice or a tourniquet to a snakebite. Venom is very irritating and may cause sloughing of the tissues. Keep the patient quiet in order to slow circulation, and transport the patient, lying down, to an emergency care facility for *antivenom injections*. If possible, take the snake along, in a closed container, for identification purposes. It may be nonpoisonous.

PATIENT EDUCATION

Patients with known allergies should be instructed on the following:

1. Be particularly careful when working outdoors and do not approach any insect nests or hives. Have lawn areas and shrubbery periodically inspected for insect nests and colonies.
2. Always wear shoes and light colored clothing when outside. If possible wear long sleeves and pant legs.
3. Remove stinger by scraping it off with the edge of something rigid such as a credit card. Pulling a stinger out with tweezers may actually cause more poison to be injected into the body as you squeeze the stinger.
4. If epinephrine or a self injected device is prescribed, the patient should be instructed on its use.

PEOPLE AT RISK

Poisonings are the leading cause of health emergencies for children in the nation and a major cause of death among young children because of their natural curiosity and active lifestyle. The danger is particularly great with flavored medications, such as aspirin or iron tablets. Great care must be taken to prevent poisoning of young children. The child between the ages of one and five years old is most at risk.

Keep all chemicals in a locked cupboard. Keep infrequently used drugs, for example, pain medications, in a lockable box such as a tackle box or file box. Be sure that medications taken daily by adults are always in childproof containers. Be particularly vigilant when visiting with older adult friends or relatives who may not have childproof containers for their pills.

The Food and Drug Administration (FDA) reports that iron pills are the leading cause of poisoning deaths in children under six. Although iron supplements have been sold in bottles with child-resistant caps, in the last decade more than 110,000 children were poisoned by eating adult iron pills and at least 33 have died. Children have an inability to metabolize iron at the same rate as an adult and therefore can build up toxicity rapidly. Therefore, in 1994 the FDA proposed requiring iron supplements to be sold in special "blister packs."

The health care practitioner can play a major role in reducing the number of accidental poisonings in children by stressing preventive measures to parents. One educational program teaches the child to stay away from dangerous products by labeling them with a "Mr. Yuk" sticker. Figure 10-1 is a warning label for children who cannot read. These stickers are available from many poison information centers throughout the United States.

Another group at risk for poisoning is older adults. Overdoses of medication can result in toxicity, with symptoms of confusion, dizziness, weakness, lethargy, ataxia, tremors, or cardiac irregularities. Toxic reactions from medications taken by older adults can possibly result from

1. Slower metabolism, impaired circulation, and decreased excretion, causing medication to remain in the body longer and build up to dangerous levels
2. Wrong dosage caused by impaired vision or poor memory (patients may forget that they have taken medicine and take a double dose)
3. Interactions when many different medications are taken and over-the-counter medications, or herbal remedies are self-administered with inadequate medical supervision
4. Medical conditions affecting absorption

(See Chapter 27: Drugs and Older Adults.)

Source: Permission to reproduce Mr. Yuk has been granted by Children's Hospital of Pittsburgh.

FIGURE 10-1 Mr. Yuk and similar stickers may be obtained from many Poison Control Centers throughout the United States. The telephone number of the nearest Poison Control Center is frequently printed on these stickers.

Many medicines and common household products resemble candy or food. Children may be attracted to the unique shapes and bright colors used in packaging. Impaired vision may contribute to mistakes by adults, especially older adults. It is important to keep medicines and dangerous chemicals in an area separate from food and medicines. Don't be fooled by look-alikes (Figure 10-2).

PATIENT EDUCATION

Poisons

Public education is of paramount importance in preventing poisoning. The general public must be instructed in precautions with medications, and it is especially important to inform the parents and caretakers of young children and older adults. It is the responsibility of all health care practitioners to provide the necessary information to help prevent poisoning.

To prevent poisoning, the American Medical Association recommends the following precautions:

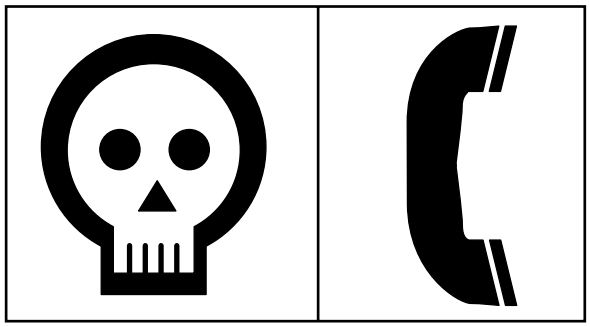
1. Keep all medicines, household chemicals, cleaning supplies, and pesticides in a locked cupboard. There is no place that is "out of reach of children."
2. Never transfer poisonous substances to unlabeled containers or to food containers such as milk or soda bottles or cereal boxes. Keep in original labeled container.
3. Never store poisonous substances in the same area with food. Confusion could be fatal.
4. Never reuse containers of chemical products.
5. Do not give or take medications in the dark.
6. Never leave medications on a bedside stand. Confusion while a person is sleepy could result in a fatal overdose.
7. Always read the label before taking any medication or pouring any solution for ingestion.
8. Never tell children the medicine you are giving them is candy. Explain to children that medication is taken for your well-being and that all medication is to be taken only as directed by a physician.
9. When preparing a baby's formula, taste the ingredients. Never store boric acid, salt, or talcum near the formula ingredients.
10. Never give or take any medication that is discolored, has a strange odor, or is outdated.
11. Don't take medicine in front of children.
12. Keep pocketbooks, purses, and pillboxes out of reach of children.
13. Rinse out containers thoroughly before disposing of them.

Note: In the past, most people flushed old medicines down the toilet to prevent accidental poisonings of children and animals who may find medicines in the trash. However, the Environmental Protection Agency (EPA) no longer recommends this as it may not be properly treated in sewage plants and return to harm humans, fish and wildlife.

Many cities and towns have household hazardous waste facilities where you can bring your old medicines. When in doubt, ask your pharmacist about proper disposal in your area.

Delmar/Cengage Learning

FIGURE 10-2 Look-alikes: Don't be fooled! Many common household products and medicines resemble candy or food. Keep these products in separate areas. The compared products are chosen for illustration purposes only. The manufacturers do not intend any misuse of their products.



POISON CONTROL CENTER ®

Source: Permission to reproduce Poison Control Center logo has been granted by the American Association of Poison Control Centers, Inc., Washington DC.

FIGURE 10-3 Obtain the number of your nearest Poison Control Center and place it near or on your telephone.

Obtain the number of your nearest Poison Control Center (Figure 10-3) and place it on or near your telephone. There are more than 70 Poison Control Centers throughout the United States and Canada with computerized data to give you the latest information about poisons. Remember, *the wrong treatment is often more dangerous than none*. You can obtain the number of the Poison Control Center in your area by calling 1-800-222-1222, or the nearest emergency care facility, or by logging on to the website (http://www.aapcc.org) of the American Association of Poison Control Centers, or check the emergency numbers in your phone book. The Poison Control Center is also a good source of information regarding poisonous plants, insects, snakes, reptiles, and poisonous marine organisms such as stingray and jellyfish.

CHAPTER REVIEW QUIZ

Complete the statements by filling in the blanks:

1. Poisons can be taken into the body in four different ways:

_____

_____

_____

_____

2. In cases of poison ingestion, vomiting is to be avoided under the following five conditions:

_____

_____

_____

_____

_____

3. Gastric lavage is contraindicated when a patient has ingested what type of substance?

_____

4. When is activated charcoal administered?

_____

5. Why are gastric contents saved after emesis or gastric lavage?

_____

6. What is the treatment for poisons that contact skin or eyes?

_____

7. What two groups of people are most at risk for poisoning?

_____

_____

8. Name four conditions that may lead to toxic medication reactions in older adults.

_____

_____

_____

_____

9. What is the leading cause of poisoning deaths in children under six years of age?

_____

10. What is the number of the National Poison Control Center?

_____

Note A Comprehensive Review Exam for Part I can be found at the end of the text following the Summary.

Answers to this comprehensive exam are available on the Instructor Resources CD-ROM.

Go to your StudyWARE™ CD-ROM and have fun learning as you play games and answer case study-related questions to help reinforce key concepts you learned in this chapter.

Go to your Study Guide and complete the review questions for this chapter.

PART 2

Drug Classifications

Chapter 11

Vitamins, Minerals, and Herbs

Objectives

Upon completion of this chapter, the learner should be able to

1. Categorize vitamins as water-soluble or fat-soluble
2. List vitamins and their sources, function, signs of deficiency, and symptoms of overdose if known
3. Identify vitamins by name as well as letter
4. List minerals and their sources, function, and signs of deficiency
5. Identify the chemical symbol for each mineral
6. Describe conditions that may require vitamin and/or mineral supplements
7. Explain the role of antioxidants in nutrition therapy
8. Describe why and how consumers should be more vigilant in the use of herbal products
9. Define the Key Terms and Concepts

Key Terms and Concepts

Antioxidants
Deficiency
Fat-soluble
Herbal
Minerals
Overdoses
Supplements
Symptoms of overdose
Toxicity
Water-soluble

The National Academy of Sciences and the National Research Council of the Food and Nutrition Board have listed U.S. Recommended Dietary Allowances (U.S. RDA) of vitamins and minerals necessary for maintenance of good nutrition in the average healthy adult under normal living conditions in the United States. This information was published by the National Academy of Sciences, Washington, DC. A major revision is currently under way to replace the RDA. The revised recommendations are called Dietary Reference Intakes (DRI) and reflect the collaborative efforts of both the United States and Canada. Until 1997, the RDA were the only standards available, and they will continue to serve health professionals until DRI can be readily accepted. For this reason and the fact that the DRI requirements will take some time to be universally accepted, both the 1989 RDA and the DRI for selected nutrients are presented here. Research is ongoing in this area. The National Academies issue periodic reports, such as those released in April 2000, urging caution with megadoses of antioxidant supplements that can cause adverse side effects.

Under special circumstances, vitamin and mineral **supplements** are required for optimal function and health. *Indications for vitamin and mineral supplements include:*

Inadequate diet. Due to anorexia, weight reduction or other special diets, illness, alcoholism, or poor eating habits

Malabsorption syndromes. Chronic gastrointestinal disorders or surgery that results in chronic diarrhea

Increased need for certain nutrients. As in pregnancy and lactation (especially iron, folic acid, and calcium), infants under one year of age, adolescence, debilitation, illness, unusual physical activity, postmenopausal women (calcium)

Deficiency due to medication interactions. For example, potassium deficiency with diuretic use

Nutrients function in groups or teams. Therefore, if diet supplementation is warranted, it is likely that both vitamins and some additional minerals are needed. An example of this teamwork is bone growth, development, and strength, which depend on calcium, magnesium, vitamin A, vitamin D, and several other nutrients (fluoride, etc.). However, patients should be advised to avoid self-medication with large doses of vitamins or minerals, which may not be indicated if the diet is well balanced and the individual is in good health. **Overdoses** of some vitamins, especially A and D, and some minerals, for example, iron, can be injurious to health. A need or **deficiency** should be established by a physician's diagnosis or blood test before exceeding Recommended Dietary Allowances (RDA). Supplementary (prophylactic) multivitamin preparations may reasonably contain 50%–150% of the RDA of vitamins (except the amount of vitamins A and D and folic acid should not exceed the RDA). Combination vitamin preparations containing iron should not be used unless a deficiency has been established with a blood test or physician's diagnosis.

It is important to differentiate between water-soluble and fat-soluble vitamins in order to avoid build-up in the body with possible symptoms of overdose. Megadoses of vitamins (more than the RDA) should be taken only if prescribed by a physician and/or approved by the FDA. *Remember, the RDA includes the amount from foods you eat as well as supplements.* Research reports have indicated a possibility of damage to tissues with large quantities of vitamins (above RDA), especially those stored in the fat cells of the body.

The Recommended Dietary Allowances (RDA's) and Dietary Reference Intakes (DRI's) listed on the following pages are established for average, normal, healthy adults. Larger amounts are required with certain conditions (e.g., pregnancy, lactation, and some illnesses). Larger amounts are required for males than females. Smaller amounts are required for children (consult references). However, megadoses should *never* be taken except under the direct supervision of a physician.

The RDA and DRI are presented here for reference only. You are not expected to remember these figures. However, before taking any supplements or educating patients on supplements it is wise to consult references for appropriate doses and to avoid overdosage. Overdosage can sometimes cause severe adverse effects and even acute toxicity, especially with the fat-soluble vitamins.

FAT-SOLUBLE VITAMINS

The **fat-soluble** vitamins are A, D, E, and K.

Vitamin A (Retinol, Retinal, Beta Carotene)

Vitamin A is processed in the body from the carotene of plants, especially yellow-orange and dark-green leafy vegetables, fruits, oily saltwater fish, dairy products, and eggs (RDA 800–1,000 units/day/DRI 700–3000 mcg/day). Beta carotene is an antioxidant. (See Antioxidants, later in this chapter.)

Necessary for:

Resistance to infection

Proper visual function at night

Normal growth and development of bones and soft tissue, and maintaining healthy epithelial tissue (skin and mucous membranes)

Healing of wounds (sometimes prescribed for acne)

Possible connection to reproduction

Deficiencies may result from:

Malabsorption of fats or diarrhea

Obstruction of bile

Presence of mineral oil in the intestines

Overcooking of vegetables in an open container (heat and air cause oxidation)

Prolonged infection or fever

Signs of deficiency include:

Night blindness

Slow growth, anorexia, weight loss, bone and teeth deformities

Dry eyes and skin, pruritus (itching)

Supplements of vitamin A (e.g., Aquasol A) may be necessary for:

Infants fed unfortified skim milk or mild-substitute formulas

Those with prolonged infection or fever

Diabetes or hypothyroidism

Liver disease

Vitamin A has been used as a screening test for fat absorption

Some dermatological disorders, for example, psoriasis, are being treated investigationally with retinoids (synthetic vitamin A products). A retinoid product, isotretinoin, is prescribed for severe acne. This product can cause fetal abnormalities and is therefore contraindicated in pregnancy. Isotretinoin has also caused increased intracranial pressure, possible liver injury, and other adverse side effects associated with hypervitaminosis A. (See Chapter 12 Skin Medications.) It is sad to note that vitamin A deficiency is the leading cause of blindness in children worldwide.

Symptoms of overdose (hypervitaminosis A) from greater than 50,000 units (15,000 mcg of retinol) in adults and 20,000 units (6,000 mcg of retinol in infants and children) include:

- Irritability and psychiatric symptoms
- Fatigue, lethargy
- Headache, insomnia
- Brittle nails, dry skin and hair
- Anorexia, nausea, diarrhea, and jaundice
- Acute toxicity with increased intracranial pressure, vertigo, coma
- Joint pain, myalgia
- Stunted growth, fetal malformations

Caution should be used with kidney or liver problems or diabetes.

- Long-term use of large doses of vitamin A is *contraindicated* for women who are, or may become, pregnant. *Fetal malformations* have been reported following maternal ingestion of large doses of vitamin A, either before or during pregnancy.

Vitamin D (Calciferol, Cholecalciferol, Ergocalciferol)

Vitamin D is synthesized in the body through the action of sunlight on the skin. Other sources include fish oils (especially salmon, tuna and mackerel), and food products fortified with vitamin D, such as milk and cereals (RDA 400 units/day/DRI 5–15 mcg/day).

Ongoing research studies have shown that people with low vitamin D levels are twice as likely to develop coronary artery disease, heart failure, stroke, high blood pressure, and diabetes as those with normal levels. Vitamin D deficiency is common in the northern latitudes where people do not get much sunlight and spend much of their time indoors.

The National Institute of health (NIH) compiled a list of individuals who need increased vitamin D and they include:

- Breastfed Infants
- Age 50 or older
- Those with limited sun exposure
- Dark-skinned people
- Obese people (BMI greater than 30)

Consequently, several researchers are suggesting that vitamin D supplement use be increased, however, the risk of overdose and toxicity must be considered. Vitamin D is fat-soluble and stays in the system longer and can accumulate to toxic levels. Those taking large doses must be assessed carefully for symptoms of toxicity which are listed shortly.

Necessary for:

Maintenance of normal nerves and muscles

Regulating the absorption and metabolism of calcium and phosphorus for healthy bones and teeth

Pregnancy and lactation, when it is especially important

Signs of deficiency include:

Poor tooth and bone structure (rickets)

Skeletal deformities

Osteoporosis, osteomalacia

Tetany (muscle spasms)

Vitamin D supplements are prescribed as calcifediol, calcitriol, or ergocalciferol to prevent or treat rickets or osteomalacia and to manage hypocalcemia in cases of parathyroid malfunction. The difference between therapeutic dosage and that causing hypercalcemia is very small and dosage must be carefully regulated and monitored.

Symptoms of vitamin D overdose and toxicity include:

Nausea, anorexia, weight loss

- Muscle and/or bone pain
- Kidney damage and kidney stone
- Heart rhythm abnormalities
- Hypercalcemia with convulsions or confusion
- Fetal disorders

Caution not to exceed the RDA of vitamin D especially with:

Cardiovascular disorders

Kidney diseases

Pregnancy (possible fetal malformations or mental retardation)

Lactation

Interactions (overdose may antagonize) with:

Digoxin

Thiazide diuretics

Mineral oil may interfere with intestinal absorption of vitamin D.

Vitamin E (Tocopherol)

Vitamin E is abundant in nature, found especially in cereals, wheat germ, seeds, nuts, vegetable oils, eggs, meat, and poultry (RDA 30 units/day/DRI 15–1,000 mg/day). Vitamin E has antioxidant properties (see Antioxidants later in this chapter).

Necessary for:

Normal metabolism

Protection of tissues of the eyes, skin, liver, breast, muscles, and lungs

Protecting red blood cells (RBCs) from damage

Decreasing platelet clumping

Research is ongoing in the use and benefits of vitamin E supplements as one of the treatment protocols for management of early Alzheimer's disease and for possibly slowing the progress of such symptoms as memory loss. However, such supplements will neither cure nor prevent the disease.

Deficiencies are found in those with:

Alcohol abuse

Malabsorption syndromes, for example, celiac disease, sprue, cystic fibrosis

Pathological conditions of liver and pancreas

Sickle-cell anemia

Also found in premature infants or low-birth-weight neonates

Signs of deficiency are not firmly established. Premature infants may show irritability, edema, or hemolytic anemia. Deficient adults may show muscle weakness and some abnormal laboratory values, such as low RBC count.

Vitamin E overdose (1200 units) can result in prolonged clotting times.

Note

Vitamin E supplements should be discontinued ten days prior to surgery because of the danger of prolonged bleeding time. Vitamin E supplements should not be taken while on anticoagulant therapy because of increased risk of bleeding.

Interactions: Excessive use of mineral oil may decrease the absorption of vitamin E.

Vitamin K (Phytonadione)

Vitamin K is found in green or leafy vegetables, cabbage, vegetable oils, cheese, eggs, and liver and is absorbed in the small intestine in the presence of bile salts (RDA 60–80 mg/day/DRI 90–120 mcg/day).

Necessary for blood clotting.

Deficiencies may result in low blood clotting factor levels caused by:

Insufficient vitamin K stores in the newborn

Malabsorption syndromes, ulcerative colitis, prolonged diarrhea

Coumadin overdose

Prolonged use of salicylates, quinine, and broad-spectrum or long-term hyperalimentation antibiotics

Signs of deficiency include:

Increased clotting time

Petechiae and bruising

Blood in the urine (hematuria)

Blood in the stool (melena)

Vitamin K is usually administered orally or intravenously. Injectable vitamin K package inserts warn against IV administration due to the possibility of severe allergic reactions. However, it is recommended as the route of choice by the American College of Chest Physicians for serious bleeding related to a vitamin K deficiency or as an antidote for bleeding complications during coumarin therapy. Vitamin K is only effective for bleeding disorders due to low concentrations of vitamin K-dependent blood clotting factors. It is not effective for bleeding from other causes such as heparin overdose.

The American Academy of Pediatrics recommends that vitamin K (phytonadione) be routinely administered to infants at birth to prevent hemorrhagic disease of the newborn. Some state regulations currently require this prophylaxis.

Adverse effects are rare, but hypersensitivity reactions have occurred with IV injections. **Toxicity** in infants can cause jaundice or hemolytic anemia.

Note Patients receiving anticoagulant therapy should be consistent in the amount of vitamin K–rich foods they eat daily in order to keep prothrombin levels stable. Large amounts of vitamin K–rich foods can counteract the anticoagulant therapy. See Chapter 25, Cardiovascular Drugs, for more information regarding anticoagulant therapy.

WATER-SOLUBLE VITAMINS

The **water-soluble** vitamins include the B-complex vitamins and vitamin C.

Vitamin B_1 (Thiamine)

Vitamin B_1 is a coenzyme utilized for carbohydrate metabolism. It is found in whole grains, wheat germ, peas, beans, nuts, yeast, meat, especially pork and organ meats, oysters, collard greens, oranges, and enriched cereals (DRI 1.1–1.4 mg/day).

Necessary for normal function of the nervous and cardiovascular systems.

Deficiencies in the United States may be due to:

Chronic alcoholism

Malabsorption

Signs of deficiency (beriberi; symptoms sometimes vague) include:

Anorexia and constipation, GI upset, nausea

Neuritis, pain, tingling in extremities, loss of reflexes

Muscle weakness, fatigue, ataxia

Mental depression, memory loss, confusion

Cardiovascular problems

Hypersensitivity reactions have occurred mainly following repeated IV administration of the drug.

Vitamin B_2 (Riboflavin)

Vitamin B_2 is a coenzyme utilized in the metabolism of glucose, fats, and amino acids. It is found in milk; eggs; nuts; meats, especially liver; yeast; enriched bread; and green leafy vegetables (DRI 1.3–1.6 mg/day).

Necessary for cell growth and metabolism with release of energy from carbohydrates, protein, and fat in food. Also functions to regulate certain hormones and in formation of RBCs.

Deficiencies of vitamin B_2 in the United States may be due to:

Chronic alcoholism

Poor diet

Signs of deficiency include:

Glossitis (inflammation of the tongue)

Cheilosis (cracking at corners of mouth)

Dermatitis, photophobia, vision loss, burning or itching eyes

Vitamin B_6 (Pyridoxine)

Vitamin B_6 is a coenzyme utilized in the metabolism of carbohydrates, fats, protein, and amino acids. It is found in meats, fish, poultry, legumes, peanuts, soybeans, wheat germ, whole-grain cereals, and bananas (DRI 1.3–1.9 mg/day). There is significant loss of B_6 when foods are frozen.

Deficiencies may be due to:

Chronic alcoholism

Drug interactions with isoniazid, other antitubercular drugs, oral contraceptives

Cirrhosis

Malabsorption syndromes

Signs of deficiency include:

Seizure activity in infants

Neuritis, dermatitis, nausea, vomiting, and depression in adults

CAUTION Overdose in pregnant women may result in newborns with seizures who have developed a need for greater than normal amounts of pyridoxine.

PATIENT EDUCATION

Patients taking levodopa alone (not combined with carbidopa) should be instructed not to take vitamin B_6 supplement because it antagonizes the action of levodopa.

Vitamin B_{12} (Cobalamin, Cyanocobalamin)

Vitamin B_{12} is found in meats (especially organ meats), poultry, fish and shellfish, milk, cheese, and eggs. Absorption of vitamin B_{12} depends on intrinsic factor, which is normally present in the gastric juice of humans. Absence of this factor leads to vitamin B_{12} deficiency and pernicious anemia (DRI 2.4 mcg/day).

The National Academy of Sciences now suggests that all Americans over the age of 50 begin taking a low-dose vitamin B_{12} supplement or regularly eat breakfast cereals that are fortified with the vitamin. The problem is that as many as 30% of adults over 50 have diminished gastric acid production, and therefore they lack intrinsic factor, which is necessary for absorption of vitamin B_{12}. This is especially true for those taking medications that reduce gastric acid, for example, cimetidine (Tagamet).

Necessary for maturation of red blood cells and maintenance of the nervous system.

Deficiencies can be associated with:

- Vegetarian diets without meat, eggs, or milk products
- Gastrectomy or intestinal resections
- Malabsorption syndromes
- Pernicious anemia, megaloblastic (macrocytic) anemia

Signs of deficiency include:

- Anemia and weakness first symptoms of clinical deficiency
- Poor muscle coordination
- Numbness of hands and feet (paresthesia)
- Mental confusion, disorientation, memory loss, and irritability

Treatment for pernicious anemia consists of vitamin B_{12}, cyanocobalamin, 100–1,000 mcg IM monthly for life to prevent neurological damage.

Side effects include:

- Transient diarrhea
- Itching and urticaria
- Anaphylaxis (rare)

Interactions may occur (decreased absorption of B_{12}) with:

- Aminoglycoside antibiotics
- Anticonvulsants
- Slow-release potassium and colchicine

PATIENT EDUCATION

Patients should avoid taking large doses of vitamin B_{12} without confirmed deficiency, as megadoses may mask symptoms of folic acid deficiency or cause complications in those with cardiac or gout conditions.

Folic Acid (Folate)

Folic acid is a vitamin included in the B-complex group and is found in leafy and green vegetables (broccoli), avocado, beets, orange juice, kidney beans, and organ meats (DRI 400 mcg/day). Folic acid is lost with overcooking and reheating.

Necessary for protein synthesis, production of RBCs, cell division, and normal growth and maintenance of all cells. Deficiency during pregnancy can result in neural tube defects, such as spina bifida, in the newborn.

Deficiencies can be associated with:

- Improper diet
- Chronic alcoholism
- Liver pathology

Intestinal obstruction

Megaloblastic and macrocytic anemia

Malabsorption syndromes, malnutrition

Renal dialysis or prolonged use of some medicines (listed below)

Signs of deficiency include:

Anorexia, weight loss, weakness

Irritability, behavior disorders

CAUTION Folic acid *should not be given to anyone with undiagnosed anemia*, since it may mask the diagnosis of pernicious anemia. OTC vitamin supplements should contain no more than 0.4 mg; however, 1-mg doses are available by prescription.

Interactions of folic acid, over DRI, could interfere with action of the following drugs:

Phenytoin (Dilantin)

Estrogen (oral contraceptives)

Barbiturates, or nitrofurantoin

PATIENT EDUCATION

Patients should avoid taking folic acid supplements without consulting a physician first.

Niacin (Nicotinic Acid, Niacinamide)

Niacin is a vitamin included in the B-complex group and is found in meat, chicken, milk, eggs, fish, green vegetables, cooked dried beans and peas, soybeans, nuts, peanut butter, and enriched cereal products (DRI 14–18 mg/day).

Necessary for lipid metabolism and nerve functioning, especially in circulation and maintenance of all cells.

Deficiency results in pellagra, a severe skin and mucous membrane disorder progressing to systemic and central nervous system disorders.

Signs of niacin deficiency include:

Peripheral vascular insufficiency

Dermatitis and varicose ulcers

Diarrhea

Dementia, hallucinations, depression

Mouth sores

Lethargy, weakness, anorexia, indigestion

Niacin is used primarily to prevent and treat pellagra. Other treatment indications (usually as an adjunct with other medications) include:

Many vascular disorders (e.g., vascular spasm, arteriosclerosis, Raynaud's disease, angina, and varicose veins and pressure ulcers)

Circulatory disturbances of the inner ear, Ménière's syndrome

Lower blood lipid levels (see Chapter 25)

Daily doses of up to 1,000 mg appear to be safe.

Side effects of niacin, especially over 1,000 mg daily, can include:

- Headache, flushing, and burning sensations of face, neck, and chest
- Postural hypotension

Jaundice

Nausea, diarrhea, vomiting

- Increased blood glucose and uric acid

Caution for patients with liver disease, gallbladder disease, gout, or diabetes

PATIENT EDUCATION

Patients should be instructed regarding possible side effects, especially flushing and a burning sensation, and should be cautioned to rise slowly from a reclining position. They should be told that the flushing usually resolves within two weeks. Taking niacin in divided doses, or extended-release products, can sometimes lessen this effect. Sometimes aspirin is prescribed to counteract flushing.

Vitamin C (Ascorbic Acid)

Vitamin C is a water-soluble vitamin found in fresh fruits and vegetables, especially citrus fruits, cantaloupe, tomatoes, cabbage, green peppers, and broccoli. It is unstable when exposed to heat or air or combined with alkaline compounds (e.g., antacids). Adding baking soda to vegetables for color retention destroys vitamin C (DRI 75–90 mg/day).

Necessary for formation of intracellular substances (collagen), and for normal teeth, gums, and bones. Also required for iron absorption. Vitamin C is considered an antioxidant. (See Antioxidants later in this chapter.) Also promotes healing of wounds and bone fractures.

Deficiencies are associated with:

Diet lacking fresh fruit and vegetables

Alcoholism, infections

Smoking

Signs of the vitamin C deficiency disease (scurvy) include:

Muscle weakness and cramping

Sore and bleeding mouth and gums, loose teeth

Capillary fragility (bruising); dry, scaly skin

Poor healing

Supplements of ascorbic acid are available in capsules, tablets (extended-release), solution, chewables, or injection form. They are indicated for:

Treatment of scurvy (adults 100–250 mg bid, children 100–300 mg/day divided doses)

Hemodialysis patients (100–200 mg daily)

Infants beginning at two to four weeks of age (20–50 mg/day)

Investigational for the prevention or treatment of the common cold (1–2 g/day)

Dosages larger than that recommended are to be avoided because of the potential for side effects. In addition, since ascorbic acid is water soluble, more than 50% of the dose is excreted in the urine of normal subjects. Excretion of less than 20% of the dose over 24 h suggests vitamin C deficiency.

Side effects of large doses of vitamin C, more than RDA, can include:

- Heartburn, abdominal cramps, nausea, vomiting, and diarrhea
- Increased uric acid levels; may precipitate gouty arthritis
- Increased urinary calcium; may precipitate kidney stone formation
- Scurvy in neonates following large amounts during pregnancy

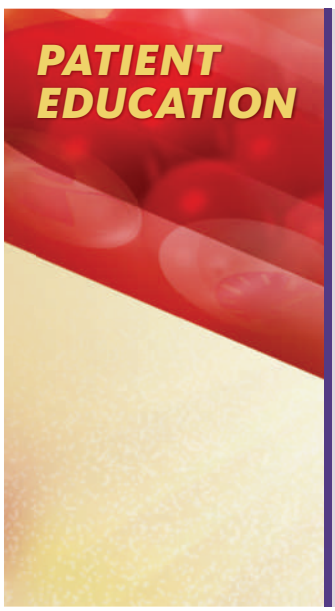
False negative for colon cancer test

Interactions may occur with:

Aspirin, causing elevated blood levels of aspirin

Barbiturates, tetracyclines, estrogens, oral contraceptives, which may increase requirements for vitamin C

Alcohol and smoking, which may decrease vitamin C level



Patients should be given the following information concerning vitamin C:

Vitamin C is destroyed by heat and air; therefore, raw fresh fruits and vegetables are best.

Large quantities of supplemental vitamin C are to be avoided, unless prescribed by a doctor, because of potential side effects, such as gastric irritation, increased uric acid, and kidney stones.

Antacids should not be taken at the same time as vitamin C supplements because the alkaline compound neutralizes the ascorbic acid.

Megadoses of vitamin C taken during pregnancy may cause the newborn to require larger than average amounts of ascorbic acid.

See Table 11-1 for a summary of water- and fat-soluble vitamins.

Table 11-1 Summary of Fat-Soluble and Water-Soluble Vitamins

NAME (WATER SOLUBLE)	FOOD SOURCES	FUNCTIONS	DEFICIENCY/TOXICITY
Vitamin A (retinol, beta carotene)	Animal Oily saltwater fish Dairy products Eggs Plants Dark-green leafy vegetables Deep yellow or orange fruit and vegetables	Dim light vision Maintenance of mucous membranes Growth and development of bones Healing of wounds Resistance to infection Beta carotene is an antioxidant	**Deficiency** Retarded growth Faulty bone and tooth development Night blindness Dry skin Xerophthalmia (dry eyes) **Toxicity** (hypervitaminosis A) Irritability, lethargy, headache Joint pain, myalgia Stunted growth, fetal malformations Jaundice, nausea, diarrhea Dry skin and hair
Vitamin D (cholecalciferol)	Animal Fish oils Fortified milk Plants Fortified cereals	Healthy bones and teeth Muscle function Enables absorption of calcium	**Deficiency** Softening bones: Rickets (in children) Osteomalacia (in adults) Poorly developed teeth Muscle spasms **Toxicity** (Hypercalcemia), convulsions Kidney stones, kidney damage Muscle/bone pain Nausea, anorexia Fetal disorders
Vitamin E (tocopherol)	Plants Vegetable oils Seeds, nuts Wheat germ, cereals	Antioxidant Decreases platelet clumping Normal metabolism and tissue protection	**Deficiency** Destruction of RBCs, muscle weakness **Toxicity** Prolonged bleeding time
Vitamin K (phytonadione)	Animal Egg yolk, cheese Liver Plants Vegetable oil Green leafy vegetables Cabbage, broccoli	Blood clotting	**Deficiency** Prolonged blood clotting time Blood in urine and stool **Toxicity** Jaundice in infants

Table 11-1 Summary of Fat-Soluble and Water-Soluble Vitamins—*continued*

NAME (WATER SOLUBLE)	FOOD SOURCES	FUNCTIONS	DEFICIENCY/TOXICITY
Vitamin B_1 (thiamine)	Animal Pork, beef, liver Oysters Plants Yeast Whole and enriched grains, wheat germ Beans, peas, collard greens, nuts, asparagus Oranges	Normal nervous and cardiovascular systems	**Deficiency** GI upset, constipation Neuritis, mental disturbance Cardiovascular problems Muscle weakness, fatigue **Toxicity** None known
Vitamin B_2 (riboflavin)	Animal Milk Meat, liver Plants Green vegetables Cereals Enriched bread Yeast	Aids in energy metabolism of glucose, fats, and amino acids	**Deficiency** Cheilosis Glossitis Photophobia, vision problems, itching eyes Dermatitis, rough skin **Toxicity** None
Vitamin B_6 (pyridoxine)	Animal Pork, beef, chicken, tuna, salmon Plants Whole-grain cereals, wheat germ Legumes, peanuts, soybeans Bananas	Synthesis of amino acids Antibody production Maintenance of blood glucose level	**Deficiency** Anorexia, nausea, vomiting Dermatitis Neuritis, depression **Toxicity** Seizures in newborn
Vitamin B_{12} (cyanocobalamin)	Animal Seafood/shellfish Meat, poultry, liver Eggs Milk, cheese Plants None	Synthesis of RBCs Maintenance of nervous system	**Deficiency** Nerve, muscle, mental problems Pernicious anemia **Toxicity** None
Niacin (nicotinic acid)	Animal Milk Eggs Fish Poultry Plants Legumes, nuts Green vegetables	Lipid metabolism Nerve functioning	**Deficiency** Pellagra **Toxicity** Headache, flushing Increased blood glucose and uric acid

(*continued*)

Table 11-1 Summary of Fat-Soluble and Water-Soluble Vitamins—*continued*

NAME (WATER SOLUBLE)	FOOD SOURCES	FUNCTIONS	DEFICIENCY/TOXICITY
Folic Acid (Folate)	Animal Organ meats Plants Green leafy vegetables Avocado, beets Broccoli, kidney beans Orange juice	Synthesis of RBCs, leukocytes, DNA and RNA Needed for normal growth and reproduction	**Deficiency** Increased risk of neural tube defects Macrocytic anemia Irritability, behavior disorders **Toxicity** None
Vitamin C (ascorbic acid)	Fruits All citrus, cantaloupe Plants Broccoli Tomatoes Brussels sprouts Cabbage Green peppers	Normal teeth, gums, and bone Prevention of scurvy Formation of collagen Healing of wounds Absorption of iron Antioxidant	**Deficiency** Scurvy Poor healing Muscle cramps/weakness Ulcerated gums/mouth, loose teeth Capillary fragility (bruising) **Toxicity** Raise uric acid level, gout GI distress Kidney stones Rebound scurvy in neonates

MINERALS

Minerals are chemical elements occurring in nature and in body fluids. The correct balance of each is required for maintenance of health. Minerals dissolved in the body fluids are called *electrolytes* because they carry positive or negative electrical charges required for body activities, such as conduction of nerve impulses, beating of the heart, skeletal muscle contraction, absorption of nutrients from the GI tract, protein synthesis, energy production, blood formation, and many other body processes.

Necessary for:

Homeostasis (body balance).

The correct ratio of fluids to electrolytes must be maintained for normal functioning of the body. Fluids and minerals are excreted daily and must be replaced with fluid and food intake.

The principal minerals in the body and their chemical symbols are sodium (Na), chloride (Cl), potassium (K), calcium (Ca), and iron (Fe).

Sodium and Chloride

Sodium and chloride are the principal minerals in the extracellular body fluids. The best source of sodium and chloride is table salt (NaCl).

Deficiencies of sodium and chloride are associated with:

Excessive fluid loss: bleeding, diarrhea, vomiting, or excessive perspiration

Insufficient oral intake (starvation or extended fasting)

Alkalosis (chloride deficiency)

Treatment consists of oral or intravenous therapy with sodium chloride (NaCl) according to needs:

Normal saline solution (0.9% sodium chloride)

Half-normal saline solution (0.45% sodium chloride)

Quarter-normal saline solution (0.225% sodium chloride)

Sometimes other minerals are required and are also added to the intravenous fluids.

Potassium (K)

Potassium (DRI 4.7 g/day) is another of the principal minerals within cells. Natural sources of potassium include citrus, bananas, tomatoes, potato skin, cantaloupe, avocadoes, dried fruits, cooked dried beans, and peas.

Necessary for:

Acid-base and fluid balance

Normal muscular irritability (heartbeat regulation)

Deficiencies are associated with:

Insufficient oral intake due to surgery, anorexia, or weight-reduction diets

Diarrhea or vomiting

Diabetic ketoacidosis

Diaphoresis (excessive perspiration)

Diuretic use, especially thiazides and furosemide

Digoxin toxicity

Long-term use of corticosteroids or long-term use of laxatives

Kidney disease

Signs of deficiency include:

Muscular weakness, paralysis

Cardiac arrhythmias

Lethargy and fatigue, mental apathy and confusion

Treatment consists of:

KCL given IV postoperatively or for severe dehydration (diluted according to directions)

One of the numerous oral products available, usually in effervescent tablet or powder form, to be dissolved in water or juice and taken after meals

(e.g., K-Lyte/Cl), or capsules to be swallowed (e.g., Micro-K), extended-release tablets (e.g., K-Dur, or Slow-K), or oral liquid preparations.

Side effects of potassium overdose can include:

Nausea, vomiting, or diarrhea

GI bleeding, or abdominal pain

Pain at the injection site or phlebitis may occur during IV administration of solutions containing 30 mEq or more potassium per liter. IV solutions containing potassium should always be run at a slow rate to prevent pain or hyperkalemia.

Hyperkalemia (excessive potassium in the blood) is not likely to result from oral administration, except in the case of severe renal impairment. Care must be taken when adding potassium to IV solutions that the dilute solution is thoroughly mixed, inverted, and agitated, before the solution is hung for administration. Never add potassium to hanging IV solution.

Symptoms of potassium overdosage can include:

Confusion

Weakness or paralysis of extremities

Fall in the blood pressure and/or *cardiac arrhythmias* from hyperkalemia

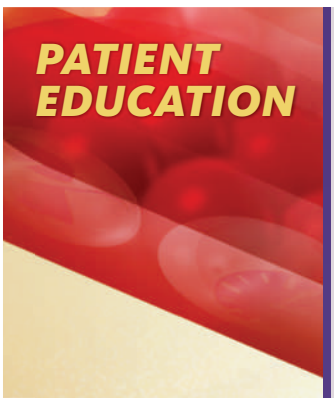
Caution with use of potassium in the following conditions:

Cardiac disease

Renal impairment

Gastric or intestinal ulcers (extended-release products contraindicated)

Mental confusion (unable to follow directions properly)



Patients taking potassium should be instructed regarding:

Natural sources of potassium-rich foods

Conditions requiring potassium supplements

Directions for taking potassium supplements with or after meals to avoid GI distress and following directions on package carefully

The importance of following specific directions carefully with certain tablets that need to be dissolved in water

Notifying a doctor immediately of any side effects

Calcium (Ca)

Calcium is a mineral component of bones and teeth. It is absorbed in the small intestine with the help of vitamin D. Natural sources include milk and dairy products (RDA 1,000–1,200 mg/day). In postmenopausal women not receiving estrogen therapy, the RDA is about 1,500 mg/day. Those who are lactose intolerant (unable to take milk) should include dark-green leafy vegetables (except spinach), broccoli, and canned fish with the bones. (DRI 1,000–1,300 mg/day, with the higher figure recommended for adolescents of both sexes and postmenopausal women.)

Necessary for:

Strong bones and teeth

Contraction of cardiac, smooth, and skeletal muscles

Nerve conduction

Blood coagulation, capillary permeability, and normal blood pressure

The balance between calcium and magnesium is important in the prevention of heart disease

Deficiencies (supplements required) are associated with:

Pregnancy and lactation

Postmenopausal women (or those with estrogen deficiency)

Hypoparathyroidism

Long-term use of corticosteroids, some diuretics, or anticonvulsants

Chronic diarrhea, pancreatitis, renal failure

Lack of weight-bearing exercise

Signs of deficiency may include:

Osteoporosis, or osteomalacia (softening of bones), including frequent fractures, especially in the elderly

Rickets in children (softening of bones)

Muscle pathology, including cardiac myopathy or tetany (muscle spasm) and leg cramps

Increased clotting time

Treatment consists of calcium supplements 400–600 mg daily PO. A higher-dosage supplement is required for those not including calcium-rich foods in the diet (e.g., without dairy products). The RDA, *including foods*, are 1,200 mg/day for adults and 1,500 mg/day for postmenopausal women not taking estrogen. Many products and combinations are available including calcium gluconate, calcium carbonate, or calcium lactate. Of these three, calcium carbonate delivers the highest amount of elemental calcium per tablet.

Adding vitamin D for calcium metabolism may be necessary without exposure to sunlight (see Vitamin D).

Side effects of calcium salts can include:

- Constipation from oral products

  Tissue irritation from IV products

- When injected IV, calcium salts should be administered *very slowly* to prevent tissue necrosis or *cardiac arrhythmias*

Caution: Calcium should be used cautiously, if at all, with:

Cardiac disease

Renal disease

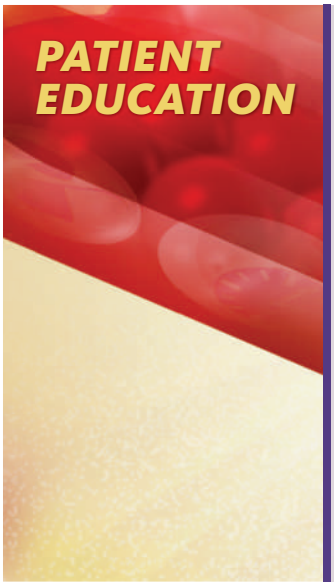
Respiratory conditions (e.g., sarcoidosis)

Administration: Most oral calcium supplements should be administered 1–1.5 h after meals, unless specified otherwise on the label.

Interactions may occur with:

Digoxin, resulting in potentiation (may cause arrhythmias)

Tetracycline, resulting in antagonism (inactivates the antibiotic)



Patients taking calcium should be instructed regarding:

Calcium-rich diet, especially dairy products and vitamin D milk, which can be low-fat

Necessity for calcium supplements, usually recommended for women beginning at age 35, and especially for postmenopausal women not on estrogen therapy

Importance of upright exercise, for example, walking at least three to four times per week to preserve bone mass

Importance of outdoor activity because sunlight helps create vitamin D necessary for calcium metabolism

Taking calcium supplements 1–1½ h after meals, unless specified otherwise on the label

Not taking calcium at the same time as other medicines

Iron (Fe)

Iron is the oxygen-carrying component of blood. Iron is a mineral found in meat (especially liver), egg yolk, beans, spinach, enriched cereals, dried fruits, prune juice, and poultry. The DRI for iron is 8-18 mg/day.

Necessary for hemoglobin formation.

Deficiencies (supplements recommended) with:

Hemorrhage and excessive menstrual flow

Internal bleeding, ulcers, and GI tumors

Pregnancy

Infancy

Puberty at time of growth spurt

Patients undergoing hemodialysis

Signs of deficiency may include:

Paleness of the skin and/or mucous membranes

Lethargy and weakness

Vertigo (dizziness, lightheadedness)

Air hunger

Decline in mental skills

Irregular heartbeat and function

Cravings for nonfood items, for example, ice, clay, or starch (called pica)

Treatment of anemia due to iron deficiency consists of administration of iron preparations:

Oral iron products. Ferrous sulfate (Feosol, Fer-in-Sol, and others). Adults 325 mg tid after meals (not with milk, coffee, or tea), infants and children 4–6 mg/kg daily in three divided doses in juice or with meals (not with milk).

Injectable iron. Iron dextran (INFeD) 50–100 mg *deep* IM by the *Z-track method only.* Extreme caution is urged to prevent solution contacting the subcutaneous tissue because of its irritating effect. A fresh 2-inch needle is recommended at the time of administration. Iron dextran also can be given IV *slowly* after testing for sensitivity with a small trial dose. Two other injectable iron preparations, iron sucrose and sodium ferric gluconate, are safer than iron dextran when given intravenously.

Side effects of taking iron preparations can include:

- Black stools
- Nausea and vomiting (GI effects can be minimized by taking iron after or with meals, *but not with coffee, tea, or milk*)
- Constipation or diarrhea

Anaphylactic reactions or phlebitis with IV administration of iron dextran

Contraindicated in patients with peptic ulcer, regional enteritis, or ulcerative colitis

Parenteral iron should *not* be administered concomitantly with oral iron therapy.

Iron should *not* be administered without confirming a diagnosis of deficiency with a blood test and determining cause of deficiency.

Interactions may occur with:

Vitamin C or orange juice, taken at same time, which *enhances* iron absorption

Coffee or tea taken within two hours of iron, which reduces iron absorption by as much as 50%

Tetracycline, absorption of which is inhibited by oral iron preparations when taken within two hours

Antacids, which decrease iron absorption (should not be given at same time)

Symptoms of acute overdose of iron may occur within minutes or days and include:

Lethargy

- Shock

Vomiting and diarrhea

Erosion of GI tract/hemochromatosis

Liver or kidney damage

Patients taking iron supplements should be instructed regarding:

- *Avoidance of self-medication* without established need (blood test) and without medical supervision to determine why hemoglobin is low. Taking iron when not prescribed could mask the symptoms of internal bleeding or GI malignancy.
- Black stools to be expected
- Taking iron at meals to minimize GI distress and with orange juice for better absorption
- Interactions (i.e., avoidance of coffee, tea, milk, or antacids at same time)
- Caution with flavored children's tablets (overdosage can be dangerous, even fatal)
- Taking liquid iron preparations with drinking straw to avoid temporary stain of dental enamel
- The iron in meats is called heme iron and is better absorbed than nonheme iron in vegetables and fruits
- Nonheme iron is absorbed better if consumed with a rich source of vitamin C (e.g., orange juice)

Zinc

Zinc is a component of numerous enzymes and is an essential element in metabolism. It is usually found in adequate amounts in a well-balanced diet. Rich sources include lean meat, organ meats, oysters, poultry, fish, and whole grain breads and cereals (DRI 8–11 mg/day). Zinc is an antioxidant.

Necessary for:

- Wound healing
- Mineralization of bone
- Insulin glucose regulation
- Normal taste

Deficiencies (supplements recommended) with:

- Inadequate or vegetarian diet
- Chronic, nonhealing wounds
- Major surgery or trauma

Deficiency symptoms can include:

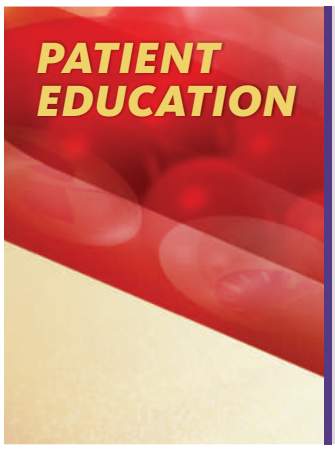
- Poor wound healing
- Reduced taste perception
- Poor alcohol tolerance, glucose intolerance
- Anemia, slowed growth, sterility
- Dermatitis and hair loss

Toxicity (more than 2 g/day) may cause:

- Nausea, GI distress, vomiting
- Copper deficiency with extended use of high levels of zinc

Treatment consists of tablets or capsules administered with meals tid to minimize gastric distress. Standard supplement of zinc is no more than 50 mg/24 h. If a zinc supplement is required for more than 90 days, blood levels should be monitored. Chronic consumption of high levels of zinc may cause copper deficiency.

Many combinations of various vitamins and minerals are available in OTC products with various strengths and forms.



Vitamins and Minerals

Patients should be instructed regarding:

- Well-balanced diets and natural sources of vitamins and minerals
- Food preparation to avoid loss of vitamins
- Information regarding signs of deficiency and overdose/toxicity
- Caution taking supplements without established need or without medical supervision, especially megadoses, fat-soluble vitamins, and iron
- Proper administration to minimize side effects

See Table 11-2 for summary of major minerals.

Table 11-2 Summary of Major Minerals

NAME	FOOD SOURCES	FUNCTIONS	DEFICIENCY/TOXICITY
Calcium (Ca) (DRI 1,000– 1,300 mg per day)	Milk, cheese, yogurt Sardines Salmon Green vegetables except spinach	Development of bones and teeth Contraction of cardiac, smooth and skeletal muscles Nerve conduction Blood clotting	**Deficiency** Osteoporosis, osteomalacia Rickets (in children) Muscle pathology Heart disease Increased clotting time **Toxicity** Kidney Stones
Potassium (K) (DRI 4.7 g per day)	Oranges, bananas Dried fruits Tomatoes	Contraction of muscles Heartbeat regulation Transmission of nerve impulses Maintaining fluid balance	**Deficiency** (Hypokalemia) Muscle weakness Cardiac arrhythmias Lethargy, mental confusion **Toxicity** (Hyperkalemia) Confusion Weakness Cardiac arrhythmias
Sodium (Na) (DRI 1,300– 1,500 mg per day)	Table salt Beef, eggs Milk, cheese	Maintaining fluid balance in blood Transmission of nerve impulses	**Deficiency** Low blood pressure **Toxicity** Increase in blood pressure

(*continued*)

Table 11-2 Summary of Major Minerals—*continued*

NAME	FOOD SOURCES	FUNCTIONS	DEFICIENCY/TOXICITY
Chlorine (Cl) (DRI 1.8–2.3 g per day)	Table salt	Gastric acidity Regulation of osmotic pressure Activation of salivary amylase	**Deficiency** Imbalance in gastric acidity Imbalance in blood pH **Toxicity** Diarrhea
Magnesium (Mg) (DRI 320–420 mg)	Green vegetables Whole grains	Synthesis of ATP (adenosine triphosphate) Transmission of nerve impulses Relaxation of skeletal muscles	**Deficiency** (seldom) Imbalance Weakness **Toxicity** Diarrhea
Iron (Fe) (DRI 8–18 mg per day)	Meat Liver Eggs Poultry Spinach Dried fruits Dried beans Prune juice	Hemoglobin formation	**Deficiency** (anemia) Pale Weak Lethargy Vertigo Air hunger Irregular heartbeat **Toxicity** Lethargy, shock Vomiting, diarrhea Erosion of GI tract Liver or kidney damage
Iodine (I) (DRI 150 mcg per day)	Freshwater shellfish and seafood Iodized salt	Major component of thyroid hormones Regulating rate of metabolism Growth, reproduction Nerve and muscle function Skin and hair growth	**Deficiency** Goiter Hypothyroidism **Toxicity** "Iodine goiter" Hyperactive, enlarged goiter
Zinc (Zn) (DRI 8–11 mg per day)	Meat Liver Oysters Poultry Fish Whole-grain bread and cereal	Wound healing Mineralization of bone Insulin glucose regulation Normal taste Antioxidant	**Deficiency** Poor wound healing Reduced taste perception Alcohol/glucose intolerance **Toxicity** GI distress Copper deficiency with extended use of high levels of zinc

PATIENT EDUCATION

Food labels provide a nutritional analysis of the food product. The Percentage (%) Daily Value is the amount of the nutrient obtained by eating the equivalent of one-serving of the product. The amount is given in a percentage based upon a 2,000-calorie daily diet. See Figure 11-1.

Nutrition Facts

Serving Size ½ cup (130g)
Servings Per Container About 4

Amount Per Serving	
Calories	110
Calories from Fat	0
	% Daily Value*
Total Fat 0g	**0%**
Sodium 340mg	**14%**
Total Carbohydrate 20g	**7%**
Dietary Fiber 6g	**25%**
Sugars 2g	
Protein 8g	
Calcium 6% •	Iron 10%

Not a significant source of saturated fat, trans fat, cholesterol, vitamin A and vitamin C.

*Percent Daily Values are based on a 2,000 calorie diet.

Delmar/Cengage Learning

FIGURE 11-1 Nutrition facts.

ANTIOXIDANTS

No discussion of nutrition would be complete without an explanation of the antioxidants, as we know them. **Antioxidants**, sometimes referred to as "anticancer foods" or "natural drugs," inhibit cell destruction in damaged or aging tissues. Nucleic acids, which make up the genetic code within the cell, usually act to regulate normal cell function and the growth and repair of damaged or aging tissues.

Free radicals attack the cells, causing damage, which prevents the transport of nutrients, oxygen, and water into the cell and the removal of waste products. This damage affects the nucleic acids in their function of growth and repair of tissue. Free radical damage is associated with several age-related diseases. For example, damage to the nucleic acids might initiate growth of abnormal cells, the first step in cancer development. Also, free radical attack to the cell membranes of the tissues lining the blood vessels can lead to cholesterol accumulation in the damaged arteries, the initial state of atherosclerosis and heart disease. Additionally, free radicals are associated with inflammation, drug-induced organ damage, immunosuppression, and possibly other disorders as well.

The body has developed an antioxidant system response to defend itself from free radicals. An antioxidant is defined as any compound that fights against the destructive effects of free radical oxidants. This system is comprised of enzymes, vitamins, and minerals. Antioxidants function in the prevention of free radical formation by binding to, and neutralizing, destructive substances before they damage cells and tissues.

The antioxidant vitamins—vitamin C, vitamin E, and beta carotene—can function independently of enzymes. Antioxidant minerals include copper, manganese, selenium, and zinc. These minerals work with antioxidant enzymes and are essential to proper enzyme function. If the diet is inadequate in these minerals, the enzyme is not produced, or is ineffective.

Research on antioxidants is ongoing. However, statistical findings at this time indicate that "natural" antioxidants in foods are much more effective than synthetic products.

A report issued in April 2000 by the National Academies stated that "insufficient evidence exists to support claims that taking megadoses of antioxidants can prevent chronic diseases." They also state that extremely large doses may lead to health problems, rather than confer benefits.

The pharmaceutical magazine, *Drug Topics*, January 2000, provides a caution that taking antioxidants while undergoing chemotherapy or radiation treatments could be contraindicated. Chemotherapy and radiation generate free radicals, and they need an oxidative process to actually kill tumor cells. By giving antioxidants concurrently with chemotherapy or radiation, you actually can increase the tumor cell's life. It is recommended that patients stop taking antioxidants two days before chemotherapy or radiation, and avoid them during the treatment and for two days after completion of the treatment.

Patients asking about antioxidants should be instructed regarding:

- Foods that provide antioxidant action
- Natural antioxidants in certain foods, which are more effective than synthetic products
- When antioxidants are contraindicated and the health problems with megadosing.

ALTERNATIVE MEDICINES

Herbs and Other Dietary Supplements

As a provider of health care, you will be asked about dietary supplements and, in particular, about **herbal** remedies. It is important for you to be able to answer these questions effectively and refer your patients to reliable sources of information. There are many books on the market and articles on the Internet describing the use of herbal remedies. In assessing the value of these resources, question the source, the credentials of the author, the research involved in collecting the data, and the reliability and validity of the statistics. Be sure that the information is based on fact, not opinion. You have a responsibility to caution your patients regarding the dangers of taking remedies not approved by the FDA, and especially the risk of possible interactions between "natural products" and prescription drugs.

The FDA has published a report entitled *A FDA Guide to Dietary Supplements*, which answers many questions on this subject. The following information was taken from that report and from the *FDA Talk Paper* of January 2000: *FDA Finalizes Rules for Claims on Dietary Supplements.*

Congress passed the Dietary Supplement Health and Education Act of 1994 (DSHEA), which amended the Food, Drug, and Cosmetic Act to recognize dietary supplements as distinct from food additives and drugs, which are monitored and regulated by the FDA. *Food supplements are not subject to the same scrutiny and restrictions*, so consumers and manufacturers have the responsibility for checking the safety of dietary supplements and determining the truthfulness of label claims.

Dietary Supplements

Dietary supplements have traditionally referred to products made of one or more of the essential nutrients, such as vitamins, minerals, and protein. DSHEA broadens the definition to include, with some exceptions, any product intended for ingestion as a supplement to the diet. This includes vitamins, minerals, herbs, botanicals, other plant-derived substances, amino acids (the individual building blocks of protein), and concentrates, metabolites, constituents, and extracts of these substances.

It is easy to spot a supplement because DSHEA requires manufacturers to include the words "dietary supplement" on product labels. Also, since March 1999, a "Supplement Facts" panel is required on the labels of most dietary supplements. The supplement manufacturers are required to document substantiation of their claims. They must also include a disclaimer on their labels that the dietary supplements *are not drugs and receive no FDA premarket approval.* The rule, published in the January 6, 2000, *Federal Register*, also prohibits "structure/function" claims (claims that the products affect the structure or function of the body) without prior FDA review. Supplement labels also *may not*, *without prior FDA review*, *bear a claim that they can prevent*, *treat*, *cure*, *mitigate*, *or diagnose disease.*

Drugs used as traditional medicines are sometimes derived from plants. However, before marketing, they must undergo extensive clinical studies to determine their effectiveness, safety, possible interactions, and appropriate dosages before FDA approval. *The FDA does not authorize or test dietary supplements.*

Dietary supplements come in many forms, including tablets, capsules, powders, softgels, gelcaps, and liquids. Though commonly associated with health food stores, dietary supplements also are sold in grocery, drug, and national discount chain stores, as well as through mail-order catalogs, TV programs, the Internet, and direct sales.

Under DSHEA, once a dietary supplement is marketed, the FDA has the responsibility for showing that a dietary supplement is *unsafe* before it can take action to restrict the product's use. This was the case when, in June 1997, the FDA proposed, among other things, to limit the amount of ephedrine alkaloids in dietary supplements (marketed as ephedra, Ma huang, and epitonin, for example) and provide warnings to consumers about hazards associated with use of dietary supplements containing the ingredients.

The hazards ranged from nervousness, dizziness, and changes in blood pressure and heart rate, to chest pain, heart attack, hepatitis, stroke, seizures, psychosis, and death. The proposal stemmed from the FDA's review of adverse event reports it had received, scientific literature, and public comments. Finally, in 2004, the FDA announced a ban on the weight-loss aid ephedra. However, there are numerous other dangerous supplements still on the market. In May 2004, *Consumer Reports* identified a dozen supplements that according to government warnings and adverse-event reports were too dangerous to be on the market. However, the following unsafe supplements were still available at that time in retail stores or by shopping online: *Aristolochia* (linked to kidney failure and cancer), *yohimbe* (linked to heart and respiratory problems), *bitter orange* (linked to high blood pressure, heart attacks and stroke), and *chapparal*, *comfrey*, *germander*, and *kava* (linked to liver failure). These products and others listed in *Consumer Reports'* "dirty dozen" (*Dangerous Supplements*), can have many other trade names. For details, consult *Natural Medicines Comprehensive Database*.

Fraudulent Products

Consumers need to be on the lookout for fraudulent products. These are products that don't do what they say they can or don't contain what they say they contain. At the very least, they waste consumers' money, and they may cause physical harm. Fraudulent products often can be identified by the types of claims made in their labeling, advertising, and promotional literature. Some possible indicators of fraud, says Stephen Barrett, M.D., a board member of the National Council Against Health Fraud, are

- Claims that the product is a secret cure and use of such terms as "breakthrough," "magical," "miracle cure," and "new discovery." "If the product were a cure for a serious disease, it would be widely reported in the media and used by health care professionals," he says.
- Claims that a product is backed by scientific studies, but with no list of references or references that are inadequate. For instance, if a list of references is provided, the citations cannot be traced, or if they are traceable, the studies are out-of-date, irrelevant, or poorly designed.

Quality Products

The growing market for supplements, with fewer regulations, creates the potential for quality-control problems. For example, the FDA has identified several manufacturers that were buying herbs, plants, and other ingredients without first adequately testing them to determine whether the product they ordered was actually what they received, whether the ingredients were free from contaminants, and were of the strength stated.

To help protect themselves, consumers should:

- Look for ingredients in products with the U.S.P. notation, which indicates that the manufacturer followed standards established by the U.S. pharmacopeia.

- Realize that the label term "natural" doesn't guarantee that a product is safe. "Think of poisonous mushrooms," says Elizabeth Yetley, Ph.D., Director of FDA's Office of Special Nutritionals. "They're natural."
- Consider the name of the manufacturer or distributor. Supplements made by a nationally known food and drug manufacturer, for example, have likely been made under tight controls because these companies already have in place manufacturing standards for their other products.
- Write to the supplement manufacturer for more information. Ask the company about the conditions under which its products were made.
- Avoid products sold for considerably less money than competing brands.

Reading and Reporting

Consumers who use dietary supplements should always read product labels, follow directions, and heed all warnings.

Supplement users who suffer a serious harmful effect or illness that they think is related to supplement use should call a doctor or other health care provider. He or she, in turn, can report it to the FDA MedWatch by calling 1-800-FDA-1088 or going to https://www.accessdata.fda.gov/scripts/medwatch/medwatch-online.htm on the MedWatch website. Patients' names are kept confidential.

Much remains unknown about many dietary supplements regarding their health benefits and potential risks. Therefore, consumers who decide to take advantage of the expanding market should do so with care, making sure to have the necessary information and consulting with their doctors regarding any health conditions that could be compromised or any medications they are taking that may interact adversely with the herbs. "The majority of supplement manufacturers are responsible and careful," FDA's Yetley says. "But, as with all products on the market, consumers need to be discriminating. FDA and industry have important roles to play, but consumers must take responsibility, too."

Your responsibility as a health care provider includes warning your clients, and others who may seek your advice, regarding the dangers of taking products not approved by the FDA and not adequately tested. You must also caution them about the possibility of fraudulent products and lack of quality control. Most importantly, you must warn them about possible interactions with the medicines they are taking and the potential for serious adverse reactions. Issue special warnings to diabetics and those taking cardiac drugs or anticoagulants because of the increased risk of very serious interactions and problems.

All of the herbal remedies on the market are too numerous to mention in this book. However, you will find some of the more popular ones, along with cautions or interactions known at this time, listed in Table 11-3. Stay informed. Some sources of current information are listed at the end of the chapter. See Table 11-3 for a list of some herbs, possible uses, cautions, and interactions.

Table 11-3 Herbs

HERBS[a]	POSSIBLE USES[b]	POSSIBLE SIDE EFFECTS, CAUTIONS, INTERACTIONS
Aloe vera	Topical use for minor burns, shallow wound healing	Not for deep, surgical wounds Can interact with diuretics to potentiate potassium loss
Black cohosh	Phytoestrogen for menopausal symptoms and premenstrual syndrome (PMS)	! Can cause bradycardia Do not take with estrogen or with history of breast cancer
Capsaicin	Topical pain reliever, anti-inflammatory for arthritis For post-herpetic neuralgia and neuropathy	Local burning sensation, may fade with time
Chamomile	Sedative tea, insomnia, nausea	Those allergic to pollens; e.g., ragweed, may be allergic to it
Chondroitin Sulfate	Anti-inflammatory for arthritis	Occasional mild GI effects Reliability of content varies Shark cartilage or cattle cartilage may be contaminated
Echinacea	Proven *ineffective* in 2005 studies for prevention and treatment of colds	Can cause allergies and rashes Contraindicated in those with autoimmune disease; e.g., HIV, MS, or lupus, and chronic use, longer than eight weeks
Ephedra	Banned by the FDA in 2004 due to danger of heart problems and stroke	
Flaxseed oil	For constipation Source of omega-3 fatty acids Possibly anti-inflammatory	! May interact with anticoagulants to cause bleeding Diarrhea possible
Feverfew	Migraine headaches, prevention and treatment	No toxic reactions known Sensitive individuals may develop dermatitis from external contact
Garlic	To lower blood pressure and cholesterol Anti-infective, immune enhancing	! Risk of bleeding with anticoagulants Nausea, vomiting, diarrhea, heartburn, flatulence
Ginger	Nausea, motion sickness	Doses higher than 6 g can cause gastric irritation
Gingko (GBE)	Antidepressant, anxiolytic, antioxidant Proven ineffective in a 2008 study for prevention or slowing of dementia or Alzheimer's disease	! May interact with anticoagulants to cause bleeding and strokes Rare GI upset, headache

Table 11-3 Herbs—*continued*

HERBS[a]	POSSIBLE USES[b]	POSSIBLE SIDE EFFECTS, CAUTIONS, INTERACTIONS
Ginseng	Antistress, antifatigue	Not for long-term use ! May cause hypertension, nausea, vomiting, diarrhea, nervousness, mental changes Contraindicated in pregnancy
Glucosamine	Anti-inflammatory for arthritis	! Elevated cholesterol ! Insulin resistance, higher blood glucose
Kava	FDA warning March 2002 Banned in Canada, Germany, So. Africa and Switzerland	Possible liver damage, often irreversible; deaths reported
Licorice	Anti-infective, for cough, anti-inflammatory, menopausal symptoms, PMS, peptic ulcer—deglycyrrhizinated licorice (DGL)	Hypertension, fluid retention Do not take with diuretics as it enhances potassium loss; decreases effects of antihypertensive drugs
Melatonin	For insomnia, improves sleep cycle, especially with older adults and for jet lag Boosts immune system Antioxidant protection	Side effects rare, nightmares Contraindicated in pregnancy
SAM-e	Anti-inflammatory for osteoarthritis and fibromyalgia Antidepressant	Not to be taken with other antidepressants Not for severe depression or bipolar disorder Package should be airtight and lightproof; not stable
Saw palmetto	For benign prostatic hypertrophy (BPH) Antiandrogen	Rare GI upset See a physician for diagnosis and treatment
Soy	Menopause symptoms Phytoestrogen Cancer-preventing qualities	No known side effects Counteracts thyroid medicine ! Do not take together
St. John's wort	Mild to moderate depression Not for severe depression or bipolar disorder	Photosensitivity—may cause hives Insomnia, irritability, headache Do not combine with other antidepressants or alcohol Interacts with warfarin, oral contraceptives, anticonvulsants, digoxin, theophylline, and other drugs
Valerian	For anxiety, insomnia	Morning-after drowsiness Avoid during pregnancy Short-term use only

[a]The listing of these herbs does not constitute a recommendation for their use. This is only a representative list of some of the more popular herbs and those that could be problematic. There are many others on the market. Always check current, reliable references for the most up-to-date information regarding dosage, adverse effects, and interactions.

[b]Although some of the herbs listed here have been tested for use with the conditions mentioned, *they are not approved by the FDA. There is no guarantee that they will help the condition. There is always the possibility of adverse effects. Use with caution and at your own risk.*

PATIENT EDUCATION

Dietary Supplements

Patients should be instructed regarding:

- Consulting a physician or pharmacist before taking any "herbal remedies." Some herbs may be contraindicated with certain diagnoses.
- Taking a list of all products you are using, including herbal remedies, herbal teas, vitamins and minerals, OTC (nonprescription) medicines, and prescription drugs to a physician or pharmacist. Many of these products can interact, with dangerous, even life-threatening results. Physician consult is important before starting any "alternative medicines." Do not mix prescription drugs and herbal remedies for the same condition.
- The fact that "natural" does not mean "safe."
- Not taking more than the recommended amount listed on the label. Even vitamins and minerals in excess of the RDA or DRI can cause serious problems. Herbs that may be safe in small doses could be harmful at larger doses or over a prolonged period of time. Products without dosage recommendations should be avoided.
- All products should carry a lot number, expiration date, and manufacturer's name, address, and phone number. Products should be *avoided* that lack this information, or that claim an effect on the body's structure or function, or claim to be able to cure a disease or condition.
- Herbal products should be stored away from young children and pets.
- Herbal products should not be used for children without the approval of a pediatrician.
- Herbal remedies should not be used if you are pregnant, trying to become pregnant, or nursing.
- These products should not be taken with alcohol without first determining the safety of such a combination.
- These products should not be used as a substitute for proper rest and nutrition. A balanced diet is necessary for good health.

Following are some of the references used in preparing the Alternative Medicine section of this book. You may find these resources useful in researching information for your patients and yourself. The most current information can frequently be found on the Internet; several Web sites are also listed. Be sure the Web sites are reliable, i.e., sites maintained by the government or pharmacists.

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The U.S. Department of Agriculture provides general information and resources at www.nal.usda.gov/

CASE STUDY – A

Vitamins and Minerals

LaQuinta Jackson, a 30-year-old secretary, calls the physician's office asking for a prescription for iron because she feels tired and weak. The patient should be given the following information:

1. No iron medication should be taken before first taking all the following steps EXCEPT
   a. Checking hemoglobin
   b. Assessing all symptoms
   c. Trying multivitamins
   d. Determining cause of deficiency
2. Symptoms of iron deficiency may include all of the following EXCEPT
   a. Nausea and diarrhea
   b. Pale skin
   c. Air hunger
   d. Dizziness
3. Iron is found in all of the following foods EXCEPT
   a. Liver
   b. Spinach
   c. Milk
   d. Red meat
4. Oral iron products can cause all of the following EXCEPT
   a. Constipation
   b. Diarrhea
   c. Black stools
   d. Nervousness
5. Iron products should be taken with which one of the following?
   a. Coffee
   b. Tea
   c. Orange juice
   d. Milk

CASE STUDY – B

Vitamins and Minerals

Jose Rodriquez, a 40-year-old physical education instructor, comes to the health fair to get the latest advice on vitamin C supplements "to prevent colds, cancer, and premature aging." He should receive the following advice:

1. Vitamin C can be found naturally in all of the following foods EXCEPT
   a. Citrus
   b. Broccoli
   c. Cabbage
   d. Cheese
2. All of the following *decrease* vitamin C levels EXCEPT
   a. Smoking
   b. Alcohol
   c. Raw vegetables
   d. Slow cooking
3. Megadoses of vitamin C can cause all of the following EXCEPT
   a. Constipation
   b. Gouty arthritis
   c. Kidney stones
   d. GI distress
4. Functions of vitamin C include all of the following EXCEPT
   a. Healing of wounds
   b. Absorption of iron
   c. Prevention of liver disease
   d. Prevention of scurvy
5. Vitamin C interacts with all of the following drugs EXCEPT
   a. Tetracycline
   b. Estrogen
   c. Aspirin
   d. Tylenol

CHAPTER REVIEW QUIZ

Multiple Choice

1. Which is *not* true of antioxidants?
   a. Inhibit cell breakdown in damaged tissue
   b. Consist of enzymes, vitamins, and minerals
   c. Only found in synthetic products
   d. Fight free radicals
2. Free radical damage can be associated with all of the following conditions EXCEPT:
   a. Stunted growth
   b. Inflammatory conditions
   c. Heart disease
   d. Immunosuppression
3. Which is *not* an antioxidant vitamin?
   a. Ascorbic acid **c.** Vitamin B
   b. Beta carotene **d.** Vitamin E
4. Which is *not* an antioxidant mineral?
   a. Copper **c.** Zinc
   b. Selenium **d.** Iron
5. Which of the following statements is true?
   a. Patients should stop taking antioxidants during chemotherapy.
   b. Patients should continue antioxidants during radiation therapy.
6. When buying dietary supplements, you should look for which term on the label?
   a. Natural **c.** U.S.P.
   b. FDA **d.** New discovery
7. All of the following herbs can interact with anticoagulants to cause bleeding EXCEPT:
   a. Flaxseed oil **c.** Gingko
   b. Garlic **d.** Ginseng
8. Which is *not* true of glucosamine?
   a. Always combined with chondroitin
   b. Can elevate cholesterol
   c. Anti-inflammatory
   d. Can raise blood glucose
9. Which is *not* true of soy products?
   a. For menopause symptoms
   b. Phytoestrogens
   c. Counteract thyroid meds
   d. Can cause bradycardia

10. Which is *not* true of St. John's wort?

a. Interacts with oral contraceptives
b. Can be combined with SSRIs
c. Causes photosensitivity
d. For moderate depression

Go to your StudyWARE™ CD-ROM and have fun learning as you play games and answer case study-related questions to help reinforce key concepts you learned in this chapter.

Go to your Study Guide and complete the review questions for this chapter.

Chapter 12

Skin Medications

Objectives

Upon completion of this chapter, the learner should be able to

1. Describe application procedures for various skin medications
2. Identify side effects of the seven major categories of skin medications and contraindications when appropriate
3. Compare and contrast scabicides and pediculicides
4. Explain the factors that influence the absorption of skin medications
5. Classify drugs according to their action: antipruritic, emollient, keratolytic, enzymatic, antifungal, anti-infective, or agents to treat acne
6. List five possible side effects of long-term topical corticosteroid therapy
7. List five contraindications for topical corticosteroid therapy
8. Describe important patient education for all skin medications in this chapter
9. Define the Key Terms and Concepts

Key Terms and Concepts

Antifungals
Antipruritics
Antiseptics
Antiviral
Bactericidal
Emollients
Enzymatics
Keratolytics
Protectants

The skin is the largest organ of the body. Since such a great area is involved, many conditions can affect the skin, causing annoyance and discomfort. Skin ailments can range from minor ones, such as pruritus (itching), to major ones, such as severe burns. Treatment is usually topical or local (applied to the affected area), but skin conditions are sometimes treated internally with oral medications or injections for their systemic effects.

This chapter primarily explains topical medications. Medications given parenterally or orally to relieve inflammation or itching, such as corticosteroids and antihistamines, are discussed more extensively in other chapters.

Topical skin preparations can be classified according to action in eight principal categories

1. Antipruritics relieve itching.
2. Emollients and protectants soothe irritation.
3. Keratolytic agents loosen epithelial scales.
4. Enzymatic agents promote the removal of necrotic or fibrous tissue.
5. Scabicides and pediculicides treat scabies or lice.
6. Antifungals control fungus conditions.
7. Local anti-infectives prevent and treat infection.
8. Agents to treat acne.

Factors that influence the rate of absorption of medication include condition and location of the skin, heat, and moisture. If the skin is thick and callused, absorption will be slower. If the skin is moist, macerated (raw), or warm, absorption will be more rapid. Sometimes the physician will order that the skin be premoistened or plastic wrap be applied over the ointment to aid absorption; in other cases, the skin must be left exposed to the air to slow absorption and reduce systemic effects. At times, the length of time for the medication to remain on the skin is very important. Complete understanding of appropriate directions for each topical medication is vital before administration.

ANTIPRURITICS

Antipruritics are used short term to relieve discomfort from dermatitis (rashes) associated with allergic reactions, poison ivy, hives, and insect bites. They relieve itching by use of products singly or in combination containing:

Local anesthetics (e.g., the "-caines," such as benzocaine, dibucaine)

Drying agents (e.g., calamine)

Anti-inflammatory agents (e.g., corticosteroids) applied locally or given PO for systemic effect. Use should be avoided in patients with pruritus without inflammation. Topical agents are preferred because of fewer adverse effects.

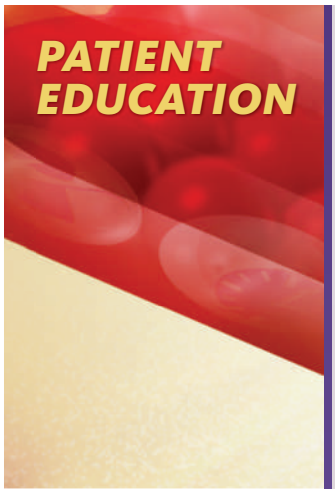
Antihistamines administered PO for systemic effect (antihistamines applied topically can cause hypersensitivity reactions—use only a few days)

See Chapter 26 for further information on antihistamines.

Side effects of antipruritics can include:

- Skin irritation, rash

  Stinging and a burning sensation
- Allergic reactions (especially with the "-caines")
- Sedation from antihistamines PO or paradoxical agitation in children. Nonsedating antihistamines may be as effective in the treatment of pruritus.



Patients being treated with antipruritics should be instructed to:

- Clean area thoroughly before application
- Rub in gently until medication vanishes
- Use caution if they have allergies
- Avoid contact with eyes or mucous membranes
- Avoid covering with dressings unless directed by physician
- Avoid prolonged use (not longer than one week)
- Discontinue if condition worsens or irritation develops
- Trim children's fingernails to reduce possibility of infection from scratching

Contraindications to antipruritics include:

On open wounds for corticosteroids—healing delayed

For prolonged use (especially corticosteroids)

Hypersensitivity (severe allergic) reaction to the active drug or any component of the formulation

CORTICOSTEROIDS

The corticosteroids are used *both topically and systemically* to treat dermatological disorders associated with allergic reactions. Most topical steroids are available in a variety of dosage forms and potencies (low, medium, high, very high); the choice depends upon the area affected and the condition being treated. Topical corticosteroids are also used to treat psoriasis and seborrheic dermatitis.

See Chapter 23, Endocrine System Drugs, for more in-depth information regarding corticosteroids.

Side effects of corticosteroid ointments and creams, especially used long term (e.g., psoriasis), can include:

- Epidermal thinning, with frequent skin tears, increased risk of infection, and frequent bruising
- Increased fragility of cutaneous blood vessels

Irritation, burning, or stinging

Ulceration, especially with occlusive dressings

- Activation of latent infections and slow healing

Hyperglycemia, glycosuria, and Cushing's syndrome, with *prolonged use* of *high-potency* products

Contraindications with corticosteroids include:

Skin infections, bacterial or fungal, and cutaneous (skin) or systemic viral infections

Open wounds

Hypersensitivity (severe allergic) reaction to the active drug or any component of the formulation

EMOLLIENTS AND PROTECTANTS

Emollients and **protectants** are used topically to soothe, protect, and seal out wetness in minor dermatological conditions, such as diaper rash, irritation, abrasions, and minor burns.

KERATOLYTICS

Keratolytic agents, for example, salicylic acid, are used to control conditions of abnormal scaling of the skin, such as dandruff, seborrhea, and psoriasis or to promote peeling of the skin in conditions such as acne, hard corns, calluses, and warts. Antifungals are also used at times for seborrheic dermatitis and dandruff. (See Table 12-1.)

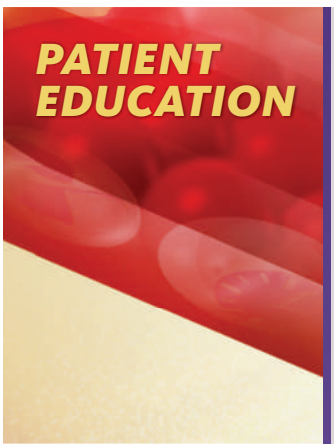
Side effects can include:

- Severe skin irritation, pruritus, or stinging
- Irritation to eyes or mucous membranes
- Photosensitivity
- Systemic effects in allergic individuals or with multiple applications and prolonged use (e.g., headache and GI symptoms)

Contraindications for keratolytics include:

Open areas of skin

Hypersensitivity (severe allergic) reaction to the active drug or any component of the formulation



Keratolytics

Patients should be instructed to:

Use only as directed, and for entire treatment period, even if improved

Avoid contact with eyes and mucous membranes

Avoid prolonged use

Discontinue and seek medical aid if irritation occurs

Avoid contact with surrounding tissues when applied as a caustic agent to corns or calluses

ENZYME PREPARATIONS

Bedridden patients are prone to decubitus (pressure sores); diabetics, to foot ulcers. Collagenase (Santyl) is a topical enzyme ointment used for the chemical debridement (removal of dead or damaged tissue) of dermal ulcers and

burns. Collagenase should only be used on wounds associated with necrotic (dead) material. If a topical antibiotic is to be applied to an infected site, the antibiotic is applied before collagenase. Avoid using detergents, povidone-iodine, and heavy metal (e.g., mercury, silver) containing agents which will inhibit the enzymatic activity of collagenase.

See Table 12-1 for Antipruritics, Emollients and Protectants, Keratolytics, and Enzyme Preparations.

Table 12-1 Topical Medications for the Skin: Antipruritics, Emollients and Protectants, Keratolytics, and Enzymatics

GENERIC NAME	TRADE NAME	AVAILABLE	COMMENTS
Antipruritics			
Local Anesthetics			
benzocaine	Lanacaine, Americaine, Orajel	Ointment, spray, gel, lotion, cream	Can cause hypersensitivity reaction
dibucaine	Nupercainal	Ointment	Potential for hypersensitivity
Antihistamine			
diphenhydramine	Benadryl	Lotion, cream, gel, spray	Not as effective as oral
Corticosteroids			
various	Cortaid, Topicort, Lidex, Kenalog, Synalar, others	Ointment, cream, lotion, solution	Also used for psoriasis and seborrhea
Emollients and Protectants vitamins A and D, **topical**	A & D	Ointment	
	Desitin (with zinc oxide)	Ointment	
Keratolytics			
coal tar	Balnetar, Polytar, Neutrogena T/Gel	Shampoo, oil, cream, lotion, ointment, soap	For dandruff, seborrheic dermatitis, or psoriasis (stains clothing)
salicylic acid	Clearasil, Salex, Compound W	Cream, liquid, gel, patches	For dandruff, psoriasis, acne, warts, corns, calluses
sulfur	Many combinations with other keratolytics	Cream, lotion, shampoo, soap	For acne, scabies, seborrheic dermatitis
Enzyme Preparations			
collagenase	Santyl	Ointment	For use on necrotic skin tissue only

Note: This table lists only typical medications and does not include all of those on the market.

SCABICIDES AND PEDICULICIDES

See It In Action! Go to the StudyWARE™ CD-ROM to view a video on *Ointments*.

Scabies is caused by an itch mite that burrows under the skin. Pediculosis is caused by infestation of lice on the hairs of the scalp, pubic area, and trunk. Both are easily transmitted from one person to another by direct contact or through contact with contaminated clothing or bed linens. Effective treatment includes laundering in hot water or dry cleaning all clothing and bedding. Sometimes concurrent treatment of close contacts is recommended.

Scabicides (permethrin or lindane) must be applied *according to directions* on the package insert, left in place the required period of time, and then rinsed thoroughly.

Pediculicides, for example, lindane, are used in topical treatment of lice infestations. Pyrethrins (e.g., RID), are considered safer for pediculosis.

Side effects, rare when applied topically according to directions, may include:

Slight local irritation, rash, or conjunctivitis

Dermatitis with frequent application

However, with excessive or prolonged use, or with oral ingestion, or inhalation of vapors, CNS symptoms and hepatic or renal toxicity may occur. Anemia and seizures have been reported, especially with lindane. Therefore, lindane should be used only in patients who cannot tolerate or have failed first-line treatment with safer medications for the treatment of lice.

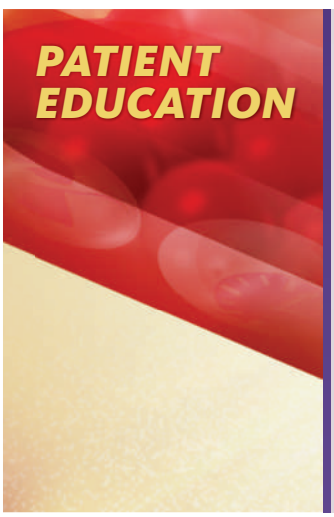
Contraindications include:

Acutely inflamed, raw, or weeping surfaces

Since lindane can be absorbed systemically following topical application, it should be avoided during pregnancy, lactation, or with infants, children, older adults, and those who weigh less than 110 pounds, or those with known uncontrolled seizure disorders.

However, permethrin is a safer alternative under these conditions for scabies. Pyrethrins (e.g., RID) are a safer alternative than lindane for pediculosis.

Due to the toxicity of lindane, the oral antiparasitic agent ivermectin (Stromectol) has been used successfully as an alternative (off-label) to treat mass scabies outbreaks in an institutional setting and to treat head lice resistant to standard therapies. It is given orally as a single dose (weight-based), with a repeat dose 10–14 days later.



Patients being treated with scabicides or pediculicides should be instructed to:

- Follow directions carefully (read and understand the medication guide dispensed with the lindane prescription); itching may still occur after the successful killing of lice and is not necessarily an indication for retreatment with lindane shampoo
- Thoroughly launder clothing and bedding
- Use caution to prevent accidental oral ingestion
- Use caution with infants who might suck their thumbs
- Inform sexual partner if condition is present in pubic area
- Alert school if head lice infestation occurs

ANTIFUNGALS

Antifungals, for example, nystatin (Mycostatin), are useful in the treatment of monilial infections (candidiasis), such as thrush, diaper rash, vaginitis, athlete's foot, and jock itch. Antifungals are also combined with corticosteroids, for example, Lotrisone (betamethasone/clotrimazole).

Effective treatment includes topical administration according to directions on the package insert and good hygiene practices, including washing, drying, and exposure to air when possible.

For the treatment of candidiasis of the oral cavity, an oral suspension administered four times daily or oral lozenges (e.g., Mycelex Troches) administered five times daily for 14 days are equally effective. For infants, administer after the feeding, which is followed by water to rinse mouth *before therapy.* Place one-half dose in each side of the mouth. For adults, apply *after meals* and *after rinsing* of mouth. Then the entire dose should be used to thoroughly coat inside the mouth, holding for as long as possible (e.g., several minutes), before swallowing. In both cases, the patient should be NPO for at least one hour after treatment.

With inadequate response to treatment, cultures should be obtained to confirm the diagnosis and assist in the selection of the most appropriate medication.

Side effects, although rare, may include:

Contact dermatitis

Itching, burning, and irritation

Contraindication or caution applies to the use of vaginal preparations during pregnancy. Use only under medical supervision. Some products can cause fetal abnormalities.

PATIENT EDUCATION

Patients being treated with antifungals should be instructed to:

- Carefully wash and *dry* affected areas
- Expose to air whenever possible
- With genital fungus, avoid tight undergarments, pantyhose, and wet bathing suits
- With athlete's foot, use open sandals instead of sneakers
- *Follow application instructions carefully.* Use for entire time, even if asymptomatic
- Remove any stains with soap and warm water
- Continue prescribed vaginal treatment even during menstruation, or if symptomatic relief occurs, until entire regimen is completed
- Consult doctor before vaginal preparations are used during pregnancy
- For oral suspensions or lozenges, apply after meals and after thorough rinsing of mouth. No food or liquids for at least 1 h after treatment.
- For vaginal infections, refrain from intercourse until treatment is complete
- Consider treating partner if reinfection occurs

ANTIVIRALS

Acyclovir has an **antiviral** effect on herpes simplex (cold sores or genital herpes), herpes zoster (shingles), and varicella zoster (chickenpox) viruses. Acyclovir (Zovirax) is available in oral and parenteral preparations (see Chapter 17), or applied topically. Zovirax *cream* is indicated *only* for the treatment of cold sores. Topical therapy is substantially less effective than systemic therapy (parenteral or oral). Topical acyclovir therapy is *not a cure*, and does not reduce the frequency or delay the appearance of new lesions. However, topical therapy generally decreases the duration of viral shedding, the duration of pain and itching, and the time required for crusting and healing of lesions. It is effective in first episode genital herpes infection, but recurrent infections have shown little, if any, therapeutic benefit from topical therapy. The ointment should be applied as soon as possible following onset of signs and symptoms of infections. Take care not to get the ointment in the eyes. It is *not effective in preventing infections.*

For more effective treatment of herpes zoster (shingles), acyclovir (Zovirax) is available orally. Valacyclovir (Valtrex) is a derivative of acyclovir, which can be dosed less frequently, improving patient compliance. *Both of these oral antivirals need to be started within 72 hours of rash onset and are most effective if started within the first 48 hours of onset.* (See Chapter 17 regarding a vaccine to prevent shingles.)

Antibacterial Agents

Mupirocin (Bactroban) is an antibiotic that is structurally unrelated to any other topical or systemic antibiotics. Mupirocin ointment is used topically to treat impetigo caused by *Staphylococcus aureus* and certain species of *Streptococci*. The ointment is used to treat secondarily infected traumatic skin lesions. Mupirocin nasal ointment is applied intranasally to reduce the risk of infection in patients with high risk during institutional outbreaks of MRSA (methicillin-resistant strains of *Staphylococcus aureus*).

There are many other prescription and over-the-counter (OTC) topical antibacterial agents on the market, including ointments, creams, and solutions too numerous to mention here. These products have the potential for adverse side effects, including local, hypersensitivity, and systemic reactions. Overuse or extended use of antibacterial agents can also lead to *resistance*. For further information regarding antibacterial agents, see Chapter 17, Anti-infective Drugs.

See Table 12-2 for a summary of Scabicides, Pediculicides, Antifungals, Antivirals and Antibacterials.

LOCAL ANTI-INFECTIVES

Antiseptics

Antiseptics are substances that inhibit the growth of bacteria (bacteriostatic). The term is used most frequently to describe chemicals applied to body tissues, especially the skin. *Disinfectants* are included in this category, but chemicals that kill bacteria (**bactericidal**) are frequently too strong to be

Table 12-2 Medications for the Skin: Scabicides, Pediculicides, Antifungals, Antivirals, and Antibacterials

GENERIC NAME	TRADE NAME	AVAILABLE	COMMENTS
Scabicides and Pediculicides			
permethrin	Acticin, Elimite	Cream, lotion	Apply from head to feet, wash off after 8–14 h
	Nix	Liquid	Apply to hair, to remain 10 min
	A-200, RID	*Spray*	For use on inanimate objects only
lindane		Lotion, shampoo	Treat all hairy areas Toxic potential
pyrethrins	RID, A-200	*Gel, shampoo, solution*	For lice only
Antifungals[a]			
terbinafine	Lamisil AT Lamisil	Cream, gel, spray, tabs	Oral form very effective for onychomycosis
clotrimazole	Mycelex, Lotrimin Gyne-Lotrimin	Troches, cream, lotion, sol, vaginal cream & supps,	For oral, topical, or vaginal application
ketoconazole	Nizoral	Cream, shampoo	Topical antifungal, shampoo for dandruff
miconazole	Monistat Lotrimin AF	Cream, gel, ointment *Powder, Spray*	Also vaginal cream & supps
nystatin	Mycostatin	Oral suspension, tabs, lozenges, cream, ointment, vaginal tab, powder	Apply oral suspension or lozenges PC, then NPO 1 h
tolnaftate	Tinactin	Aerosol spray, cream, powder, solution, gel	Avoid inhaling spray or powder
Antivirals			
acyclovir	Zovirax	Cream	For cold sores only: 5x/day for 4 days
		Ointment, orally[a]	6x/day (q3h) x7 days
valacyclovir	Valtrex	Orally[a]	
Antibacterials			
mupirocin	Bactroban	2% cream, ointment	Avoid contact with mucosa and eyes

[a]Oral preparations and dosing are discussed in Chapter 17.
Note: Other preparations are available. This is a representative list.

applied to body tissues and are *usually* applied to inanimate objects, such as furniture, floors, and instruments. Sometimes a chemical can be used as an antiseptic on skin and also as a disinfectant on inanimate objects by increasing the strength.

The two major antiseptics in use today are chlorhexidine and povidone-iodine, used for surgical scrubs and as bacteriostatic skin cleansers. Some iodine preparations are also bactericidal and are used in the treatment of superficial skin wounds and to disinfect the skin preoperatively. Chlorhexidine (Hibiclens) should not be used on wounds involving more than the superficial layers of skin. It is important to rinse thoroughly after use.

Side effects of chlorhexidine can include:

- Dermatitis and irritation
- Photosensitivity (increased reaction such as burn from brief sun exposure)
- Allergic reactions, especially in the genital area

Side effects of povidone-iodine (Betadine) can include:

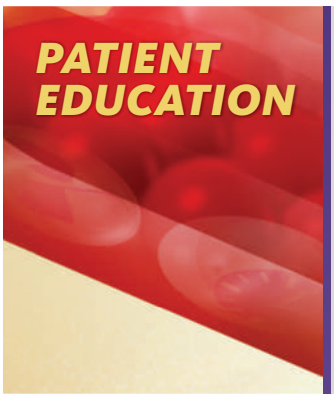
- Skin irritation or burns
- Allergic reactions

Contraindications/warnings for chlorhexidine include:

- Pregnancy category B
- Not for frequent use for total body bathing
- Not for use in eyes and ears

Povidone-iodine contraindications/warnings include:

- Not for those allergic to iodine
- Not for use on open wounds
- Not for use in newborns (risk of iodine absorption)



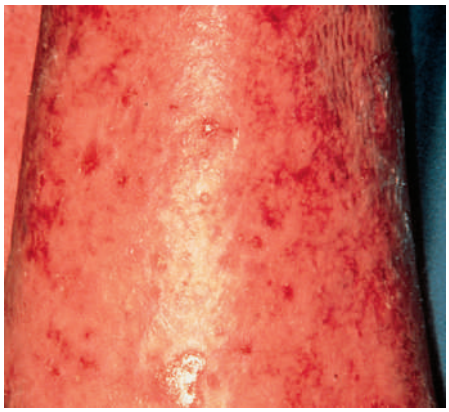
Patients being treated with local anti-infectives should be instructed to:

- Rinse chlorhexidine *thoroughly*
- Avoid chlorhexidine for total body bathing or frequent use
- Avoid use of chlorhexidine on open skin lesions, mucous membranes, and genital areas
- Take care to avoid chlorhexidine or povidone-iodine in the eyes or ears; flush thoroughly
- Use caution with povidone-iodine in anyone with allergies

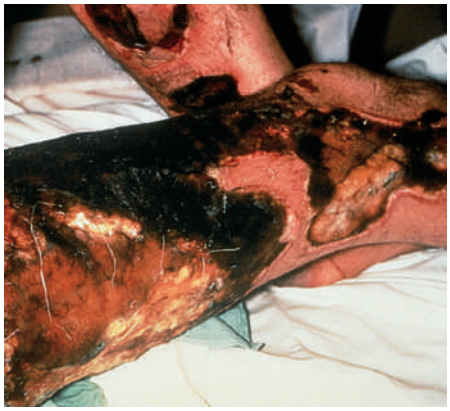
Burn Medications

Burn treatments include topical application of medications to prevent or treat infections. The two most commonly used agents for this purpose are silver sulfadiazine (Silvadene) and mafenide (Sulfamylon). These agents should be applied with a sterile-gloved hand. See Figure 12-1 which shows the various types of burns.

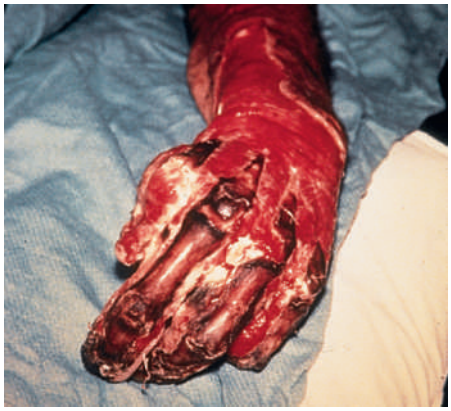
A. First-Degree Burn



B. Second-Degree Burn



C. Third-Degree Burn



D. Fourth-Degree Burn

Source: Courtesy of the Phoenix Society for Burn Survivors, Inc.

FIGURE 12-1 Types of burns.

Side effects of burn medications can include:

- Pain, burning, and itching
- Allergic reactions
- Staining of the skin temporarily

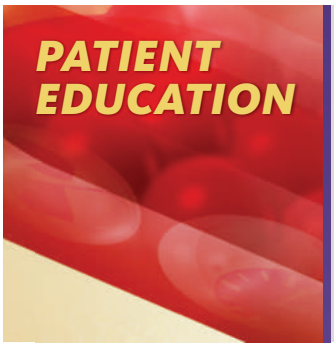
Contraindications or extreme caution applies to newborns or to patients with:

- Impaired kidney or liver function (cumulative effects)
- History of allergy, especially to sulfa drugs
- Do not use silver sulfadiazine with collagenase or trypsin-containing enzymatic debriding agents—silver will inactivate these enzymes

PATIENT EDUCATION

Patients using burn medications should be instructed to:

- Use aseptic technique to prevent infection
- Watch for allergic reactions
- Keep careful intake and output record
- Keep area covered at all times with cream and sterile dressing



Patients using any topical antibacterial agent should be instructed to:

Read and follow carefully all directions on the package

Check all ingredients carefully for possible allergies

If there is no improvement, the condition worsens, or there are other untoward reactions (e.g., inflammation, itching, rash, or swelling), stop the medication and consult a physician.

AGENTS USED TO TREAT ACNE

Acne is a common condition of the skin that affects almost everyone to some degree during the teenage years and even some people into adulthood. Acne is most commonly seen on the face, scalp, neck, chest, back, and shoulders. *Acne is graded depending upon the degree of severity from type 1 (least) to type 4 (most).*

Patients with *type 1* acne may choose from several relatively mild *non-prescription topical* medications such as sulfur, salicylic acid, and benzoyl peroxide. A patient with *type 2* acne might be *prescribed topical antibiotics*, such as, tetracycline or erythromycin. For *Type 3* acne, a course of *oral antibiotics* (tetracyclines or erythromycin—see Chapter 17) may be prescribed in addition to topical products. *Type 4 acne does not respond to topical therapy;* rather *systemic hormones ("birth control pills")* or retinoids (e.g., Accutane) may be prescribed.

Accutane, a retinoid prescribed to treat type 4 acne was taken off the market in November 2009 amid signs the drug may be linked to inflammatory bowel disease. Generic versions (e.g., isotretinoin) are still available as of this date however they may be removed from the market completely upon further investigation.

Side effects of benzoyl peroxide can include:

- Skin irritation, mild stinging, redness, dry skin

Precautions for benzoyl peroxide include:

Pregnancy, breast-feeding

Use in patients with skin diseases (dermatitis, eczema, sunburn, etc.) may increase risk of skin irritation

Benzoic acid or paraben hypersensitivity

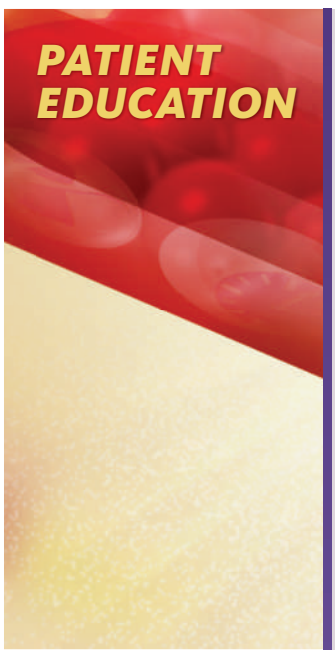
Avoid exposure to the eyes or mucous membranes, can cause severe irritation

See Table 12-3 for a summary of topical anti-infectives and antiseptics, burn medications, and acne medications. See Figure 12-2 for various skin conditions.

Table 12-3 Medications for the Skin: Topical Anti-infectives and Antiseptics, Burn Medications, and Acne Medications

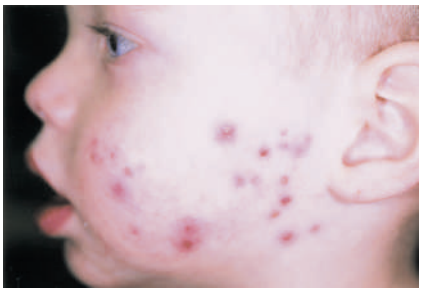
TOPICAL ANTI-INFECTIVES AND ANTISEPTICS	GENERIC NAME	TRADE NAME	AVAILABLE AS
chlorhexidine	Hibiclens	Solution, liquid, foam	Antimicrobial skin cleanser, surgical scrub; rinse thoroughly
	Peridex	Oral rinse for Tx of gingivitis	
povidone-iodine	Betadine	Aqueous solution, ointment, liquid scrub, spray	Bactericidal, antiseptic, surgical scrub; watch for allergies
Burn Medications			
silver sulfadiazine	Silvadene	Cream	Watch for allergies
mafenide	Sulfamylon	Cream, powder for solution	Watch for allergies
Acne Medications			
benzoyl peroxide	Benzac, Desquam-X, Panoxyl-5 and 10	Bar, cream, gel, liquid, lotion	Antibacterial activity Drying actions, for type 1 acne
isotretinoin	Sotret	10, 20, 30, 40 mg caps	Absolutely contraindicated in pregnancy, for type 4 acne
salicylic acid	Clearasil, Neutrogena	Cream, liquid, gel	For type 1 acne
sulfur	Many combinations with other keratolytics	Cream, lotion	For type 1 acne

Note: Other preparations are available. This is a representative list.



Patients being treated with acne agents should be instructed to:

- Use preparations every day as directed; often takes several weeks to be effective (your acne may actually get worse during the first few weeks of treatment, then start to improve)
- Do not use benzoyl peroxide with other topical acne products or retinoids
- Avoid prolonged exposure to sunlight (UV)—use sunscreen and protective clothing; avoid drugs such as sulfas that make you more sensitive to the sun
- Avoid multivitamins or nutritional supplements that contain vitamin A, tetracycline antibiotics, certain antacids (aluminum hydroxide), and certain birth control pills (progestin-only) while taking isotretinoin
- Make sure you receive, read, and understand the *Isotretinoin Medication Guide* every time you get a prescription or refill



Source: Courtesy of Robert A. Silverman, M.D., Clinical Associate Professor, Department of Pediatrics, Georgetown University.

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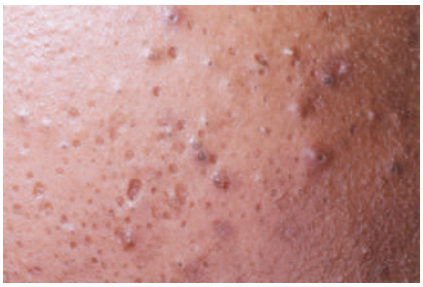

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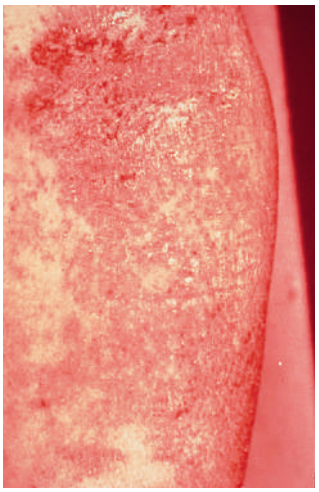

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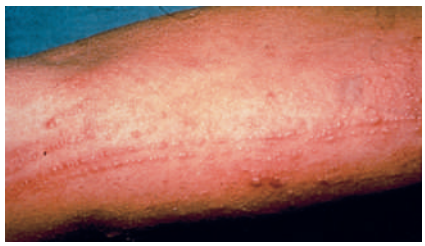

Source: Courtesy of the Centers for Disease Control and Prevention.

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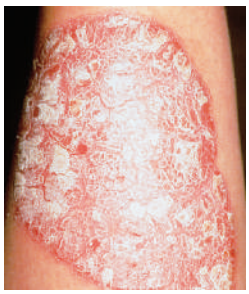

Source: Courtesy of the Centers for Disease Control and Prevention.

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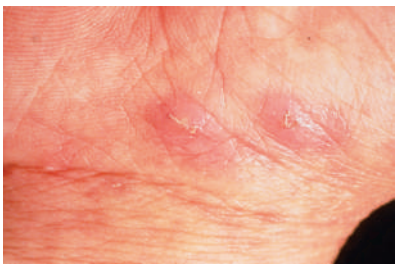

Source: Courtesy of Robert A. Silverman, M.D., Clinical Associate Professor, Department of Pediatrics, Georgetown University.

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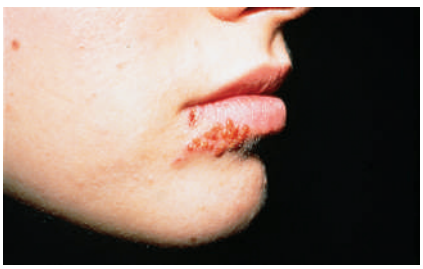

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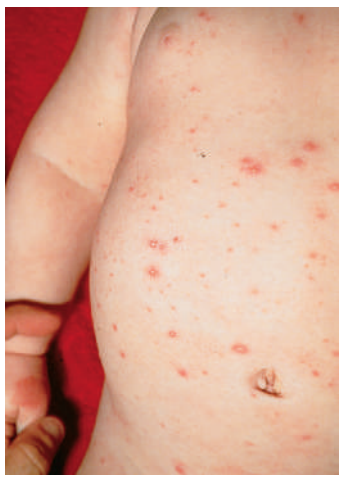

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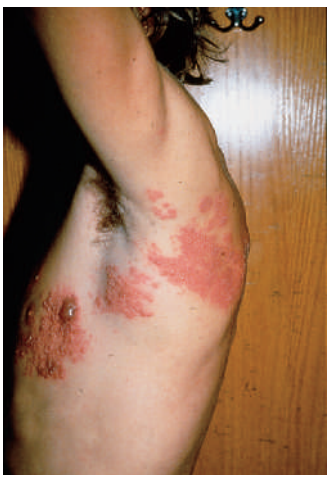


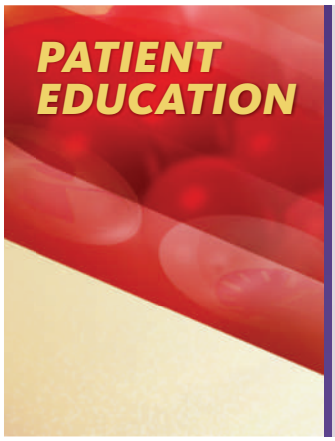
Source: Courtesy of Robert A. Silverman, M.D., Clinical Associate Professor, Department of Pediatrics, Georgetown University.

(I)

FIGURE 12-2 (A) Acne papules and nodules are visible on this child's face. (B) Acne scarring. (C) **Psoriasis.** (D) Eczema. (E) Allergic Contact Dermatitis. (F) Scabies. (G) Herpes Simplex. (H) Varicella. (I) Herpes Zoster.

CAUTIONS FOR TOPICAL MEDICATIONS

Skin medications by prescription or OTC are too numerous to mention. Many patients use products without adequate instruction in administration, side effects, or precautions. The health care practitioner has a responsibility to advise patients whenever possible to use great caution with self-medication to avoid ineffective or dangerous treatment. Both the health care practitioner and the lay person should *read instructions completely* before administration of any medication.



Patients using topical medications should be instructed regarding:

- *Never* taking by mouth
- Keeping out of reach of children
- Being sure labels are not obscured and are read completely
- Discontinuing at once with any side effects and seeking medical advice
- Not taking beyond time limit listed on medication container
- If allergies are known, avoiding self-medication without medical advice

CASE STUDY – **A**

Skin Medications

Barak Saloom, a 35-year-old male, comes to the dermatologist's office with a request for corticosteroid cream for an outbreak of psoriasis on his hands. He asks if he will be able to use the same medicine for his jock itch and athlete's foot and for an abrasion on his son's knee. He will need the following information.

1. Topical corticosteroids are contraindicated for many conditions. The only appropriate use listed below is for
   a. Open wounds
   b. Viral infections
   c. Fungal conditions
   d. Allergic reaction

2. Topical corticosteroids should be used with caution in many circumstances. Which condition would be the most appropriate use?
   a. With immunosuppression
   b. With children's rash
   c. With psoriasis
   d. With chemotherapy

3. Corticosteroid cream can be used for all of the following EXCEPT
   a. Jock itch
   b. Poison ivy
   c. Hives
   d. Insect bites

4. Side effects of prolonged use of corticosteroid cream can include all of the following EXCEPT
   a. Easy bruising
   b. Thick scabs
   c. Thin skin
   d. Slow healing

5. Other medications to treat psoriasis include keratolytics listed below EXCEPT
   a. Polytar
   b. Neutrogena T/Gel
   c. Salicylic acid
   d. Lindane

CASE STUDY – B

Skin Medications

Melody Smith goes to the physician for her 6-week postpartum check. She complains of vaginal itching and says that her baby has "white spots in his mouth." The following information would be helpful:

1. Fungal infections (candidiasis) can cause all of the following EXCEPT
   a. Thrush
   b. Acne
   c. Diaper rash
   d. Vaginitis

2. Oral candidiasis can be treated with all of the following EXCEPT
   a. Lozenges
   b. Suspension
   c. Extended-release capsules
   d. Topical application

3. Treatment for oral candidiasis includes all of the following instructions EXCEPT
   a. Treat ac
   b. Rinse first
   c. NPO after
   d. Swallow solution

4. Customary treatment of monilial vaginal infections can include all the following EXCEPT
   a. Cream
   b. Lotion
   c. NPO after
   d. Tablets

5. Treatment for vaginal monilial infections includes all of the following instructions EXCEPT
   a. Avoid tight undergarments
   b. Continue during menstruation
   c. Discontinue when better
   d. Consult M.D. if pregnant

CHAPTER REVIEW QUIZ

Multiple Choice

1. For the treatment of scabies in an extended care facility, which is the safest treatment?
   a. Lindane **c.** Ketoconazole
   b. Ivermectin **d.** Nystatin
2. Treatment for type I acne could include any of the following medicines EXCEPT:
   a. Salicylic acid **c.** Isotretinoin
   b. Sulfur **d.** Benzoyl peroxide
3. The most effective treatment for shingles includes all of the following EXCEPT:
   a. Start within 72 h **c.** Valacyclovir caps
   b. Zovirax **d.** Acyclovir ointment
4. Collagenase (Santyl) would be indicated to treat:
   a. hives **c.** dermal ulcers and burns
   b. scaly skin **d.** Psychiatric disorders
5. Mycostatin can be used to treat all of the following EXCEPT:
   a. jock itch **c.** thrush
   b. vaginitis **d.** Increased salivation
6. Which antipruritic would be most likely to cause a hypersensitivity reaction?
   a. Synalar **c.** Cortaid
   b. Benzocaine **d.** Benadryl
7. Lindane, used to treat lice infestations, is contraindicated in all of the following conditions EXCEPT:
   a. Infancy **c.** Pregnancy
   b. Older adult **d.** Obesity
8. Which statement is NOT true with chlorhexidine (Hibiclens)?
   a. Used with deep wounds **c.** Rinse after use
   b. Can cause photosensitivity **d.** Can cause dermatitis
9. An antibacterial cream used topically to treat impetigo:
   a. Lindane **c.** Mycostatin
   b. Bactroban **d.** Monistat
10. Patients with *type 1* acne would most likely be treated with:
    a. benzoyl peroxide. **c.** systemic hormones
    b. tetracycline **d.** Isotretinoin

Go to your StudyWARE™ CD-ROM and have fun learning as you play games and answer case study-related questions to help reinforce key concepts you learned in this chapter.

Go to your Study Guide and complete the review questions for this chapter.

Chapter 13

Autonomic Nervous System Drugs

Objectives

Upon completion of this chapter, the learner should be able to

1. Compare and contrast characteristics of the four categories of autonomic nervous system drugs
2. List the most frequently used (key) drugs in each of the four categories and the purpose of administration
3. Describe the possible side effects of each of the key drugs
4. Define the Key Terms and Concepts

Key Terms and Concepts

Adrenergic

Alpha-blockers

Anticholinergics

Autonomic

Beta-blockers

Cholinergic drugs

The **autonomic** nervous system (ANS) can be thought of as being *automatic*, self-governing, or involuntary. That is to say, we have no control over the action of the autonomic nervous system. The autonomic system can be divided into the sympathetic and parasympathetic nervous system. The sympathetic system is your "alert system" that can quickly ready your body to face emergencies. The parasympathetic system can be thought of as your "resting and digesting" system and automatically helps to maintain the normal day-to-day body functions. Chemical substances called *neurotransmitters* are released at the nerve endings within these systems to transmit the nerve impulses from nerve to nerve at the synapses or from nerve to muscle at the myoneural junctions.

Drugs that affect the function of the autonomic nervous system are divided into four categories based on whether they mimic or block the response of the sympathetic and parasympathetic nervous system:

1. Adrenergics (sympathomimetics = mimic sympathetic responses)
2. Adrenergic blockers (alpha- and beta-blockers = block sympathetic responses)
3. Cholinergics (parasympathomimetics = mimic parasympathetic responses)
4. Cholinergic blockers (anticholinergics = block parasympathetic responses)

ADRENERGICS

The sympathetic nervous system can be thought of as the emergency system used to mobilize the body for quick response and action. Key words to illustrate this action are *fright*, *fight*, and *flight*. If someone is startled in a dark place by a sudden motion, the body automatically mobilizes the sympathetic nerves to prepare the body to handle the fright by flight or a fight. The blood pressure, pulse, and respiration increase to supply more oxygen to the tissues. The peripheral blood vessels constrict, sending more blood inward to the vital organs and skeletal muscles needed for the fight or flight action. The bronchioles dilate to allow for a greater oxygen supply. The pupils dilate to allow more light to see the situation at hand.

The chemical substances (neurotransmitters) released at the sympathetic nerve endings are called catecholamines and include epinephrine *(adrenalin)*, norepinephrine, and dopamine. Drugs that mimic the action of the sympathetic nervous system are called sympathomimetic or **adrenergic**.

Actions of the adrenergics include:

Cardiac stimulation

Increased blood flow to skeletal muscles

Peripheral vasoconstriction

Bronchodilation

Dilation of pupils (mydriatic action)

Uses for the adrenergics include:

Restoring rhythm in cardiac arrest

Elevating blood pressure in shock of all kinds

Constricting capillaries (e.g., applied topically to relieve nosebleed or nasal congestion or combined with local anesthetics for minor surgery)

Dilating bronchioles in acute asthmatic attacks, bronchospasm, or anaphylactic reaction

Ophthalmic procedures (See Chapter 18 Eye Medications)

Side effects of the adrenergics may include:

- Palpitations
- Nervousness or tremor
- Tachycardia
- Cardiac arrhythmias
- Anginal pain
- Hypertension
- Hyperglycemia

Tissue necrosis (when applied to laceration of periphery, for example, nose, fingers, and toes)

Headache and insomnia

Contraindications or extreme caution with adrenergics applies to:

Angina
Coronary insufficiency
Hypertension
Cardiac arrhythmias
Angle-closure glaucoma
Organic brain damage
Hyperthyroidism

Caution for adrenergics also with administration; check dosage carefully (small amounts only). Give subcutaneous, IM (deltoid), or IV.

Interactions of adrenergics may occur with:

CNS drugs (e.g., alcohol, monoamine oxidase inhibitors [MAOIs], and antidepressants)
Propranolol (Inderal) or other beta-adrenergic blockers
Terazosin (Hytrin) or other alpha-adrenergic blockers

See Table 13-1 for a summary of the adrenergics.

Table 13-1 Adrenergics

GENERIC NAME	TRADE NAME	DOSAGE	COMMENTS
epinephrine	Adrenalin	0.1–0.5 mL 1:1,000 sol subcu or IM[a] (deltoid) 5–10 mL 1:10,000 sol IV	For bronchospasm, asthma, cardiac arrest, anaphylaxis
	EpiPen, EpiPen Jr.	0.3 mL (1:1000 or 1:2000) IM	
ephedrine		25–50 mg IM, subcu, or slow IV	To raise blood pressure
dopamine		2–5 mcg per kg per min IV	To raise blood pressure, cardiotonic
isoproterenol	Isuprel	0.02–0.2 mg IV or IM	For asthma or bronchospasm; for heartblock or ventricular arrhythmias
norepinephrine	Levophed	2–30 mcg per min IV	For severe shock, cardiac arrest
phenylephrine	Neo-Synephrine	0.5–9 mcg per kg per min IV	To raise blood pressure, ventricular arrhythmias

[a]Use caution with dosage. This caution applies to both dosages.

ADRENERGIC BLOCKERS

Drugs that block the action of the sympathetic nervous system are called adrenergic blockers. The most commonly used drugs in this category are the alpha- and beta-adrenergic blockers, or **alpha-blockers** and **beta-blockers**. Alpha-adrenergic blockers are discussed in Chapters 15 and 25. The prototype of the beta-adrenergic blockers is propranolol (Inderal) (Table 13-2).

Uses of the beta-blockers include treatment of the following:

Hypertension
Cardiac arrhythmias
Angina pectoris
Migraine headache

Side effects of beta-blockers may include:

- Hypotension
- Bradycardia
- Fatigue or lethargy
- Bronchospasm

Nausea and vomiting
Hypoglycemia

- Confusion

Contraindications or extreme caution applies to use of beta-blockers with:

Congestive heart failure or atrioventricular block
Hypotension

Table 13-2 Adrenergic Blockers

GENERIC NAME	TRADE NAME	DOSAGE	COMMENTS
propranolol[a]	Inderal	PO 40–160 mg daily in two divided doses	Begin with smaller dose and increase gradually to optimum dose for blood pressure control
		PO 10–20 mg 4x per d (initial dose)	For angina
		PO 10–30 mg 4x per d IV 0.5–3 mg slowly Use extreme caution	For arrhythmias
		PO 80 mg initial dose, increase to 160–240 mg daily divided doses	For migraine

[a]A beta-adrenergic blocker or beta-blocker. Others available and vary with condition (see Chapter 25).

Asthma

Diabetes

Interactions of beta-blockers may occur with:

Digoxin

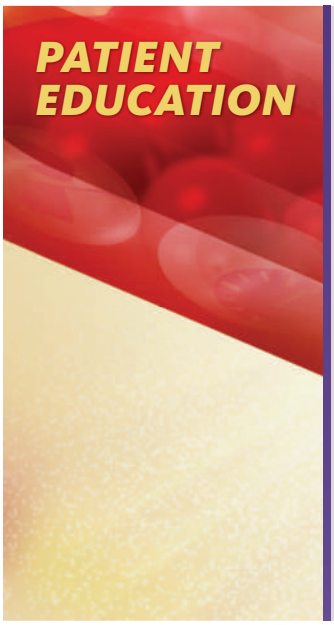
Insulin or oral antidiabetic agents

Theophylline

MAOIs and tricyclic antidepressants

Epinephrine

Alcohol



Patients taking beta-blockers, frequently given for cardiovascular disease, should be instructed regarding:

- Rising slowly from reclining position to avoid postural hypotension
- Possible slow heartbeat and reporting dizziness, difficulty breathing, or excessive weakness to the physician
- Avoiding alcohol, antihistamines, muscle relaxants, tranquilizers, and sedatives because they potentiate CNS depression and sedation
- Reporting sexual dysfunction or depression to the physician for possible dosage regulation or change to different medication
- Not discontinuing the medication abruptly, except on advice of physician
- Consulting physician or pharmacist before using over-the-counter (OTC) cold preparations

CHOLINERGICS

The parasympathetic nerve fibers synthesize and liberate *acetylcholine* as the mediator. Drugs that mimic the action of the parasympathetic nervous system are called parasympathomimetic or **cholinergic drugs** (e.g., bethanechol, neostigmine, and pilocarpine).

Actions of the cholinergics include:

Increased gastrointestinal (GI) peristalsis

Increased contraction of the urinary bladder

Increased secretions (sweat, saliva, and gastric juices)

Increased skeletal muscle strength

Lowered intraocular pressure

Constriction of pupils

Slowing of the heart

Uses for the cholinergics include treatment of:

Non-obstructive urinary retention (bethanechol)

Non-obstructive abdominal distention (neostigmine)

Myasthenia gravis (neostigmine)

Open-angle glaucoma (pilocarpine)

Side effects of the cholinergics may include:

- Nausea, vomiting, and diarrhea
- Muscle cramps and weakness
- Slowing of the heart, hypotension
- Sweating, excessive salivation, lacrimation (discharge of tears), and flushing
- Respiratory depression, bronchospasm

Acute toxicity or cholinergic crisis is treated with atropine sulfate IV. Atropine is a cholinergic blocker and thus would block the effects of a cholinergic crisis.

Contraindications or extreme caution with the cholinergics applies to:

Benign prostatic hypertrophy (BPH)

GI disorders (e.g., ulcer and obstruction)

Asthma

Cardiac disorders

Hyperthyroidism

Interactions of cholinergics may occur with:

Procainamide

Quinidine

See Table 13-3 for a summary of the cholinergics.

Table 13-3 Cholinergics

GENERIC NAME	TRADE NAME	DOSAGE	COMMENTS
bethanechol	Urecholine	10–50 mg PO 4 × per d	For postpartum or postoperative urinary retention, **not** with benign prostatic hypertrophy
neostigmine	Prostigmin	15–125 mg PO 3 × per d 0.5–2 mg IM, subcu or IV q1–3h	Treatment for myasthenia gravis Neuromuscular blockade reversal
pilocarpine	Isopto Carpine	Ophthalmic drops, dose varies	To lower intraocular pressure in glaucoma

Patients taking cholinergic drugs, or exposed to insecticides containing cholinergic agents (e.g., malathion), should be instructed regarding:

- Reporting immediately to physician or emergency room any symptoms of prolonged GI distress (e.g., nausea, vomiting, and diarrhea), excessive perspiration, slow heartbeat, or depressed respiration
- Avoiding combination of cholinergic medications with heart medications or cholinergic blockers

CHOLINERGIC BLOCKERS

Cholinergic blockers, or **anticholinergics**, are drugs that block the action of the parasympathetic nervous system. Therefore, they are also called parasympatholytic. Atropine is the classic example of a cholinergic blocker.

Anticholinergics most commonly used as preoperative medications include atropine and glycopyrrolate (Robinul). They reduce the secretions of the mouth, pharynx, bronchi, and GI tract and reduce gastric activity. Anticholinergics, as preoperative medication, also are used to prevent cholinergic effects during surgery, such as hypotension or bradycardia and some cardiac arrhythmias associated with general anesthetics or vagal stimulation. The vagus nerve is the major nerve of the parasympathetic nervous system and can be stimulated during intubation procedures and surgery. However, only *atropine* acts as a bronchodilator and reduces the incidence of laryngospasm that can occur during general anesthesia. (See Table 13-4 for anticholinergics.)

Actions include:

- Drying (all secretions decreased)
- Decreased GI and genitourinary (GU) motility
- Dilation of pupils

Uses of anticholinergics:

- Antispasmodic and antisecretory for GI or GU hypermotility
- Preoperative and preanesthetic uses
- Neuromuscular block and other spastic disorders
- Antidote for insecticide poisoning, cholinergic crisis, or mushroom poisoning
- Emergency treatment of bradycardia and atrioventricular heart block with hypotension
- Dilation of pupils (mydriatic)
- Prevention and treatment of bronchospasm (bronchodilator, e.g., Atrovent inhaler)

Side effects of anticholinergics may include:

- Fever or flushing
- ! Blurred vision, headache
- ! Dry mouth, constipation, and urinary retention
- ! Confusion and/or excitement, especially older adults
- ! Palpitations and tachycardia (abnormally fast heartbeat)

Interactions with potentiation of sedation and drying occur with antihistamines (e.g., diphenhydramine).

Contraindications or extreme caution applies to use of atropine with:

Asthma and other chronic obstructive pulmonary disease (COPD)—atropine type *inhalations of aerosols are recommended* rather than oral or parenteral administration, which can reduce and dry bronchial secretions and obstruct airflow. More on this in Chapter 26 concerning inhaled medications.

Angle-closure glaucoma

GI or GU obstruction

Cardiac arrhythmias

Hypertension

Hypothyroidism, hepatic, or renal disease

PATIENT EDUCATION

Patients receiving cholinergic blockers should be instructed regarding:

Dried secretions (e.g., dry mouth)

Possible blurring of vision

Reporting fast heartbeat or palpitations

Avoiding oral anticholinergics with chronic obstructive lung disease and asthma, using inhalants only as prescribed, never OTC

See Table 13-4 for a summary of the anticholinergics.

See Figure 13-1 for a summary of the autonomic nervous system drugs.

Table 13-4 Cholinergic Blockers

GENERIC NAME	TRADE NAME	DOSAGE[a]	COMMENTS
atropine		0.4–0.6 mg IM, IV, subcu 2 mg IM or IV qh 0.5–1 mg IV	Preoperative For insecticide or mushroom poisoning For bradycardia or atrioventricular block
glycopyrrolate	Robinul	0.1–0.2 mg IM or IV	Preoperative
propantheline	Pro-Banthine	15 mg PO AC and 30 mg at bedtime	For bladder spasm
scopolamine	Transderm Scop	72-h patch	Prevent motion sickness; reduce salivary flow
homatropine	Isopto Homatropine	Ophthalmic drops[b] dosage varies	Mydriatic

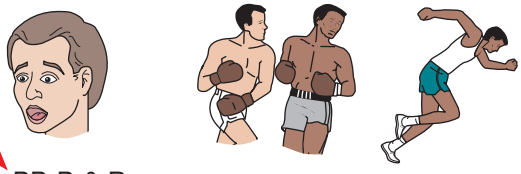
[a]Use caution to give correct dosage.
[b]Other anticholinergics used in ophthalmic conditions are discussed in Chapter 18.

The Autonomic Nervous System

Sympathetic

A = Adrenergic Action

fright fight flight



BP, P, & R. Fast

Bronchioles dilate
Pupils dilate

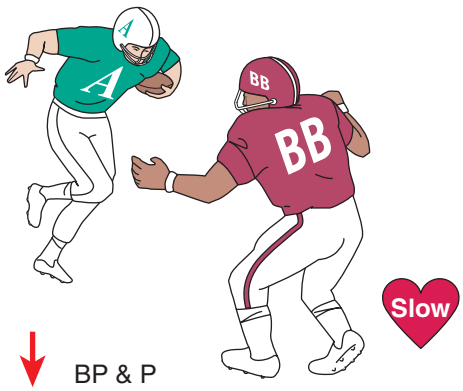
Peripheral blood vessels constrict

Adrenergic Drugs:

epinephrine (Adrenalin)
isoproterenol (Isuprel)
norepinephrine (Levophed)

Side effects: tachycardia, palpitations, hypertension, nervousness, hyperglycemia

B = β-adrenergic Blockers



Slow

BP & P

Beta-blocker:

propranolol (Inderal)

Side effects: hypotension, bradycardia, fatigue, depression, hypoglocemia

Parasympathetic

C = Cholinergic Action

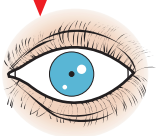
Secretion = fluids flow

Peristalsis and bladder contractions

Increased muscle strength

Respiration depressed

Slow



Pupils constrict ↓ intraocular pressure

Cholinergic Drugs:

bethanechol (Urecholine)
neostigmine (Prostigmin)
pilocarpine ophthalmic gtts

Side effects: nausea, vomiting, diarrhea, sweating, bradycardia, bronchospasm, respiratory depression.

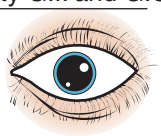
D = Cholinergic Blockers

3D (3D effects)

Drying

Decreased motility G.I. and G.U.

Dilated pupils



↑ Heart rate Fast

Anticholinergic:

Atropine

Side effects: dry mouth, urinary retention, constipation, blurred vision, confusion, tachycardia

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FIGURE 13-1 The automatic nervous system drugs can be simple as A, B, C, D.

CASE STUDY – A

Autonomic Nervous System Drugs

Shanelle Woods, a 33-year-old, receives epinephrine (Adrenalin) in the emergency room for a severe asthma attack. Health care personnel should have the following information.

1. Adrenalin has all of the following actions EXCEPT
   a. Peripheral vasodilator
   b. Dilation of pupils
   c. Bronchodilator
   d. Cardiac stimulant
2. All of the following doses of Adrenalin are appropriate EXCEPT
   a. 0.4 mL IM (deltoid)
   b. 0.3 mL subcu
   c. 5 mL subcu
   d. 1 mL IV
3. Epinephrine is also used to treat all of the following conditions EXCEPT
   a. Nosebleed
   b. Hypertension
   c. Anaphylaxis
   d. Cardiac arrest
4. Side effects can include all of the following EXCEPT
   a. Tremors
   b. Hypoglycemia
   c. Tachycardia
   d. Insomnia
5. She should be told all of the following about epinephrine EXCEPT
   a. May cause sedation
   b. Avoid alcohol
   c. May cause headaches
   d. Palpitations possible

CASE STUDY – B

Cholinergic Blockers

Milton Shapiro was brought into the emergency room with complaints of nausea, diarrhea, and sweating. He says that he "ate mushrooms found in the woods." The following information would be helpful.

1. Mushroom poisoning mimics parasympathetic nervous system (cholinergic) action with all of the following symptoms EXCEPT
   a. Increased peristalsis
   b. Urinary retention
   c. Salivation
   d. Bradycardia
2. Treatment includes cholinergic blockers. Which of the following is not a cholinergic blocker?
   a. Urecholine
   b. Pro-Banthine
   c. Atropine
   d. Scopolamine
3. Which is the drug of choice to treat cholinergic toxicity (e.g., mushroom or insecticide poisoning)?
   a. Urecholine
   b. Pro-Banthine
   c. Atropine
   d. Scopolamine
4. Side effects of cholinergic blockers include all of the following EXCEPT
   a. Dry mouth
   b. Diarrhea
   c. Urinary retention
   d. Dilated pupils
5. Other side effects of cholinergic blockers can include all of the following EXCEPT
   a. Flushing
   b. Confusion
   c. Blurred vision
   d. Bradycardia

CHAPTER REVIEW QUIZ

Match the type of drug with the action. The type of drug may be used more than once.

	Action	ANS drugs
1. _____	Increases muscle strength	**a.** Adrenergic
2. _____	Drying secretions	**b.** Adrenergic blocker
3. _____	Increases blood pressure	**c.** Cholinergic
4. _____	Increases peristalsis	**d.** Anticholinergic
5. _____	Lowers intraocular pressure	
6. _____	Antispasmodic	
7. _____	Bronchodilator	
8. _____	Lowers blood pressure	
9. _____	Constricts pupils	
10. _____	Antiarrhythmic	

Match the type of drug with possible side effects. The type of drug may be used more than once.

	Side Effects	ANS Drugs
11. _____	Bronchospasm	**a.** Adrenergic
12. _____	Hyperglycemia	**b.** Adrenergic blocker
13. _____	Diarrhea	**c.** Cholinergic
14. _____	Flushing	**d.** Anticholinergic
15. _____	Lethargy	
16. _____	Hypoglycemia	
17. _____	Constipation	
18. _____	Nervousness	
19. _____	Confusion	

20. The effects of a sympathetic drug would include all of the following EXCEPT:
    a. Pupil dilation
    b. Increased respirations
    c. Decreased heart rate
    d. Increased blood pressure

Go to your StudyWARE™ CD-ROM and have fun learning as you play games and answer case study-related questions to help reinforce key concepts you learned in this chapter.

Go to your Study Guide and complete the review questions for this chapter.

Chapter 14

Antineoplastic Drugs

Objectives

Upon completion of this chapter, the learner should be able to

1. Name three characteristics associated with administration of antineoplastic drugs
2. Name the six major groups of antineoplastic agents
3. List the side effects common to most of the antineoplastic agents
4. Describe appropriate interventions in caring for patients receiving antineoplastic agents
5. Explain precautions in caring for those receiving radioactive isotopes
6. Describe the responsibilities of those caring for patients receiving chemotherapy
7. Explain appropriate education for patient and family when antineoplastic agents are administered
8. List safety factors for those who care for patients receiving cytotoxic drugs
9. Define the Key Terms and Concepts

Key Terms and Concepts

Antineoplastic
Chemotherapy
Cytotoxic
Immunosuppressive
Palliative
Proliferating

Antineoplastic (against new tissue formation) refers to an agent that counteracts the development, growth, or spread of malignant cells. Cancer therapy frequently includes a combination of surgery, radiation, and/or chemotherapy.

Chemotherapy is a constantly growing field in which many old and new drugs and drug combinations are used for **palliative** effects (alleviation of symptoms) or for long-term or complete remissions in early treatment of cancer. Antineoplastic drugs are **cytotoxic** (destructive to cells), especially to cells that are **proliferating** (reproducing rapidly). Unfortunately, the toxic effects of the antineoplastic drugs are not confined to malignant cells alone, but also affect other proliferating tissue, such as bone marrow, gastrointestinal epithelium, skin, hair follicles, and epithelium of the gonads, resulting in numerous adverse side effects.

One of the most significant developments in cancer treatment today is the use of targeted therapies. *Monoclonal antibodies* are designed to target only

cancer cells, thereby sparing normal tissues. This reduces host toxicity while simultaneously increasing toxicity to cancer cells and improving survival rates in cancer patients.

Many antineoplastic agents also possess **immunosuppressive** properties, because they may decrease the production of white blood cells, antibodies and reduce the inflammatory reaction. Suppression of the immune response results in increased susceptibility of the patient to infection.

Antineoplastic drugs are frequently administered in high doses on an *intermittent* schedule. Most normal tissues have a greater capacity for repair than do most malignant tissues, and therefore normal cells may recover during the drug-free period.

Chemotherapy is *individualized* and frequently modified according to the patient's response to treatment. A *combination of several drugs* is frequently prescribed to delay the emergence of resistance, with the choice of agents based on the type of malignancy, areas involved, extent of the cancer, physical condition of the patient, and other factors. Careful planning is required to maximize the effectiveness of therapy and to minimize the side effects and discomfort for the patient. Understanding the treatment program and possible side effects is essential for all concerned: the health care practitioner, the patient, and the family. Preplanning includes provision for symptomatic relief, such as antiemetics (drugs to prevent nausea), as well as reassurance and availability of support staff to answer questions, explore feelings, and allay fears.

The treatment of cancer is highly complex. Only health care practitioners on oncology units, in cancer treatment centers, or in oncologist's offices would be expected to know the names of the numerous drugs. However, anyone who is in contact with patients on antineoplastic therapy should be aware of the frequent possible side effects to expect and appropriate interventions for the comfort of the patient. Patient education and support are extremely important.

Antineoplastic agents can be generally classified into six major groups: antimetabolites, alkylating agents, mitotic inhibitors (plant alkaloids, taxanes), antitumor antibiotics, hormone therapies (corticosteroids, antiestrogen, antiandrogen), and immunotherapies (interferons, monoclonal antibodies).

Another exciting and growing field is radiation oncology, in which radioactive substances are placed close to or implanted in the cancerous tissues or the cancer is treated with external-beam radiation in three dimensions made possible with computer technology.

Only one or two examples of medications are presented for each category in order to identify the side effects specific to that group. It is not necessary to remember the names of these drugs as they are only representative of the many antineoplastic agents available. However, if you work extensively with cancer patients, knowing the drug names would become important.

ANTIMETABOLITES

Antimetabolites are used in the treatment of various malignancies, especially those involving rapidly proliferating neoplasms (new growth or tumor). Some antimetabolites include methotrexate and fluorouracil. Methotrexate has also been used for severe, resistant cases of psoriasis, rheumatoid arthritis, and lupus. Fluorouracil is also available in a topical formulation (Efudex) to treat certain skin cancers.

Side effects of antimetabolites can include:

- Anorexia, nausea, vomiting, and diarrhea
- Ulceration and bleeding of the oral mucosa and gastrointestinal (GI) tract
- Bone marrow suppression, including leukopenia (abnormal decrease in WBC) with infection, anemia, and thrombocytopenia (abnormal decrease in blood platelets) with hemorrhage
- Rash, itching, photosensitivity, and scaling
- Alopecia (regrowth of hair may take several months)

> ***Note*** Leucovorin (a reduced form of folic acid) is sometimes used as a "rescue agent" following methotrexate administration to reduce the side effects of methotrexate-induced hematological and GI toxicity.

Contraindications or extreme caution with antimetabolites applies to:

Renal and hepatic disorders

Pregnancy

GI ulcers

ALKYLATING AGENTS

Alkylating agents are used in the treatment of a wide range of cancers. Some alkylating agents include cisplatin (Platinol) and cyclophosphamide (Cytoxan).

Since these agents damage DNA, they can cause long-term damage to the bone marrow. In a few rare cases, this can eventually lead to acute leukemia 5 to 10 years after treatment.

Side effects of alkylating agents can include:

- Nausea, vomiting, and diarrhea
- Mucosal ulceration, bone marrow suppression, including leukopenia, with infection, anemia, and thrombocytopenia with hemorrhage
- Neurotoxicity, including headache, vertigo, and seizures

Rash and alopecia

Loss of reproductive capacity

Pulmonary fibrosis

Contraindications or extreme caution with alkylating agents applies to:

Debilitated patients

Pregnancy

Renal disease (with cisplatin)

MITOTIC INHIBITORS

Mitotic inhibitors are often plant alkaloids and other compounds derived from natural products. They are used to treat many different types of cancer. These agents are also known for their potential to cause peripheral nerve damage, which can be a dose-limiting side effect.

Plant Alkaloids

Plant alkaloids, for example, vinblastine (Velban) or vincristine (Oncovin), which are derived from the periwinkle plant, are used in combination with other chemotherapeutic agents in the treatment of various malignancies.

Side effects of plant alkaloids can include:

- Neurotoxicity, including numbness; tingling; ataxia; foot drop; pain in the jaw, head, or extremities; and visual disturbances (less common with vinblastine)
- Severe constipation or diarrhea, nausea, and vomiting
- Oral or GI ulceration
- Rash, phototoxicity (increased reaction to sunlight), and alopecia

Leukopenia with vinblastine (hematological effects less common with vincristine)

Necrosis of tissue if intravenous drug solution infiltrates into tissue

Contraindications or caution with plant alkaloids applies to:

Pregnancy, hepatic dysfunction, infection

> ***Note*** Intrathecal administration (into the spinal canal) of these agents is fatal. This route must not be used. Syringes containing these agents should be labeled, "Warning—For IV use only, fatal if given intrathecally."

Taxanes

Paclitaxel (Taxol), another plant alkaloid, was originally extracted from the bark of the Western (Pacific) yew. It is structurally different from other available antineoplastic agents. It is used as second-line or subsequent therapy in patients with metastatic breast or ovarian carcinoma refractory to conventional chemotherapy.

Adverse side effects of Taxol are frequent and include:

- Bone marrow suppression: neutropenia, leukopenia, thrombocytopenia, and anemia
- Hypersensitivity reactions—can be severe, with flushing, rash, dyspnea, chest pain, hypotension, bradycardia
- Peripheral neuropathy
- Nausea, vomiting, diarrhea, mucositis (inflammation of the mucous membranes)
- Alopecia

Contraindications and cautions with Taxol applies to pregnancy, hepatic dysfunction, infection.

Since paclitaxel (Taxol) is so toxic, the drug is only administered IV under constant supervision of an oncologist, with frequent monitoring of vital signs, and facilities available for emergency interventions if required.

ANTITUMOR ANTIBIOTICS

Antitumor antibiotics are used to treat a wide variety of malignancies. Doxorubicin (Adriamycin) is considered the most active chemotherapy agent and is a critical component of breast cancer and lymphoma treatment protocols, but can permanently damage the heart if given in high doses. Other antitumor antibiotics include bleomycin (Blenoxane), daunorubicin (Cerubidne), mitomycin (Mutamycin), and others. They are frequently used in combination with other drugs.

Note Side effects vary depending on specific medications. Always check side effects for each drug in this classification.

Side effects of antitumor antibiotics can include:

- Anorexia, nausea, vomiting, and diarrhea
- Bone marrow suppression (with some medications)
- Cardiotoxicity, including arrhythmias and congestive heart failure (with some medications)
- Pneumonitis and dyspnea; pulmonary fibrosis with bleomycin
- Ulceration of mouth or colon
- Alopecia, rash, and scaling
- Tissue necrosis if intravenous infiltrates (with most meds)

Contraindications or caution with antitumor antibiotics applies to:

- Pregnancy
- Liver disorders
- Cardiac disease

HORMONE THERAPIES

Corticosteroids

Corticosteroids, such as prednisone, are frequently used in combination with other chemotherapeutic agents in the treatment of some types of cancer and before chemotherapy to help prevent severe allergic reactions. In addition, large doses of dexamethasone (Decadron) have been found effective in the prevention and treatment of nausea and vomiting associated with many antineoplastic agents, when administered before or with chemotherapy. Dexamethasone is also used to treat cerebral edema associated with brain tumors.

Side effects with prolonged use of corticosteroids (see Chapter 23) include:

- Fluid retention
- Cushingoid features (moon face)
- Fatigue and weakness
- Osteoporosis

Antiestrogen

A *nonsteroidal antiestrogen*, *tamoxifen (Nolvadex)*, can be used as both primary hormonal therapy for metastatic estrogen receptor–positive breast cancer in both men and postmenopausal women and also for palliative treatment. Serious adverse side effects are rare and usually dose related. Nausea, vomiting, hot flashes, and night sweats can occur in up to 66% of cases, but usually do not require discontinuation.

Anastrozole (Arimidex), which inhibits the final step in estrogen production, offers an alternative to tamoxifen in postmenopausal women with breast cancer. It can also cause nausea, vomiting, and hot flashes similarly to tamoxifen, but is more likely than tamoxifen to cause osteoporosis.

Antiandrogen

Antiandrogen drugs include leuprolide acetate (Lupron Depot), which is usually administered IM once monthly for prostate cancer. See Chapter 24 for more details.

Bicalutamide (Casodex) is an oral antiandrogen used simultaneously with leuprolide in the treatment of metastatic prostate cancer.

Side effects of antiandrogens can include:

- Impotence
- Hot flashes, generalized pain, infection, constipation, nausea

Patients should be advised that the drug should be continued even when signs or symptoms of the disease improve.

Sex hormones, including the estrogens, progestins, and androgens, are also used as antineoplastic agents in the treatment of malignancies involving the reproductive system (e.g., cancer of the breast, uterus, or prostate). These hormones are discussed in Chapter 24.

IMMUNOTHERAPIES

These agents are given to some cancer patients to stimulate their natural immune systems to more effectively recognize and attack cancer cells. There are different types of immunotherapy—the *active* type (such as interferons) stimulate the body's own immune system to fight the disease. *Passive* immunotherapies (such as monoclonal antibodies) use immune system components created outside the body.

Interferons

Interferon alfa (Intron A, Roferon A) is a complex combination of many proteins that boost immune system response. Its antiviral action is described in Chapter 17. Interferons are used in the treatment of many malignancies, especially those resistant to standard treatments. Some interferons are used to treat multiple sclerosis and many other conditions, and research is ongoing.

Adverse side effects of interferons, sometimes severe, are experienced by almost all patients receiving interferon, varying with the dosage and condition.

Most common side effects include:

- Flulike syndrome—fever, fatigue, chills, headache, muscle aches, and pains
- GI symptoms—anorexia, nausea, vomiting, diarrhea, and dry mouth
- Nervous system effects—sleep disturbances, depression
- Hematological effects—especially leukopenia

Dyspnea, cough, nasal congestion

Alopecia—transient

MONOCLONAL ANTIBODIES

Monoclonal antibodies (MABs) are *exogenous* (*outside of body*) antibodies genetically engineered in the laboratory. MABs are designed to target only cancer cells, thereby sparing normal tissues (i.e., not *directly* cytotoxic). This reduces host toxicity while simultaneously increasing toxicity to cancer cells.

MABs have fairly specific mechanisms of action that result in fairly specific indications. Bevacizumab (Avastin), in combination with fluorouracil, is indicated for first-line treatment of patients with metastatic carcinoma of the colon or rectum. Trastuzumab (Herceptin), combined with paclitaxel, is indicated for first-line treatment of metastatic breast cancer. All MABs are administered intravenously.

Side effects of MABs are common, especially with the first infusion, and can include:

- Fever and chills, headache, dizziness
- Nausea and vomiting

Itching, rash, generalized pain

These reactions should occur less frequently with subsequent infusions.

Severe reactions can be minimized by *premedicating* with acetaminophen (Tylenol), diphenhydramine (Benadryl), and/or meperidine (Demerol). Signs of severe reaction can include:

- Angioedema, hypotension, dyspnea, bronchospasm (may be necessary to stop infusion)
- Hypersensitivity reactions (including anaphylaxis)
- Cardiac arrythmias, angina, heart failure, cardiomyopathy; hypertensive crisis (with Avastin)

Acute renal failure (not with Herceptin)

- Hematological toxicity (i.e., reduced white blood cells [WBCs]); complete blood count (CBC) and platelet count should be monitored frequently
- GI perforation, GI bleed; impaired wound healing (all with Avastin)

RADIOACTIVE ISOTOPES

Radioactive isotopes are also used in the treatment of certain types of cancer. Sometimes the radioactive material is injected into the affected site (e.g., radiogold, injected into the pleural or peritoneal cavity to treat the abnormal

accumulation of fluid called ascites caused by the cancer). Radioactive sodium iodine is administered PO to treat thyroid cancer. Radioactive material is sometimes implanted in the body in the form of capsules, needles, or seeds.

The newest targeted therapy provides the added benefit of radiation. Radioimmunotherapy consists of MABs that have radioisotopes attached to them so that whatever the targeted antibody binds to can also be irradiated. Tositumomab (Bexxar) with iodine 131 is indicated for patients with refractory non-Hodgkin's lymphoma. The primary side effect after radioimmunotherapy is a decreased blood count occurring four to six weeks after treatment. The counts remain low for two to three weeks and then returns to normal. The distinct advantage of radioimmunotherapy is that it is usually given one time.

Health care practitioners caring for patients receiving radioactive isotopes must observe special precautions to prevent unnecessary radiation exposure. Gowns and gloves should be worn when handling patient excreta such as feces, urine, and body secretions. Other isolation procedures, such as handling of linens, will be outlined in the facility's procedure manual. This protocol should be followed with great care by all those who come in contact with patients receiving radioactive materials, for the protection of patients, as well as the health care practitioner.

CAUTIONS AND RESPONSIBILITIES FOR ANTINEOPLASTIC DRUGS

Health care practitioners involved in the administration of antineoplastic agents, as well as those who care for these patients, have a number of very important responsibilities.

1. All medications should be given on time and exactly as prescribed to keep the patient as comfortable as possible and maximize efficacy and safety. Check package inserts on all new drugs.
2. Intravenous sites must be checked with great care because some antineoplastic agents can cause extreme tissue damage and necrosis if infiltration into surrounding tissues occurs. (Gloves should be worn when handling IVs with antineoplastic agents.)
3. Intravenous fluids containing antineoplastic agents should not be allowed to get on the skin or into the eyes of the patient or the one administering the medication. Flush skin or eyes copiously if spills occur.
4. Antiemetics should be immediately available and administered as prescribed to minimize nausea and vomiting. Ondansetron (Zofran), dolasetron (Anzemet), and granisetron (Kytril) are examples of antiemetics for this purpose (see Chapter 16).
5. Careful and frequent oral hygiene is essential to minimize the discomfort and ulceration.
6. Soft foods and cool liquids should be available to the patient as required.
7. Accurate intake and output is important for adequate assessment of hydration.

8. Careful observation and reporting of symptoms and side effects is an essential part of chemotherapy.
9. Aseptic technique is necessary to minimize the chance of infection in patients with reduced resistance to infection.
10. Careful assessment of vital signs is important to identify signs of infection, cardiac irregularities, and dyspnea.
11. The health care practitioner and family must be informed about all aspects of chemotherapy and answer the patient's questions honestly. Awareness of verbal and nonverbal communication that gives clues to the patient's needs is absolutely necessary.
12. Careful attention to detail, astute observations, appropriate interventions, and compassion are an integral part of care when the patient is receiving chemotherapy.
13. The health care practitioner should reassure the patient that someone will be available to help at all times. Identify these resources.

PATIENT EDUCATION

Patients being treated with antineoplastic drugs and their families should be instructed regarding:

- Side effects to expect, how long they can be expected to continue, and that they are frequently temporary
- Comfort measures for coping with unpleasant side effects, (e.g., antiemetics and antidiarrhea agents as prescribed)
- Appropriate diet with foods that are more palatable and more likely to be tolerated (e.g., soft foods, bland foods, a variety of liquids, and especially cold foods in frequent, small quantities)
- Careful aseptic technique to decrease the chance of infections and reporting any signs of infection (e.g., fever)
- Careful oral hygiene with swabs to prevent further trauma to ulcerated mucosa
- Observation for bleeding in stools, urine, and gums and for bruises, and reporting this to medical personnel
- Reporting of any persistent or unusual side effects, such as dizziness, severe headache, numbness, tingling, difficulty walking, or visual disturbances
- Available community resources to assist and support the patient (e.g., Cancer Society, Hospice, or Home Health Services) as required and recommended by the physician
- How to obtain information and answers to questions regarding treatment
- The right of patients to terminate therapy if they wish

See Table 14-1 for a summary of antineoplastic agents side effects.

Table 14-1 Side Effects of Antineoplastic Agents

DRUG CATEGORIES

	ANTIMETA-BOLITES	ALKYLATING AGENTS	MITOTIC INHIBITORS (PLANT ALKALOIDS)	ANTITUMOR ANTIBIOTICS	ANTIESTROGEN, ANTIANDROGEN	INTERFERONS	MONOCLONAL ANTIBODIES (MABS)
Possible side effects							
GI Effects; nausea, vomiting, diarrhea,	X	X	X	X	X	X	X
Alopecia	X	X	X	X		X	
Suppressed bone marrow*	X	X	X	X		X (especially leukopenia)	X
Ulcerated mucosa	X	X	X				
Photosensitivity	X		X				
Neurotoxicity	X	X	X			X	
Hypersensitivity			X				X
Cardiotoxicity			X	X			X
Respiratory dysfunction	X	X		X		X	X
Hot flashes					X		
Impotence					X		
Flu-like syndrome						X	X

*Includes leukopenia (low WBC count) and prone to infections, anemias, thrombocytopenia and prone to hemorrhage.

Cytotoxic Drug Dangers to Health Care Personnel

Most cytotoxic drugs are toxic substances known to be carcinogenic, mutagenic, or teratogenic. Anyone who prepares, administers, or cares for patients receiving cytotoxic drugs should be aware of the dangers involved. The American Society of Health-System Pharmacists (ASHP) has published a *Technical Assistance Bulletin (TAB)* that provides detailed advice on recommended policies, procedures, and equipment for safe handling of cytotoxic drugs (see AHFS Drug Information). It is essential that policies and procedures are followed exactly as outlined on the labels provided by the drug company. Guidelines of the individual health care agency must also be followed to the letter for the safety of all concerned.

The danger to health care personnel from handling a hazardous drug stems from a combination of its inherent toxicity and the extent to which practitioners are exposed in the course of carrying out their duties. This exposure may be from inadvertent ingestion of the drug on foodstuffs, inhalation of drug dust or droplets, or direct skin contact.

Recommended safe handling methods include four broad goals:

1. Protect and secure packages of hazardous drugs. Store separately from nonhazardous drugs.
2. Inform and educate all involved personnel about hazardous drugs and train them in safe handling procedures.
3. Do not let the drugs escape from containers when they are manipulated (i.e., dissolved, transferred, administered, or discarded).
4. Eliminate the possibility of inadvertent ingestion or inhalation and direct skin or eye contact with the drugs.

Specific recommendations for cytotoxic drugs include:

1. When preparing these drugs, wear gloves, long-sleeved gowns, splash goggles, and disposable respirator masks.
2. For administration, wear long-sleeved gowns and gloves. Syringes and IV sets with Luer-Lock fittings should be used and care taken that all fittings are secure.
3. Dispose of syringes, IV tubing and bags, gauze, or any other contaminated material such as linens in a leak proof, puncture-resistant container that is labeled "HAZARD."
4. Wear gloves and gown when handling excreta from patients receiving cytotoxic drugs.
5. Those who are pregnant, breast-feeding, or actively trying to conceive a child should not care for patients receiving cytotoxic drugs.

For more detailed instructions, see *ASHP Technical Assistance Bulletin on Handling Cytotoxic and Hazardous Drugs*, which is reproduced in the AHFS Drug Information book and updated based on information from OSHA (Occupational Safety and Health Administration), National Institutes of Health (NIH), National Study Commission on Cytotoxic Exposure, and the AMA (American Medical Association) Council on Scientific Affairs.

Antineoplastic therapy is complex and changes frequently with ongoing research. Therefore, you are not expected to remember the names of all of the antineoplastic agents. However, you need to know the *common side effects*, *interventions*, *cautions*, *and appropriate patient education*.

CASE STUDY – A

Antineoplastic Drugs

Maria Vasquez, a 36-year-old patient with leukemia, has begun chemotherapy at the oncologist's office. She will need the following information.

1. Her therapy will include all of the following EXCEPT
   a. Individualized dosage
   b. Intermittent schedule
   c. Radioactive iodine
   d. Several drugs

2. All of the following side effects are possible EXCEPT
   a. Nausea
   b. Alopecia
   c. Constipation
   d. Photosensitivity

3. Many antineoplastic drugs cause bone marrow suppression, which can result in all of the following EXCEPT
   a. Susceptibility to infection
   b. Increased clotting time
   c. Anemia
   d. Jaundice

4. The following advice is appropriate EXCEPT
   a. Practice good oral hygiene
   b. Exercise briskly
   c. Eat soft foods
   d. Watch for hematuria

5. The following should be reported to the physician EXCEPT
   a. Fever
   b. Dyspnea
   c. Blood in stools
   d. Hair loss

CASE STUDY – B

Antineoplastic Drugs

Joan Witoski, a 40-year-old patient with metastatic breast cancer, will be followed by the oncologist. The nurse or medical assistant in the office will need the following information.

1. Treatment of breast cancer with antiestrogens (e.g. tamoxifen) can cause the following adverse effects EXCEPT:
   a. nausea
   b. impotence
   c. hot flashes
   d. night sweats

2. The patient will need a supply of all of the following EXCEPT
   a. Analgesics
   b. Antiemetics
   c. Diuretics
   d. Antidiarrhea drugs

3. If the patient is treated with a MAB (e.g. Herceptin) severe reactions can occur and monitoring of the following is necessary EXCEPT
   a. Vital signs
   b. CBC and platelet count
   c. Hydration
   d. Blood glucose

4. Patient education includes all of the following EXCEPT
   a. Careful handwashing
   b. Adequate fluids
   c. Brush teeth briskly
   d. Report air hunger

5. Health care practitioners who handle cytotoxic drugs should observe the following precautions EXCEPT
   a. Wear gloves
   b. Avoid pregnancy
   c. Wear long-sleeved gowns
   d. Dispose of waste in dumpster

CHAPTER REVIEW QUIZ

Match the term with the definition:

1. _____ Palliative
2. _____ Cytotoxic
3. _____ Antineoplastic
4. _____ Monoclonal antibodies
5. _____ Proliferating
6. _____ Exogenous antibodies
7. _____ Refractory
8. _____ Immunosuppressive
9. _____ Endogenous antibodies
10. _____ Clone

a. Target only cancer cells
b. Unresponsive to treatment
c. Within the cell
d. Produce a copy
e. Decreases antibody production
f. Alleviation of symptoms
g. Engineered in a laboratory
h. Reproducing rapidly
i. Destructive to cells
j. Counteracts malignant cell growth

Multiple Choice

11. Severe reactions from MABs can be minimized by premedicating with the following drugs EXCEPT
    a. Tylenol **c.** Toradol
    b. Benadryl **d.** Demerol
12. Which is NOT a side effect of many antineoplastic drugs?
    a. Alopecia **c.** Bone marrow suppression
    b. Rash **d.** Constipation
13. Which is NOT a side effect with some antineoplastic drugs?
    a. GI symptoms **c.** Mouth ulcers
    b. Jaundice **d.** Photosensitivity
14. Bone marrow suppression can result in all of the following complications EXCEPT
    a. Anemia **c.** Thrombophlebitis
    b. Hemorrhage **d.** Infection
15. The monoclonal antibodies (MABs) can be administered by which route?
    a. Intramuscular **c.** Oral
    b. Intravenous **d.** Subcutaneous

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Chapter 15

Urinary System Drugs

Objectives

Upon completion of this chapter, the learner should be able to

1. Compare and contrast the four types of diuretics for uses, side effects, cautions, and interactions and give examples of each type
2. Describe two interactions of other medications with probenecid
3. Identify one medication given for chronic gout that is not uricosuric and one that is
4. Explain the role of certain antispasmodics used to reduce contractions of the urinary bladder
5. Identify the actions of phenazopyridine (Pyridium) and bethanechol (Urecholine)
6. Describe two different treatments for benign prostatic hypertrophy (BPH)
7. Describe appropriate patient education for all medications listed in this chapter
8. Define Key Terms and Concepts

Key Terms and Concepts

Alpha-blockers

Antispasmodics

Antiandrogens

Benign prostatic hypertrophy (BPH)

Calculus

Cholinergics

Diuretics

Gout

Hyperkalemia

Hypokalemia

Osmotic agents

Uricosuric agents

Urinary analgesic

DIURETICS

The most commonly used drugs influencing function of the urinary tract are the **diuretics**, which increase urine excretion. Diuretics are divided into four categories according to their action: thiazides, loop diuretics, potassium-sparing diuretics, and osmotic agents. The type of diuretic used is determined by the condition being treated. Carbonic anhydrase inhibitors such as acetazolamide (Diamox), which are diuretics used to lower intraocular pressure, are discussed in Chapter 18, Eye Medications.

Thiazides and Related Diuretics

Thiazides are the most frequently used type of diuretic, increasing excretion of water, sodium, chloride, and potassium. An example is hydrochlorothiazide.

Uses of the thiazides include treatment of:

Edema from many causes although loop diuretics are more commonly used (e.g., heart failure and cirrhosis)

Hypertension, either alone or combined with drugs from other classes (blood pressure is lowered by reducing peripheral vascular resistance as well as by decreasing fluid retention)

Prophylaxis of **calculus** (stone) formation in those with hypercalciuria (excess calcium in the urine)

Electrolyte imbalance from renal dysfunction (metolazone is diuretic of choice)

Side effects of the thiazides may include:

- **Hypokalemia** (potassium deficiency), may lead to cardiac arrhythmias
- Hyponatremia (low serum sodium)
- Muscle weakness or spasm
- Gastrointestinal (GI) reactions (e.g., anorexia, nausea, vomiting, diarrhea)
- Postural hypotension, vertigo, and headache
- Fatigue, weakness, and lethargy
- Skin conditions (e.g., rash and photosensitivity; rare)
- Hyperglycemia and increased uric acid

Contraindications or caution with thiazides applies to:

Diabetes (may cause hyperglycemia and glycosuria)

History of gout (increased uric acid level)

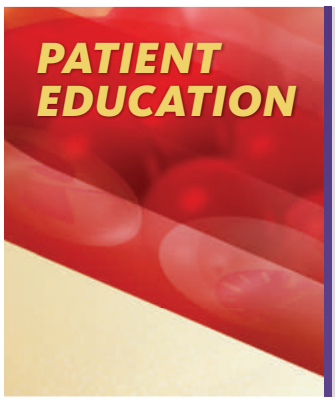
Severe renal disease

Impaired liver function

Prolonged use (periodic serum electrolyte checks indicated, and potassium supplements may be necessary to prevent hypokalemia)

Older adults due to greater sensitivity to thiazides (may cause low sodium)

Patients with sulfonamide hypersensitivity



Patients being treated with thiazides should be instructed regarding:

Diet including potassium-rich foods (e.g., citrus fruits and bananas) or potassium supplements (check with the physician first)

If diuretic prescribed for hypertension, a low-sodium diet may be prescribed by the physician

Notifying the physician of persistent or severe side effects

Administration with food (to reduce gastric irritation)

Administration in the morning to prevent disruption of sleep

Rising slowly from reclining position to counteract postural hypotension

Limitation of alcohol

Consulting physician before adding other medications

Necessity for regular blood test to monitor electrolytes

Interactions with thiazides may occur with:

Nonsteroidal anti-inflammatory agents—risk of renal insufficiency and reduced blood pressure control

Corticosteroids to increase potassium loss

Lithium, to cause lithium intoxication

Hypotensive agents, which potentiate blood pressure decrease

Digoxin with increased potential for digoxin toxicity

Probenecid to block uric acid retention

Antidiabetic agents (loss of diabetic control)

Loop Diuretics

These diuretics act directly on the loop of Henle in the kidney to inhibit sodium and chloride reabsorption, which in turn inhibits water reabsorption back into the bloodstream leading to increased urine formation. Potent diuretics such as furosemide (Lasix), bumetanide (Bumex), and torsemide (Demadex) are not thiazides but act in a similar way to increase excretion of water, sodium, chloride, and potassium. Their action is more rapid and effective than that of thiazides, with a greater diuresis.

Uses of loop diuretics include treatment of:

Edema associated with impaired renal function, heart failure or hepatitic disease

Pulmonary edema

Ascites caused by malignancy or cirrhosis

Hypertension (if thiazides ineffective, loop diuretics sometimes combined with other antihypertensives)

Side effects of loop diuretics may include:

- Fluid and electrolyte imbalance with dehydration, circulatory collapse, chest pain
- Hypokalemia with weakness (potassium supplements may be indicated especially for cardiac patients to prevent arrhythmias)
- Hypotension (close blood pressure checks required)

GI effects, including anorexia, nausea, vomiting, diarrhea, and abdominal pain

- Hyperglycemia and increased uric acid
- Hematologic disease with prolonged use
- Tinnitus, hearing impairment, and blurred vision
- Rash, urticaria, pruritus, and photosensitivity
- Headache, muscle cramps, mental confusion, dizziness

Contraindications or caution with loop diuretics applies to:

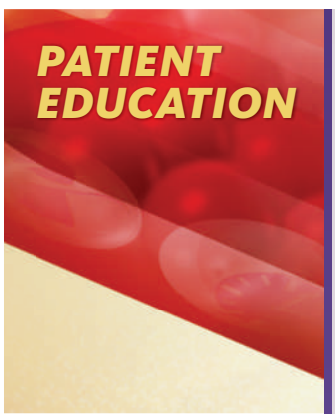
- Cirrhosis and other liver disease—careful monitoring required
- Kidney impairment
- Alkalosis and dehydration
- Patients on digoxin (cardiac arrhythmias possible unless potassium supplemented)
- Those allergic to sulfa
- Diabetes
- History of gout
- Pregnancy and lactation
- Children under 18 years of age (Bumex and Demadex)

Interactions of loop diuretics are similar to those of the thiazides:

- Corticosteroids—potentiate potassium loss
- Lithium—toxicity risk increased
- Hypotensive agents—potentiation of effects
- Digoxin with increased potential for digoxin toxicity and arrhythmias

Additional interactions of loop diuretics may include:

- Aminoglycosides increase chance of deafness
- Indomethacin decreases diuretic effect
- Salicylates with furosemide increase chance of salicylate toxicity
- Anticonvulsants (e.g., phenytoin) reduce the diuretic effect of furosemide



Patients being treated with loop diuretics should be instructed regarding the same information as patients taking thiazides:

- Dietary or other potassium supplements as prescribed
- Notifying the physician of side effects immediately
- Taking with food before 6 P.M.
- Rising slowly from reclining position
- Avoiding alcohol
- Reporting sudden changes in urinary output, especially decrease

Reporting abrupt or severe weight loss

Limiting exposure to sunlight with furosemide, due to photosensitivity

Not taking any other prescribed or over-the-counter drugs without consulting the physician first

Potassium-Sparing Diuretics

Potassium-sparing diuretics such as spironolactone (Aldactone) and triamterene (Dyrenium) are sometimes administered under conditions in which potassium depletion can be dangerous. Potassium-sparing diuretics may also counteract the increased glucose and uric acid levels associated with thiazide diuretic therapy. Spironolactone is the diuretic of choice in patients with cirrhosis. It has also been shown to reduce deaths in patients with severe heart failure.

Potassium-sparing (saving) diuretics are seldom used alone, but are usually combined with thiazide diuretics to increase the diuretic and hypotensive effects and to reduce the danger of **hyperkalemia** (excessive potassium retention). When combination products (e.g., Aldactazide or Dyazide) are given, supplemental potassium is usually *not* indicated, but this varies with individual circumstances and other medications taken concomitantly. *Periodic serum electrolyte checks are indicated.*

Side effects of potassium-sparing diuretics are usually mild and respond to withdrawal of the drug, but may include:

- *Hyperkalemia* (especially with potassium supplements), which may lead to *cardiac arrhythmias*
- Dehydration or weakness
- GI symptoms, including nausea, vomiting, and diarrhea
- Fatigue, lethargy, and profound weight loss
- Hypotension
- Gynecomastia (enlargement of breast tissue in males) with spironolactone

Caution with potassium-sparing diuretics is indicated in patients with:

- Renal insufficiency
- Cirrhosis and other liver disease
- Pregnancy and lactation

Interactions may occur with potassium-sparing diuretics and:

- Potassium supplements, angiotensin-converting enzyme (ACE) inhibitors, angiotensin receptor blockers (ARBs), salicylates, and nonsteroidal anti-inflammatory drugs (NSAIDs), to cause hyperkalemia
- Lithium to reduce clearance and cause lithium toxicity

PATIENT EDUCATION

Patients being treated with potassium-sparing diuretics should be instructed regarding:

- Avoidance of potassium-rich foods and salt substitutes
- Reporting signs of excessive dehydration (e.g., dry mouth, drowsiness, lethargy, and fever)
- Reporting GI symptoms (e.g., nausea, vomiting, and diarrhea)
- Reporting persistent headache and mental confusion
- Reporting irregular heartbeat
- Monitoring weight and reporting sudden, excessive weight loss
- Rising slowly from reclining position
- Taking medications after meals

Osmotic Agents

Osmotic agents (e.g., mannitol) are most frequently used to reduce intracranial or intraocular pressure.

Side effects of osmotic agents can include:

- Fluid and electrolyte imbalance
- CNS symptoms, including headache, vertigo, mental confusion, nausea, and vomiting
- Tachycardia, hypertension, and hypotension
- Allergic reactions
- Severe pulmonary edema

Extreme caution is indicated, and kidney and cardiovascular function should be evaluated before administration of osmotic agents to anyone with:

- Kidney failure
- Heart failure
- Active intracranial bleeding (except during craniotomy)
- Severe pulmonary edema
- Pregnancy and lactation

PATIENT EDUCATION

Patients being treated with osmotic agents should be instructed regarding side effects to be reported to the physician immediately. The patient should be reassured that osmotic agents are always given under close medical supervision and serum electrolytes will be monitored frequently by blood tests to detect adverse reactions.

See Table 15-1 for a summary of drugs for diuresis.

Table 15-1 Drugs for Diuresis

GENERIC NAME	TRADE NAME	DOSAGE (VARIES WITH CONDITION)[a]
Thiazide and Related Diuretics		
(representative list—many others)		
indapamide	Lozol	2.5–5 mg daily PO
hydrochlorothiazide	Microzide	12.5–100 mg daily
metolazone	Zaroxolyn	2.5–20 mg daily
Loop Diuretics		
furosemide	Lasix	20–80 mg daily, PO, IM, or IV
bumetanide	Bumex	0.5–2 mg daily, PO, IM, or IV
torsemide	Demadex	5–20 mg daily, PO; slow IV dosage not to exceed 200 mg
Potassium-Sparing Diuretics		
spironolactone	Aldactone	25–100 mg daily
triamterene	Dyrenium	50–100 mg bid pc
Combination Potassium-Sparing and Thiazide Diuretics		
spironolactone and hydrochlorothiazide	Aldactazide	25–50 mg daily (each component)
triamterene and hydrochlorothiazide	Dyazide, Maxzide	1 cap or tab daily
Osmotic Agents		
mannitol	Osmitrol	Parenteral only, dose varies with condition

[a]Dose may be higher for edema and heart failure

MEDICATIONS FOR GOUT

Gout is a form of arthritis in which uric acid crystals are deposited in and around joints, causing inflammation and pain. Joints affected may be at any location but gout usually begins in the knee or foot.

Medications to treat gout include uricosuric agents and allopurinol, which lower uric acid levels.

Uricosuric Agents

Uricosuric agents, such as probenecid, act on the kidney by blocking reabsorption and thereby promoting urinary excretion of uric acid. This type of drug is used in the treatment of chronic cases of gout and frequent disabling attacks of gouty arthritis. However, the uricosuric agents have no analgesic or anti-inflammatory activity and are therefore not effective in the treatment of acute gout. During acute attacks of gout, the probenecid dosage is supplemented

with colchicine, which has anti-inflammatory action. (See Chapter 21, Anti-inflammatory Drugs.)

Probenecid is sometimes given with penicillin to potentiate the level of the antibiotic in the blood, for example, with amoxicillin for some gonococcal infections. Probenecid is also given with cefoxitin to treat acute pelvic inflammatory disease.

Side effects of probenecid are rare but may include:

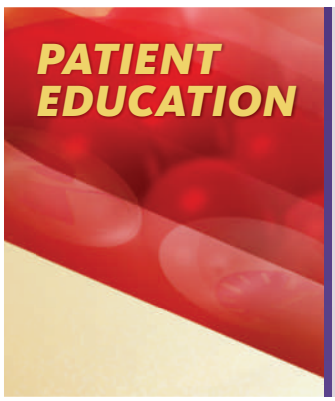
- Headache
- Nausea and vomiting
- ! Kidney stones and renal colic if large volume of fluids is not maintained
- Hypersensitivity reactions, rash, hypotension, and anaphylaxis are rare

Contraindications or cautions for probenecid apply to patients with:

- History of uric acid kidney stones
- History of peptic ulcer
- Renal impairment
- Hematologic disease

Interactions may occur with:

- Penicillins and cephalosporins, potentiating therapeutic effect of antibiotics
- Oral hypoglycemics, which could cause hypoglycemia through potentiation
- Salicylates, which antagonize uricosuric action
- NSAIDs (probenecid decreases renal clearance)



Patients being treated with uricosuric agents should be instructed regarding:

- Drinking large amounts of fluid
- Avoiding taking any aspirin products
- Taking other medications at the same time only with physician's order
- Taking medications with food
- Reporting rash immediately

Allopurinol

Allopurinol (Zyloprim) is another medication used to treat chronic gout. This drug acts by inhibiting an enzyme responsible for the production of uric acid resulting in decreased serum and urinary levels of uric acid. It has no analgesic or anti-inflammatory activity and therefore is not effective in the treatment of acute gout.

Note Medications of choice for acute gouty arthritis are nonsteroidal anti-inflammatory drugs (NSAIDs) (discussed in Chapter 21, Anti-inflammatory Drugs).

Allopurinol is also used for the prevention of renal calculi in patients with a history of frequent stone formation and prevention of acute hyperuricemia during radiation of certain tumors or antineoplastic therapy.

Side effects of allopurinol can include:

Rash

Allergic reactions, also fever, chills, nausea, vomiting, diarrhea, drowsiness, and vertigo

Severe hypersensitivity reactions are rare, but increase in older adult patients with renal impairment who receive allopurinol and thiazide diuretics in combination

Contraindications or caution with allopurinol applies to:

Impaired renal function

History of hypersensitivity reactions

Liver disease

Pregnancy and lactation

Interactions may occur with allopurinol and:

Antineoplastic drugs, potentiating side effects (azathioprine, mercaptopurine)

Alcohol and diuretics, which increase serum urate concentrations

Patients being treated with allopurinol should be instructed regarding:

Drinking large quantities of fluid

Taking medication after meals

Stopping medication and reporting rash to physician immediately

Avoiding alcohol, which increases uric acid

Avoiding other medications unless prescribed by physician

ANTISPASMODICS

Antispasmodics, which are anticholinergic in action (blocking parasympathetic nerve impulses), are used to reduce the strength and frequency of contractions of the urinary bladder (see Chapter 13, Cholinergic Blockers). Antispasmodics, such as tolterodine (Detrol) and oxybutynin (Ditropan), are used to decrease bladder tone and suppress bladder contractions in patients with neurogenic bladder resulting in decreased incontinence.

These drugs are used for the relief of symptoms such as urgency, frequency, nocturia, and incontinence. They have similar adverse side effects, especially in older adults.

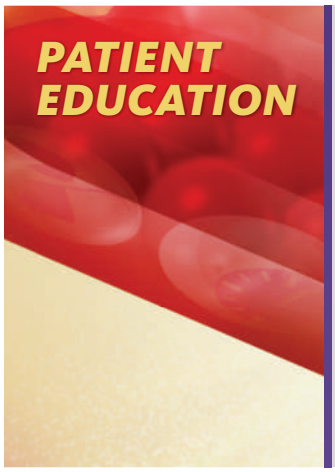
Extended release formulations (Ditropan XL, Detrol LA), patches (Oxytrol), and newer agents (Enablex, VESIcare) are less than or equally effective as oxybutynin IR (immediate release), but may cause fewer anticholinergic adverse effects. Another anticholinergic, less commonly used as an antispasmodic, is hyoscyamine (Cystospaz, Levsin) but adverse side effects are common in older adults.

Side effects of antispasmodics are *anticholinergic* in action and can include:

- Drying of all secretions (especially in the eyes and mouth)
- Drowsiness and dizziness—headache
- Urinary retention and constipation
- Blurred vision
- Mental confusion (especially with older adults)
- Tachycardia, palpitations
- Nausea and vomiting
- Rash, urticaria, allergic reactions

Cautions with antispasmodics for:

- Older adults
- Hepatic or renal disease, obstructive uropathy
- Bladder or GI obstruction, or ulcerative colitis
- Cardiovascular disease
- Prostatic hypertrophy
- Children under five years old—contraindicated
- Pregnant or nursing women
- Narrow angle glaucoma



Patients being treated with antispasmodics should be instructed regarding:

- Reporting side effects that are troublesome for possible dosage adjustment
- Reporting effectiveness; inform patients that it may take several months to see effects
- Using caution driving or operating machinery
- Avoiding alcohol or other sedatives that potentiate drowsiness
- Do not crush or chew extended release formulations; do not cut or trim patches

CHOLINERGICS

Bethanechol (Urecholine) is a **cholinergic** drug, stimulating parasympathetic nerves, to bring about contraction of the urinary bladder in cases of non-obstructive urinary retention, usually postoperatively or postpartum. It has been called the "pharmacological catheterization." (See Chapter 13, Cholinergics.)

Side effects of bethanechol are cholinergic in action and usually dose related, and can include:

- GI cramping, diarrhea, nausea, and vomiting
- Sweating and salivation
- Headache and bronchial constriction
- Slow heartbeat or reflex tachycardia, and orthostatic hypotension
- Urinary urgency

Contraindications of bethanecol include:

Obstruction of the GI or urinary tract

Hyperthyroidism

Peptic ulcer, irritable bowel syndrome

Asthma

Cardiovascular disease—bradycardia

Parkinsonism, seizure disorder

Pregnancy and lactation

Interactions may occur with bethanecol and:

Other cholinergic or anticholinesterase agents (e.g., neostigmine) administered concomitantly, which can potentiate effects, with increased possibility of toxicity

Quinidine or procainamide, which antagonize cholinergic effect

Atropine, which antagonizes cholinergic effect (antidote in cases of cholinergic toxicity)

URINARY ANALGESICS

Phenazopyridine (Pyridium) is an oral **urinary analgesic** or local anesthetic for urinary tract mucosa. It is used to relieve burning, pain, discomfort, and urgency associated with cystitis; with procedures causing irritation to the lower urinary tract, such as cystoscopy and surgery; or with trauma. It should not be taken for more than two days when used with an antibacterial agent.

Phenazopyridine is used *only for symptomatic* relief and is not a substitute for treatment of causative conditions. For treatment of urinary tract infections, anti-infective medication is required (see Chapter 17).

Side effects of Pyridium are rare for the most part but can include:

Headache or vertigo

Mild GI disturbances

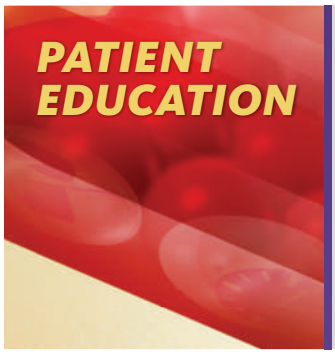
- Orange-red urine (common)—may stain fabric and contact lenses

Contraindications and cautions for urinary analgesics include:

Impaired kidney function, especially in older adults

liver disease

Phenazopyridine may interfere with various urine, kidney function, or liver function tests.



Patients being treated with phenazopyridine (Pyridium) for urinary tract distress should be instructed regarding color change of urine to orange-red, which may stain fabric, and tears may stain contact lenses.

Phenazopyridine is only temporarily effective against discomfort in the lower urinary tract and is not effective against infection. The cause of the discomfort must be determined and appropriate therapy, such as surgery or anti-infective medication, may be necessary to correct the condition.

TREATMENT OF BENIGN PROSTATIC HYPERTROPHY (BPH)

Antiandrogens

Finasteride (Proscar) and dutasteride (Avodart) are used to reduce prostate size and associated urinary obstruction and manifestations, for example, urgency, nocturia, and urinary hesitancy in patients with **benign prostatic hypertrophy (BPH)**. Proscar 5 mg, or Avodart 0.5 mg, is administered daily for a minimum of 6–12 months. This therapy appears to be suppressive rather than curative, and return of the hypertrophy is likely if the drug is withdrawn.

Side effects of **antiandrogens** include impotence, decreased libido, decreased ejaculate, and gynecomastia (including breast tenderness and enlargement).

Cautions: Patients should be screened first for cancer, infection, or other urinary dysfunctions. Antiandrogens can affect a blood test called PSA, used for screening of prostate cancer. Liver function abnormalities may be exacerbated. Crushed tablets and soft gelatin capsules should *not be handled by pregnant women* (causes fetal damage).

ALPHA-BLOCKERS

Tamsulosin (Flomax) blocks alpha-1 receptors found in smooth muscle in the bladder neck and prostate, causing them to relax. Consequently, the urine flow rate is improved and the symptoms of BPH are decreased. Other examples of **alpha-blockers** are doxazosin (Cardura) and terazosin (Hytrin), which are used in the treatment of hypertension, as well as for BPH (see Chapter 25, Cardiovascular Drugs).

Side effects of alpha-blockers are infrequent, but can include:

- Dizziness, headache, nasal congestion
- Orthostatic hypotension

Palpitations (not Flomax)

Ejaculation dysfunction, decreased libido, impotence

Cautions: Patients with a history of serious or life threatening sulfonamide allergy (with Flomax). Notify ophthalmologist of current or previous treatment with alpha-blockers—may be at risk for Intraoperative Floppy Iris Syndrome during cataract surgery.

Combination therapy with an antiandrogen (Proscar) and an alpha-blocker (Cardura) in patients with large prostates has recently been shown to significantly reduce the overall clinical progression of BPH and may reduce the need for invasive therapy compared to either agent alone.

See Table 15-2 for a summary of uricosuric agents, antigout medication, antispasmodics, cholinergic agents, analgesic agents, and agents for BPH.

Table 15-2 Other Drugs Affecting the Urinary Tract

GENERIC NAME	TRADE NAME	DOSAGE
Uricosuric Agents		
probenecid		250–500 mg BID
probenecid w/colchicine		1 tab (500 mg / 0.5 mg) BID
Antigout Medication		
allopurinol	Zyloprim	100–600 mg daily
Antispasmodics		
tolterodine	Detrol	1–2 mg BID
	Detrol LA	2–4 mg daily
oxybutynin	Ditropan	2.5–5 mg 2–4 × per d
	Ditropan XL	5–30 mg daily
	Oxytrol patch	3.9 mg per day patch twice weekly
darifenacin	Enablex	7.5–15 mg daily
solifenacin	VESIcare	5–10 mg daily
hyoscyamine	Cystospaz, Levsin	0.125–0.25 mg PO, SL, 3–4 × per d
Cholinergica[a]		
bethanechol	Urecholine	10–50 mg 3–4 × per d
Analgesic		
phenazopyridine	Pyridium, Azo Standard	200 mg TID pc for 48 hours only
Agents for BPH		
Antiandrogens		
finasteride	Proscar	5 mg daily
dutasteride	Avodart	0.5 mg daily
Alpha-Blockers		
doxazosin	Cardura	1–8 mg at bedtime
tamsulosin	Flomax	0.4–0.8 mg once daily pc
terazosin	Hytrin	1–10 mg at bedtime

[a]For bladder contraction.

CASE STUDY – A

Urinary System Drugs

Lee Chan, a 60-year-old diabetic with a history of heart disease and hypertension, comes to the clinic complaining of swollen ankles, shortness of breath, weakness, and nausea. He is taking hydrochlorothiazide. You will need to answer his questions with the following information.

1. Hydrochlorothiazide causes increased excretion of all of the following EXCEPT
   a. Sodium
   b. Glucose
   c. Chloride
   d. Potassium
2. Side effects of the thiazides can include all of the following EXCEPT
   a. Fatigue
   b. Nausea
   c. Muscle spasms
   d. Low blood glucose
3. What advice should be given if he is prescribed furosemide
   a. watch for skin color changes
   b. Eat citrus
   c. limit sun exposure
   d. urine may be orange
4. Because of the edema, he will probably be put on a more potent loop diuretic, such as
   a. Dyazide
   b. Osmitrol
   c. Aldactone
   d. Lasix
5. Patients like Mr. Chan taking loop diuretics should be given all of the following advice EXCEPT
   a. Avoid sunlight
   b. Avoid alcohol
   c. Take medicine at bedtime
   d. Check blood glucose

CASE STUDY – B

Urinary System Drugs

Juanita Grove, an 85-year-old Alzheimer's patient with cardiac arrhythmias is brought to the physician's office by her daughter with a request for medication to decrease her mother's incontinence. She will need the following information:

1. The following medications can reduce bladder contractions EXCEPT
   a. Urecholine
   b. Detrol
   c. Ditropan
   d. VESIcare
2. Side effects of the antispasmodics can include all of the following EXCEPT
   a. Constipation
   b. Drooling
   c. Blurred vision
   d. Mental confusion
3. Other side effects can include all of the following EXCEPT
   a. Nausea
   b. Dizziness
   c. Frequency
   d. Palpitations
4. Which of the following conditions would be treated with antispasmodics?
   a. Renal disease
   b. Kidney stones
   c. Prostatic hypertrophy
   d. Neurogenic bladder
5. Antispasmodics, for example Ditropan, are contraindicated or given with caution in the following conditions EXCEPT
   a. Geriatrics
   b. Renal disease
   c. Neurogenic bladder
   d. Cardiovascular disease

CHAPTER REVIEW QUIZ

Match the medication in the first column with the conditions in the second column that it is used to treat. Conditions may be used more than once.

	Medication	Condition
1. _____	Proscar	**a.** Congestive heart failure
2. _____	Probenecid	**b.** Gout
3. _____	Hydrochlorothiazide	**c.** Benign prostatic hypertrophy (BPH)
4. _____	Ditropan	**d.** Incontinence
5. _____	Allopurinol	**e.** Edema
6. _____	Lasix	
7. _____	Cardura	
8. _____	Detrol	
9. _____	Bumex	
10. _____	Microzide	

Choose the correct answer.

11. Patients taking combination potassium-sparing diuretics and thiazides, for example Dyazide, should be given the following instructions EXCEPT:
a. Avoid salt substitutes
b. Rise slowly
c. Take before meals
d. Report sudden weight loss

12. Osmotic agents, for example mannitol, are used in all of the following conditions EXCEPT:
a. Hypertension
b. Intraocular pressure
c. Traumatic Brain injury
d. Craniotomy with increased cerebral edema

13. The following statements are true of probenecid EXCEPT:
a. Can cause kidney stones
b. Anti-inflammatory
c. Used for chronic gout
d. Interacts with penicillin

14. The following statements are true of urecholine EXCEPT:
a. Stimulates bladder contractions
b. For postoperative urinary retention
c. Cholinergic action
d. For BPH

15. The following statements are true of Pyridium EXCEPT:

a. Colors urine orange-red
b. May interfere with kidney tests
c. Anti-infective
d. Analgesic

Go to your StudyWARE™ CD-ROM and have fun learning as you play games and answer case study-related questions to help reinforce key concepts you learned in this chapter.

Go to your Study Guide and complete the review questions for this chapter.

Chapter 16

Gastrointestinal Drugs

Objectives

Upon completion of this chapter, the learner should be able to

1. Describe side effects, contraindications, and interactions of antacids, antiulcer agents, antidiarrhea agents, antiflatulents, cathartics and laxatives, and antiemetics
2. Compare and contrast the seven types of laxatives according to use, side effects, contraindications, and interactions
3. Identify examples of drugs from each of the eight categories of gastrointestinal drugs
4. Explain important patient education for each category of gastrointestinal drugs
5. Define the Key Terms and Concepts

Key Terms and Concepts

Antacids

Antidiarrhea

Antiemetics

Antiflatulents

Antiulcer

Gastroesophageal reflux disease (GERD)

Laxatives

Gastrointestinal drugs can be divided into the following eight categories based on the action:

antacids,

drugs for treatment of ulcers and Gastroesophageal reflux disease (GERD),

antispasmodics,

management of inflammatory bowel disease,

antidiarrhea agents,

antiflatulents,

laxatives and cathartics,

antiemetics.

ANTACIDS

Antacids act by partially neutralizing gastric hydrochloric acid and are widely available in many over-the-counter (OTC) preparations for the relief of indigestion, heartburn, and sour stomach. Antacids are also prescribed at times

(between meals and at hour of sleep) to help relieve pain and promote the healing of gastric and duodenal ulcers even though their effectiveness for these conditions has not been well studied. Other antiulcer agents are discussed later in this chapter. Antacids are also used at times in the management of esophageal reflux.

Antacid products may contain aluminum, calcium carbonate, or magnesium, either individually or in combination. Most antacids also contain sodium. Sodium bicarbonate alone is not recommended because of flatulence, metabolic alkalosis, and electrolyte imbalance with prolonged use. Calcium carbonate, for example Tums, may cause constipation.

The choice of a specific antacid preparation depends on palatability, cost, adverse effects, acid neutralizing capacity, the sodium content, and the patient's renal and cardiovascular function. Magnesium and/or aluminum antacids are the most commonly used. Magnesium can cause diarrhea, and aluminum is constipating. Therefore, combinations are frequently used to control the frequency and consistency of bowel movements, for example, Maalox, Gelusil, and Mylanta.

Side effects with frequent use of antacids may include:

- Constipation (with aluminum or calcium carbonate antacids)
- Diarrhea (with magnesium antacids)
- Electrolyte imbalance
- Urinary calculi (stone formation) and renal complications
- Osteoporosis (with aluminum antacids)
- Belching and flatulence (with calcium carbonate and sodium bicarbonate)

Contraindications or extreme caution with antacids applies to:

Heart failure

Chronic kidney disease or history of renal calculi

Cirrhosis of the liver or edema

Dehydration or electrolyte imbalance

Antacids may either increase or decrease the absorption of other medications. For many medications, this interaction does not result in patient harm. However, because they may decrease effectiveness of the drug, antacids should not be taken within two hours of the following medications:

Anti-infectives, especially tetracyclines, quinolones, and isoniazid

Digoxin, indomethacin, and iron

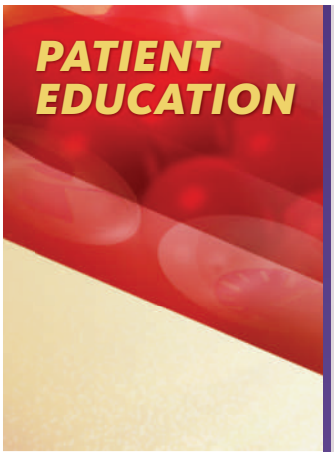
Salicylates and thyroid hormones

Antacids with the following drugs may increase action and precipitate side effects:

Diazepam, which increases sedation

Amphetamines and quinidine, which increase cardiac irregularities

Enteric-coated drugs may be released prematurely in the stomach (separate doses from antacids by two hours).



Patients should be instructed regarding:

- Avoiding prolonged use (no longer than two weeks) of OTC antacids without medical supervision because of the danger of masking symptoms of gastrointestinal (GI) bleeding or GI malignancy
- Avoiding the use of antacids at the same time as any other medication because of many interactions (check with a pharmacist or physician concerning clinically important interactions)
- Avoiding the use of antacids entirely or use with caution if patient has cardiac, renal, liver disease or fluid retention

Patients taking medicines for the management of esophageal reflux should also be instructed regarding avoidance of constrictive clothing, treatment of obesity (if appropriate), reducing meal size, avoiding lying down after meals, restriction of alcohol use, elimination of smoking, and elevating the head of the bed during sleep.

AGENTS FOR TREATMENT OF ULCERS AND GASTROESOPHAGEAL REFLUX DISEASE

H_2-Blockers

The histamine receptors found in the stomach are called H2-receptors. Some **antiulcer** agents *reduce gastric acid secretion* by acting as *histamine*$_2$ blockers. The drugs in this category, cimetidine (Tagamet), famotidine (Pepcid), and ranitidine (Zantac) are used *short term* for the relief of "acid indigestion and heartburn," **gastroesophageal reflux disease (GERD)**, and upper GI bleeding or esophagitis.

Side effects of H_2-blockers, usually transient and dose related, can include:

- Diarrhea, dizziness, rash, and headache
- Mild gynecomastia with Tagamet occurs infrequently and is reversible.
- Mental confusion (especially in older or debilitated adults)—rarely with Pepcid

Contraindications or extreme caution with H_2-blockers applies to:

- pregnancy
- lactation

Interactions with Tagamet may occur with increased blood concentrations of:

- Coumarin anticoagulants (also with high doses of Zantac)
- Phenytoin
- Propranolol
- Diazepam

Lidocaine

Theophylline (also with high doses of Zantac)

Tricyclic antidepressants

Antacids may interfere with absorption of Tagamet and Zantac; separate administration by at least one hour.

There is less likelihood for drug interactions with Pepcid.

Proton Pump Inhibitors (PPI)

Omeprazole (Prilosec) is a gastric antisecretory agent (proton pump inhibitor), unrelated to the H_2-receptor antagonists. It is used for the short-term (four to eight weeks) symptomatic relief of GERD, for the *short-term* treatment of *confirmed* gastric and duodenal ulcer, and for erosive esophagitis and "heartburn." Other drugs in this category include lansoprazole (Prevacid), rabeprazole (Aciphex), pantoprazole (Protonix), and esomeprazole (Nexium).

Side effects of proton pump inhibitors can include:

- Diarrhea, constipation, nausea, vomiting, abdominal pain
- Headache, dizziness

Long-term use on a regular basis of agents that reduce gastric acid can possibly result in vitamin B_{12} deficiency, especially in older adults. In patients older than 50, long-term PPI therapy, particularly at high doses, is also associated with an increased risk of hip fracture. A potential mechanism for this is interference with calcium absorption.

Interactions of proton pump inhibitors may occur with:

H_2-blockers (decrease proton pump inhibitor effectiveness)

Sucralfate (delays absorption of most proton pump inhibitors)

Diazepam, phenytoin, warfarin (increased serum levels)

Ampicillin, ketoconazole, iron (results in poor bioavailability)

Food—Nexium, Prevacid, and Prilosec should be given on an empty stomach; Aciphex and Protonix can be given without regard to meals.

Note

Proton pump inhibitors available as slow release (SR) tabs should *not* be chewed, broken, or crushed. Proton pump inhibitors available as SR caps may be opened and sprinkled on applesauce or yogurt, given with fruit juices, and swallowed immediately with water (do not chew or crush).

GASTRIC MUCOSAL AGENTS

Misoprostol (Cytotec)

Misoprostol (Cytotec), a synthetic form of prostaglandin E_1, inhibits gastric acid secretion and protects the mucosa from the irritant effect of certain drugs, for example nonsteroidal anti-inflammatory drugs (NSAIDs—see Chapter 21),

especially in those at risk, for example debilitated patients or older adults or those with a history of gastric ulcers. It is not FDA-approved for the treatment of gastric or duodenal ulcers.

Side effects of Cytotec can include:

- Diarrhea, nausea, and abdominal pain (occurs early in treatment and is usually self-limiting; take with food to minimize)
- Menstrual irregularities (begin therapy on the second or third day of next normal menstrual period)
- Spontaneous abortion, possibly incomplete, with potentially dangerous uterine bleeding, maternal or fetal death

Contraindications for Cytotec include:

- Women of childbearing age (unless woman is capable of using effective contraceptives)
- Pregnant women
- Children under age 12

Interactions with antacids decrease the rate of absorption. Therefore, it is recommended that antacids should be given at least two hours away and should not be of a magnesium type (which exacerbates diarrhea).

Sucralfate (Carafate)

Sucralfate (Carafate), an inhibitor of pepsin, is another antiulcer agent that acts in a different way. Sucralfate is *administered on an empty stomach* and then reacts with hydrochloric acid in the stomach to form a paste that adheres to the mucosa, thus protecting the ulcer from irritation. The therapeutic effects of the drug result from local (i.e., at the ulcer site) rather than systemic activity.

Side effects of sucralfate are rare, with constipation occurring occasionally.

Interactions are possible with sucralfate altering absorption and, therefore, other drugs should not be given within two hours of sucralfate.

Antacids may decrease binding of sucralfate to mucosa, decreasing effectiveness. Separate administration times by 30 min.

Helicobacter Pylori Treatment

Since most peptic ulcer disease is related to the consumption of nonsteroidal anti-inflammatory drugs or infection with *Helicobacter pylor* it makes sense to consider these causes immediately. *Helicobacter pylor* infection has been treated successfully with multiple-drug regimens (over 14 days) combining three medications. One such combination package, called Prevpac, contains amoxicillin with clarithromycin and lansoprazole (Prevacid). Another combination, the Helidac pack, contains tetracycline with metronidazole (antibacterial and antiprotozoal), and bismuth salicylate. This treatment and possible side effects are discussed further in Chapter 17, Anti-infective Drugs. See Table 16-1 for a listing of the antacids, agents for Ulcers and GERD, and protective gastric mucosal medications.

Table 16-1 Antacids, Antiulcer Agents, and Gastric Mucosal Agents

GENERIC NAME	TRADE NAME	DOSAGE
Antacids (only a sample, many other products available)		
aluminum hydroxide gel	AlternaGel	Suspension, 600 mg per 5 mL between meals & hs
calcium carbonate	Tums	Tabs, 500–2,000 mg orally in 2–4 divided doses daily
aluminum-magnesium combinations with simethicone	Maalox, Gelusil, Mylanta	Suspension, tabs; dose varies with product
Agents for Ulcers and GERD		
H_2-Blockers		
cimetidine	Tagamet	300 mg q6h PO or IV per IM
	Tagamet HB (OTC)	200 mg daily-BID PO (2 weeks maximum)
famotidine	Pepcid	20–40 mg PO tabs at bedtime
		20 mg IV diluted q12h
	Pepcid AC (OTC)	20 mg daily or 10 mg BID (2 weeks max)
ranitidine	Zantac	150 mg tabs BID
		50 mg IV diluted or IM q6-8h
	Zantac 75,150 (OTC)	150 mg daily or 75 mg BID (2 weeks max)
Proton Pump Inhibitors		
esomeprazole	Nexium	20–40 mg ac daily SR caps, susp, IV diluted
lansoprazole	Prevacid	15–30 mg ac daily SR caps,
		SoluTab; 30 mg daily IV diluted
omeprazole	Prilosec	20–40 mg qAM ac, SR caps
	Prilosec OTC	20 mg daily ac SR tab (2 weeks maximum)
pantoprazole	Protonix	20–40 mg orally daily SR tabs, susp; 40 mg daily IV diluted
rabeprazole	Aciphex	20 mg daily SR tab
Gastric Mucosal Agents		
misoprostol	Cytotec	100–200 mcg 4 × per d with meals and at bedtime with food
sucralfate	Carafate	1 g 4 × per d (1 h ac and at bedtime), tabs, susp

ANTISPASMODICS/ANTICHOLINERGICS

Dicyclomine

Antispasmodics/anticholinergics help to calm the bowel. Dicyclomine (Bentyl) is an anticholinergic/antimuscarinic agent used for the treatment of irritable bowel syndrome and other functional disturbances of GI motility. GI anticholinergics work by decreasing motility (smooth muscle tone) in the GI tract.

Side effects of dicyclomine, especially in older adults, can include:

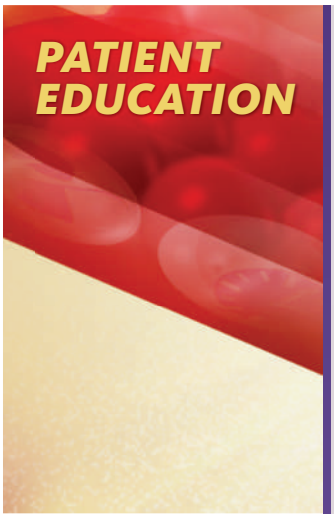
- Dry mouth, constipation
- Blurred vision, dizziness, drowsiness
- Urinary retention
- Tachycardia, palpitations
- Confusion (especially in older adults)

Contraindications of dicyclomine include:

- Glaucoma (narrow angle)
- Cardiovascular disease
- Obstructive GI disease, ulcerative colitis
- Obstructive uropathy (BPH, bladder obstruction)
- Myasthenia gravis
- Lactation

Interactions of dicyclomine include:

- Phenothiazines (decreased antipsychotic effectiveness, increased anticholinergic side effects)
- Tricyclic antidepressants (increased anticholinergic side effects)
- Opiate agonists (additive depressive effects on GI motility/bladder function)



Patient Education for Those Undergoing Ulcer Therapy

Patients should be instructed regarding:

- Avoiding cigarette smoking, which seems to decrease the effectiveness of medicines in the healing of duodenal ulcers
- Importance of close communication with the physician for possible dosage regulation of other medications taken at the same time
- Structuring of environment to reduce stress factors and decrease tension in order to facilitate healing of ulcers and reduce gastric motility and hypersecretion, as an adjunct therapy
- Not taking antacids, if ordered, within two hours of taking cimetidine, ranitidine, or any other drug

Taking medications on a regular basis and avoiding abrupt withdrawal, which could lead to rebound hypersecretion of gastric acid

Taking sucralfate (Carafate) one hour before meals, on an empty stomach, and not within two hours of any other medicine

Taking misoprostol (Cytotec) with meals and at bedtime with food, and avoiding magnesium products to lessen incidence of diarrhea

Taking proton pump inhibitors, esomeprazole (Nexium), lansoprazole (Prevacid), and omeprazole (Prilosec), on an empty stomach; rabeprazole (Aciphex) and pantoprazole (Protonix) can be given without regard to meals.

Proton pump inhibitors available as delayed release dosage forms should NOT be chewed, broken, or crushed; proton pump inhibitors available as delayed release capsules may be opened and sprinkled on applesauce or yogurt, given with fruit juices, and swallowed immediately with water (do not chew or crush).

FOR INFLAMMATORY BOWEL DISEASE

Salicylates

Mesalamine (Asacol, Rowasa) and sulfasalazine (Azulfidine) have chemical structures similar to those of aspirin and exhibit anti-inflammatory activity in the GI tract. They are used in the management of Crohn's disease and ulcerative colitis. These salicylates are all designed to reach the ileum and colon, bypassing the stomach and upper intestines. They are safe for long-term use and are well tolerated in most patients.

Side effects of salicylates (often more frequent and severe with sulfasalazine) can include:

- Anorexia, nausea, vomiting, diarrhea, abdominal pain, cramps
- Headache, weakness, dizziness

Intolerance to sulfasalazine can be minimized by taking the enteric-coated product.

Caution with sulfasalazine applies to:

- Allergy to salicylates
- Allergy to sulfonamides with sulfasalazine (can cause anaphylaxis or asthma attacks)
- Allergy to sulfites (Rowasa enema)

Renal impairment

Hepatic impairment (with sulfasalazine)

Interactions with sulfasalazine include:

Warfarin (increased risk of hemorrhage)

Methotrexate (increased bone marrow suppression)

Cyclosporine (decreased efficacy)

Oral diabetic agents (hypoglycemia)

Glucocorticoids

Glucocorticoids (prednisone, prednisolone, hydrocortisone enema) are used to treat moderate to severe forms of inflammatory bowel disease in patients who are inadequately controlled with salicylates. The oral steroids do not require direct contact with inflamed intestinal tissue to be effective. For a detailed discussion on these agents, see Chapter 23, Endocrine System Drugs.

ANTIDIARRHEAL DRUGS

Antidiarrheal agents act in various ways to reduce the number of loose stools.

Bismuth Subsalicylate

Bismuth subsalicylate (e.g., Kaopectate, Pepto-Bismol) has anti-infective and antisecretory properties, a direct mucosal protective effect, and weak antacid and anti-inflammatory effects. Kaopectate brand products have been reformulated several times over the years. Be aware that several formulations of "generic" Kaopectate are still available—check label contents and dosing carefully.

Side effects of bismuth subsalicylate are relatively uncommon at normal doses, and include:

- Transient constipation on occasion
- Discoloration of tongue and stool

Ringing in ears

Interactions with bismuth subsalicylate are possible, when these agents are administered concurrently with medications such as:

Warfarin (increases bleeding)

Aspirin, methotrexate, valproic acid (increases toxicity)

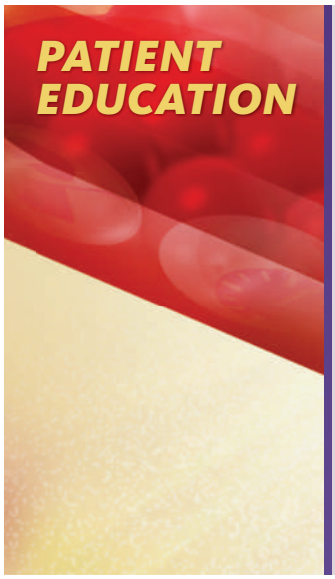
Contraindications for bismuth subsalicylate include:

Salicylate (including aspirin) hypersensitivity

Children or teenagers recovering from chickenpox or influenza (risk of Reye's Syndrome)

Coagulation abnormalities, ulcers

Pregnancy, breast feeding



Patients with diarrhea should be instructed regarding:

- Avoiding self-medication for longer than 48 hours or if fever develops without consulting a physician
- Diet of a bland nature, excluding roughage, and including foods containing natural pectin (e.g., apple *without* peelings and without sugar added to apple)
- Adequate fluid intake (especially tea *without* sugar for its astringent effect) or Gatorade to prevent dehydration
- Contacting the physician immediately if complications develop or condition worsens and if observing blood in stool
- Do not use bismuth subsalicylate if allergic to salicylates (including aspirin) and in children or teenagers recovering from chickenpox or influenza

Diphenoxylate with Atropine and Loperamide

Diphenoxylate with atropine (Lomotil) and loperamide (Imodium) act by slowing *intestinal motility* thus allowing for more reabsorption of fluid.

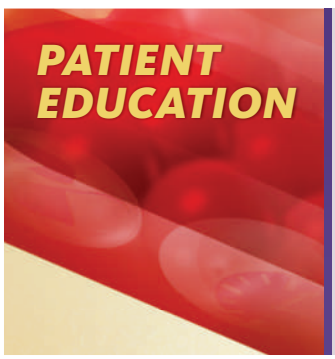
Side effects can include:

- With Lomotil, anticholinergic effects (e.g., drying of secretions, blurred vision, urinary retention, lethargy, confusion, or flushing)
- With Lomotil or Imodium, abdominal distention, nausea, or vomiting

Contraindications include:

- Diarrhea caused by infection or poisoning
- Young children and pregnancy
- Colitis associated with broad-spectrum antibiotics
- Obstructive jaundice

Caution with older adults.



Patients taking antidiarrheal drugs should be instructed regarding:

- Not exceeding the recommended dosage; short-term only
- Adequate fluid intake and bland diet
- Reporting side effects or complications to the physician immediately, or if symptoms persist
- Not taking these medications if diarrhea is caused by infection or food poisoning.

Probiotics

Probiotics are living microorganisms that can alter a patient's intestinal flora and may provide benefit in numerous GI diseases. The body's naturally occurring gut flora may fall out of balance in a wide range of circumstances, including the use of antibiotics or other drugs, excess alcohol, stress, certain diseases, or exposure to toxic substances.

Lactobacillus acidophilus (Lactinex) is an acid-producing bacterium in culture administered orally for simple diarrhea caused by antibiotics, infection, irritable colon, colostomy, or amebiasis. Lactobacillus bacteria help to reestablish normal intestinal flora. The capsules, tablets, or granules may be taken or mixed with cereal, food, juice, or water.

Side effects tend to be mild and digestive (gas, bloating) in nature.

Contraindications or warnings for Lactinex apply to:

- Anyone with a high fever; weakened immune system
- Those sensitive to milk products
- Long-term use, unless directed by physician
- Patients with prosthetic heart valves/valvular heart disease (risk of bacteremia)

Saccharomyces boulardii (Florastor) is a yeast used in dairy fermentation or derived from the intestinal microbiota of healthy humans. It is a probiotic often started within 3 days of antibiotic initiation and continued for 3 days after discontinuation to prevent diarrhea. Probiotic bacteria are also found in yogurt (Activia) and other foods for replacement of beneficial intestinal tract bacteria.

ANTIFLATULENTS

Antiflatulents (e.g., simethicone) are used in the symptomatic treatment of gastric bloating and postoperative gas pains, by helping to break up gas bubbles in the GI tract.

No side effects, contraindications, or drug interactions have been reported.

Contraindications apply only to infant colic because of limited information on safety in children.

PATIENT EDUCATION

Patients should be instructed to avoid gas-forming foods (e.g., onions, cabbage, and beans).

See Table 16-2 for a summary of antispasmodics, inflammatory bowel disease, antidiarrhea, and antiflatulent agents.

Table 16-2 Antispasmodic, Inflammatory Bowel Disease, Antidiarrhea, and Antiflatulent Agents

GENERIC NAME	TRADE NAME	DOSAGE
Antispasmodic/Anticholinergic		
dicyclomine	Bentyl	PO 20 mg 4 × per d caps, tabs; IM 20 mg q6h (2 days max)
For Inflammatory Bowel Disease		
Salicylates		
mesalamine	Asacol	800 mg PO TID (up to 6 weeks), DR tab
	Rowasa	4 g R at bedtime (retain 8 h; use 3–6 weeks), enema
sulfasalazine	Azulfidine	500 mg tab or EC tab
		500 mg–1 g 4 × per d
Antidiarrhea Agents		
diphenoxylate with atropine	Lomotil	Sol or tabs, 2.5–5 mg 4× per d (max 20 mg per day)
bismuth subsalicylate	Kaopectate, Pepto-Bismol	Susp, 30 mL or 2 tabs q30-60 min after each BM (max 8 doses per day)
loperamide	Imodium	Sol, tabs, caps; 4 mg initially, 2 mg after each loose BM
	Imodium A-D (OTC)	(Rx maximum 16 mg per day; OTC maximum 8 mg per day × 2 days)
Probiotics		
lactobacillus acidophilus	Lactinex, Bacid	2 caps, 4 tabs, or 1 pkg granules 3 or 4 × per d
saccharomyces boulardii	Florastor	2 caps PO BID (start within 3 days of antibiotic; continue for 3 days after discontinuation)
Antiflatulent		
simethicone	Mylicon	Liquid, tabs pc and at bedtime 160–500 mg daily in divided doses

LAXATIVES AND CATHARTICS

Laxatives promote evacuation of the intestine. Included in the laxative category are *cathartics*, or *purgatives*, which promote rapid evacuation of the intestine and alteration of stool consistency. Laxatives can be subdivided into seven categories according to their action: bulk-forming laxatives, stool softeners, emollients, saline laxatives, stimulant laxatives, osmotic laxatives, and chloride channel activator.

Many over-the-counter (OTC) laxatives are self-prescribed and overused by a large portion of the population. Prevention and relief of constipation is

better achieved through natural methods (e.g., high-fiber diet, adequate fluid intake, good bowel habits, and exercise). Normal frequency of bowel movements varies from daily to several times weekly. When constipation occurs, the cause should be identified before laxatives are used.

Bulk-Forming Laxatives

Bulk-forming laxatives, also known as fiber supplements (e.g., psyllium, cellulose derivatives, polycarbophil, and bran) soften the stool and increase bulk to facilitate defecation. They are the treatment of choice for simple constipation unrelieved by natural methods. These products are available in powders, flakes, granules, tablets, wafers, or liquids and *must be dissolved and/or diluted* according to manufacturers' directions (note label). The usual procedure is to dissolve the product in one *full glass* of water or juice to be taken orally and followed immediately with another glass of fluid. The proper dosage is administered one to three times per day. Laxative effect is usually apparent within 12–72 h.

Bulk-forming laxatives are the choice for older adults or laxative-dependent patients. They have been useful in maintaining regularity for patients with diverticulosis, and they have also been used to increase the bulk of stools in patients with chronic, watery diarrhea.

Contraindications for bulk-forming laxatives apply to patients with acute abdominal pain, partial bowel obstruction, dysphagia (difficulty in swallowing), or esophageal obstruction.

PATIENT EDUCATION

Patients should be instructed regarding *dissolving all bulk-forming products completely* in one full glass of liquid and following that with another glass of fluid to prevent obstruction.

Administer immediately when dissolved, before thickening occurs.

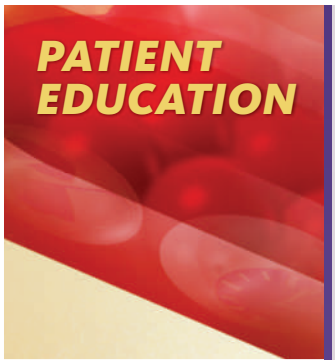
Stool Softeners

Stool softeners (e.g., docusate) are surface-acting agents that moisten stool through a detergent action and are administered orally. Dosage required to soften stools varies widely depending on the condition and patient response. Stool softeners are the choice for pregnant or nursing women and children with hard, dry stools. Onset of action is usually 12–72 h.

Side effects are rare, with occasional mild, transitory GI cramping or rash.

Contraindications include acute abdominal pain or prolonged use (more than one week) without medical supervision

Caution to avoid stool softeners that also contain stimulant laxatives, for example, Peri-Colace, Senokot-S.



Patients taking stool softeners should be instructed regarding:

- Discontinuance with any signs of diarrhea or abdominal pain
- Avoiding use for longer than one week without medical supervision
- Interaction with mineral oil, which leads to mucosal irritation
- Taking large quantities of fluids to soften stool
- Checking package label to be sure no cathartics are included

Emollients

Emollients promote stool movement through the intestines by softening and coating the stool. Mineral oil may be administered orally and is usually effective in six to eight hours. Mineral oil is sometimes administered rectally as an oil-retention enema (60–120 mL).

Side effects of emollients may include:

- Seepage of oil from rectum, causing anal irritation
- Malabsorption of vitamins A, D, E, and K only with prolonged oral use

Contraindications for oral mineral oil include:

- Children under 5 years old
- Bedridden, debilitated, or geriatric patients
- Patients with dysphagia, gastric retention, or hiatal hernia
- Pregnancy
- Prolonged use
- Concomitant use of stool softeners

Patients taking mineral oil should be instructed regarding:

- Avoiding frequent or prolonged use
- Caution with anyone who might have trouble swallowing or who might aspirate the oil
- Interaction with docusate (stool softener), which can facilitate absorption of mineral oil, possibly increasing risk of toxicity.

Saline Laxatives

Saline laxatives (e.g., milk of magnesia, or citrate of magnesia) promote secretion of water into the intestinal lumen and should be taken only infrequently in single doses. Saline laxatives should not be taken on a regular or repeated basis unless directed by a physician. Onset of action is 0.5–3 h.

Side effects of saline laxatives used for prolonged periods or in overdoses can include:

- Electrolyte imbalance
- CNS symptoms, including weakness, sedation, and confusion
- Edema
- Cardiac, renal, and hepatic complications

Contraindications or warnings include:

Long-term use
Heart failure or other cardiac disease
Edema, cirrhosis, or renal disorders
Those taking diuretics
Acute abdominal pain
Colostomy

PATIENT EDUCATION

Patients taking saline laxatives should be instructed regarding:

Avoiding saline cathartics with the contraindicated medical conditions
Avoiding frequent or regular use of saline cathartics

Stimulant Laxatives

Stimulant laxatives (e.g., senna, castor oil, and bisacodyl) are cathartic in action, producing strong peristaltic activity, and may also alter intestinal secretions in several ways. Stimulant laxatives are habit-forming, and long-term use may result in laxative dependence and loss of normal bowel function. All stimulant laxatives produce some degree of abdominal discomfort. Their use should be confined to conditions in which rapid, thorough emptying of the bowel is required (e.g., before surgical, proctoscopic, sigmoidoscopic, or radiological examinations, or for emptying the bowel of barium following GI X-rays) or for patients on opioid therapy. Sometimes a combination of oral preparations, suppositories, and/or enemas may be ordered for these purposes. Onset of action is 0.25–8 h, depending on preparation.

Side effects of stimulant laxatives are common, especially with frequent use, and can include:

- Abdominal cramps or discomfort and nausea (frequent)

Rectal and/or colonic irritation with suppositories

- Loss of normal bowel function with prolonged use
- Electrolyte disturbances with prolonged use

Discoloration of urine with senna

Contraindications with stimulant laxatives include:

Acute abdominal pain or abdominal cramping—danger of ruptured appendix

Ulcerative colitis

Children, pregnancy, and lactation

Long-term use

PATIENT EDUCATION

Patients taking stimulant laxatives should be given strong warnings against frequent or prolonged use because of danger of laxative dependence and loss of normal bowel function.

Osmotic Laxatives

Osmotic laxatives such as glycerin, lactulose, polyethylene glycol (PEG), and sorbitol exert an action that draws water from the tissues into the feces and reflexively stimulates evacuation. Response and side effects vary with preparation. Lactulose response may take 24–48 h. Side effects include nausea, vomiting, flatulence, and abdominal cramps.

Glycerin rectal suppositories or enemas usually cause evacuation of the colon within 15–60 min. Glycerin may produce rectal irritation or cramping pain. Polyethylene glycol (Miralax) response can be seen in 0.5-3 h, however, two to four days of therapy may be required to produce a bowel movement. Side effects are similar to other drugs in this category; high doses of Miralax can cause electrolyte imbalances (hyponatremia, hypokalemia) with prolonged or excessive use.

Chloride Channel Activator

Lubiprostone (Amitiza) is a unique oral agent for the treatment of constipation. It increases intestinal fluid secretion by activating specific chloride channels in the intestinal epithelium. Lubiprostone alters stool consistency and promotes regular bowel movements without altering electrolyte balance or producing tolerance. Most patients experience a bowel movement within 24 hours of the first dose.

Side effects of lubiprostone can include:

- nausea, diarrhea

headache

abdominal bloating/pain and flatulence

Contraindications/Precautions include:

severe diarrhea, bowel obstruction

renal/hepatic impairment

pregnancy and breast feeding

PATIENT EDUCATION

Patients should be instructed regarding:

- High-fiber diet to prevent constipation, including roughage (e.g., bran, whole-grain cereals, and fresh fruits and vegetables)
- Adequate fluid intake
- Developing good bowel habits (e.g., regular, at an unrushed time of day)
- Regular exercise to develop muscle tone
- Avoiding any laxative with acute abdominal pain, nausea, vomiting, or fever
- Avoiding laxatives if any medical condition is present, unless prescribed by a physician. Bulk-forming laxatives are safest in the long term.
- Use of only the mildest laxatives (e.g., stool softeners) on a short-term, infrequent basis
- Reporting any prolonged constipation, if above measures are ineffective, to a physician for investigation

Please see Table 16-3 for a summary of laxatives.

Table 16-3 Laxatives

GENERIC NAME	TRADE NAME	DOSAGE
Laxatives (only a sample, many other products available)		
Bulk-forming		
psyllium	Metamucil, Konsyl-D, Hyrocil, others	Powder, 1 tsp, dissolved in full glass of fluid 1–3 × per d
Stool softener		
docusate	Colace, others	Oral caps, liquid 50–300 mg daily
Emollient		
mineral oil	Fleet Mineral Oil	15–45 mL PO daily; 60–120 mL R daily
Saline laxative		
magnesium hydroxide	Milk of Magnesia	Susp, 15–60 mL daily
Stimulant laxatives		
senna	Senokot	8.6 mg tab, 1–4 BID or 10–15 mL syrup BID
with docusate	Peri-Colace, Senokot-S	2 tabs daily - BID
bisacodyl	Dulcolax	5–15 mg tabs, 10 mg Supp
	Fleet	10 mg/30 mL enema
Osmotic laxatives		
glycerine	Colace suppository	1 suppository R prn
lactulose	Enulose	15–60 mL PO daily (10 g per 15 mL)
polyethylene glycol	Miralax	17 g (1 capful) in 4-8 oz liquid daily (OTC-7 days max; Rx-14 days+)
sorbitol		30–150 mL PO of 70% solution
Chloride channel activator		24 mcg cap BID w/food (constipation)
lubiprostone	Amitiza	8 mcg cap BID w/food (IBS w/constipation)

Note: This is only a representative sample. Others are available. Always read labels carefully, especially with OTC medications.

ANTIEMETICS

Antiemetics are used in the prevention or treatment of nausea, vomiting, or motion sickness. Many different types of products are available, varying in their actions, the condition treated, and route of administration. Prevention is preferred over treatment of established nausea and vomiting.

Anticholinergics

Motion sickness is mediated by cholinergic and histaminic receptors in the inner ear. For prophylaxis of motion sickness, anticholinergic drugs such as dimenhydrinate (Dramamine) or scopolamine are used. For greatest effectiveness, the Transderm-Scop patch is applied behind the ear 4 h before anticipated exposure to motion and is effective up to 72 h. Dramamine is administered orally 30 min before exposure to motion. Both of these drugs are also available for IM injection in patients who have already developed motion sickness.

Meclizine (Antivert) is an antihistamine used in the prevention and treatment of nausea, vomiting, and/or vertigo associated with motion sickness, and in the symptomatic treatment of vertigo associated with the vestibular system (e.g., Meniere's disease). The onset of action is about 1 h and effects persist 8–24 h after a single oral dose. Although meclizine produces fewer adverse anticholinergic effects than scopolamine, it can cause drowsiness, but to a lesser degree than dimenhydrinate (Dramamine). It is not recommended for children under age 12.

Antidopaminergics

Dopamine receptor antagonists interfere with stimulation of the chemoreceptor trigger zone (CTZ) in the brain, thereby blocking messages to the GI tract. The most frequently used agents to control nausea and vomiting in this class are prochlorperazine (brand name Compazine which is no longer marketed) and Phenergan, which are related to the phenothiazines, discussed in Chapters 20 and 26 respectively. These drugs are used for symptomatic relief and their use must be supplemented by restoration of fluid and electrolyte balance, as well as determination of the cause of vomiting.

Antagonism of dopamine receptors in other areas of the brain, including those involved with movement, can lead to extrapyramidal reactions (tremors, difficulty walking, and muscular rigidity) which are common for drugs in this class at high doses. Prochlorperazine shows a high incidence of extrapyramidal reactions, especially in psychiatric patients receiving phenothiazines long term or in children. It is not recommended for children under age 12. *Caution with older adults. Not for long-term use!*

For *preoperative* preventive antiemetic effect or *postoperative* treatment for nausea and vomiting, promethazine (Phenergan) is usually the drug of choice. Phenergan can be given *deep* IM or IV, but *never* subcutaneously. Metoclopramide (Reglan), a dopamine-receptor antagonist unrelated to other agents, is an antiemetic and a stimulant of upper GI motility. It accelerates gastric emptying and intestinal transit. It is used in a variety of GI motility disorders, especially gastric stasis, *short-term* (*up to 12 weeks*)

treatment of GERD, and for the prevention of cancer chemotherapy–induced emesis.

Serotonin Receptor Antagonists

Serotonin is a major neurotransmitter involved in emesis located in the gut. Serotonin receptor antagonists preferentially block serotonin receptors found centrally in the CTZ and peripherally in the intestines to control emesis. Ondansetron (Zofran) and dolasetron (Anzemet) are used for the prevention and treatment of post-operative nausea and vomiting and for control of emesis *with chemotherapy*. These agents have fewer side effects (mainly headache, dizziness, drowsiness, and diarrhea) and are usually well tolerated.

Side effects of the antiemetics vary with the drug and dosage, but the most common include:

- Confusion, anxiety, restlessness (especially with older adults)
- Sedation, drowsiness, vertigo, weakness
- Diarrhea, depression (with Reglan)
- Dry mouth and blurred vision
- Extrapyramidal reactions (involuntary movements), especially in children and older adults with the antidopaminergics

Cardiac arrhythmias with IV administration if too fast

Contraindications or extreme caution with antiemetics applies to:

Children and adolescents (increased risk of movement disorders) with antidopaminergics

Pregnancy and lactation

Debilitated, emaciated, or geriatric patients (require reduced dose)

Angle-closure glaucoma

Prostatic hypertrophy

Cardiac arrhythmias or hypertension

Seizure disorders

COPD and asthma (Phenergan suppresses cough reflex.)

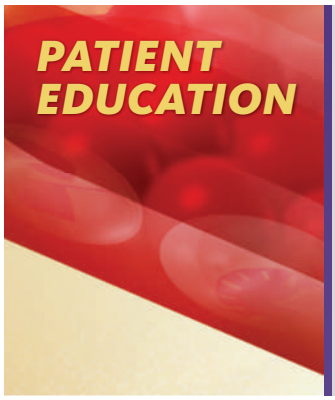
Interactions of antiemetics resulting in potentiation of a sedative effect occur with:

CNS depressants, including tranquilizers, hypnotics, analgesics, antipsychotics

Alcohol

Muscle relaxants

Metoclopramide (other antiemetics also antagonize the stimulant effects of metoclopramide on the GI tract)



Patients taking antiemetics should be instructed regarding:

- Taking these medications under medical supervision
- Determining the cause of nausea and vomiting
- Reporting effectiveness or complications
- Administering only as directed
- Not combining with any other CNS depressants, alcohol, or muscle relaxants unless prescribed by a physician (e.g., with cancer patients)

See Table 16-4 for a summary of antiemetics.

Table 16-4 Antiemetics

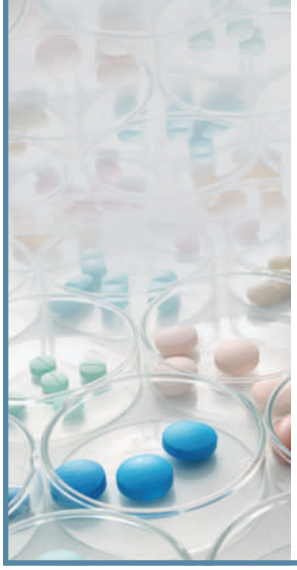
GENERIC NAME	TRADE NAME	DOSAGE
Antiemetics		
Anticholinergics		
dimenhydrinate	Dramamine	50–100 mg PO or IM, IV q4h PRN for motion sickness (max 400 mg PO, 300 mg IM)
meclizine	Antivert	25–50 mg daily, 1 h before motion (repeat q24h PRN)
scopolamine	Transderm-Scop	25–100 mg in divided doses/Meniere's 72 hour patch for motion sickness
Antidopaminergics		
metoclopramide	Reglan	PO, IM, IV; dose varies with condition
prochlorperazine	(Compazine)[a]	5–10 mg PO, IM, IV, 4 × per d; 25 mg suppository BID
promethazine	Phenergan	Tabs, syrup, deep IM, IV, or suppository 12.5–25 mg; (never subcu)
Serotonin Receptor Antagonists (Postoperative Nausea and Vomiting (PONV) or with Chemotherapy—Chemotherapy Induced Nausea and Vomiting (CINV)		
dolasetron	Anzemet	CINV: 100 mg slow IV, 100 mg PO; PONV: 12.5 mg IV, 100 mg PO
ondansetron	Zofran	CINV: 32 mg IV (over 15 min); 24 mg PO; PONV: 4 mg IM, IV (over 2–5 min), 16 mg PO

Note: This is only a representative sample. Others are available. Always read labels carefully, especially with OTC medications.

[a]Brand name no longer marketed.

CASE STUDY – A

Gastrointestinal Drugs



Henry Johnson, a 55-year-old salesman, has been taking antacids for years for recurrent gastric distress. X-ray has confirmed a gastric ulcer. The following information will be helpful.

1. All of the following can result from antacids EXCEPT
   a. Gastric acid decrease
   b. Urinary calculi
   c. Constipation
   d. Diarrhea

2. All of the following are antiulcer drugs EXCEPT
   a. Prilosec
   b. Pepcid
   c. Azulfidine
   d. Cytotec

3. All of the following are true of sucralfate (Carafate) EXCEPT
   a. Take before meals
   b. Decreases gastric acid
   c. Coats the stomach
   d. Action is local

4. The following are true of Tagamet and Zantac EXCEPT
   a. Reduces gastric acid
   b. Used long-term for GERD
   c. Can cause confusion in older adults
   d. Can cause dizziness

5. Patients with recurrent, resistant peptic ulcers might be treated with a combination of all of the following EXCEPT
   a. Bismuth salicylate
   b. Tetracycline
   c. Metronidazole
   d. Gentamicin

CASE STUDY – B

Gastrointestinal Drugs

Conessa Alvarez, a 70-year-old woman, has been taking cathartics for years, and they are now ineffective. She requests a new one she can take daily. She needs the following information.

1. The only laxative that should be taken daily is
   a. Dulcolax
   b. Senokot
   c. Metamucil
   d. Milk of Magnesia

2. Stimulant laxatives can cause all of the following EXCEPT
   a. Electrolyte imbalance
   b. Reduced peristalsis
   c. Dependence
   d. Cramping

3. The following is true of bulk-forming laxatives EXCEPT
   a. Given with liquids
   b. Useful for diverticulosis
   c. Used for chronic diarrhea
   d. Used for acute abdominal pain

4. The following is true of mineral oil EXCEPT
   a. Can cause anal irritation
   b. Used with stool softener
   c. Can cause vitamin deficiency
   d. Contraindicated with dysphagia

5. Patient education includes all of the following EXCEPT
   a. Increase fluids
   b. High-fiber diet
   c. Stool softeners used short term
   d. Milk of magnesia used long term

CHAPTER REVIEW QUIZ

Match the medication in the first column with the condition in the second column that it is used to treat. Conditions may be used more than once.

Medication	Condition
1. _____ Nexium	**a.** Diarrhea
2. _____ Antivert	**b.** Flatulence
3. _____ Rowasa	**c.** GERD
4. _____ Lactinex	**d.** Meniere's disease
5. _____ Prevacid	**e.** Nausea and vomiting
6. _____ Transderm-Scop	**f.** Constipation
7. _____ Dulcolax	**g.** Inflammatory bowel disease
8. _____ Simethicone	**h.** Motion sickness
9. _____ Imodium	
10. _____ Phenergan	

Choose the correct answer.

11. With antacids, which of the following applies to administration?
- **a.** Before meals
- **b.** Two hours from other medications
- **c.** With Tagamet
- **d.** With milk

12. Misoprostol (Cytotec) can cause all of the following EXCEPT:
- **a.** Constipation
- **b.** Menstrual irregularities
- **c.** Spontaneous abortion
- **d.** Gastric distress

13. Dicylomine (Bentyl), an anticholinergic drug, can cause all of the following EXCEPT:
- **a.** Decreased GI motility
- **b.** Confusion in older adults
- **c.** Urinary incontinence
- **d.** Dry mouth

14. The following statements regarding proton pump inhibitors, for example Prilosec, are true EXCEPT:
- **a.** Treat GERD
- **b.** Used long-term
- **c.** Interact with anticoagulants
- **d.** GI side effects

15. Prochlorperazine, a phenothiazine antiemetic, can cause all of the following EXCEPT:
- **a.** Confusion
- **b.** Sedation
- **c.** Gastric distress
- **d.** Extrapyramidal reactions

16. The following statements regarding Reglan are true EXCEPT:

a. Short-term use only
b. Extrapyramidal effects possible
c. Can cause depression
d. Decreases GI motility

Go to your StudyWARE™ CD-ROM and have fun learning as you play games and answer case study-related questions to help reinforce key concepts you learned in this chapter.

Go to your Study Guide and complete the review questions for this chapter.

Chapter 17

Anti-infective Drugs

Objectives

Upon completion of this chapter, the learner should be able to

1. Identify side effects, contraindications, and interactions common to each category of anti-infectives
2. Explain the unique features of patient education appropriate for each category of anti-infectives
3. Describe general instructions that should be given to every patient undergoing anti-infective therapy
4. Define Key Terms and Concepts

Key Terms and Concepts

Adverse reactions
Aminoglycosides
Anaphylaxis
Antifungal
Antituberculosis agents
Antiviral
Broad-spectrum
Cephalosporins
Culture and sensitivity (C&S) tests
Direct toxicity
Hypersensitivity
Macrolides
Opportunistic infections
Penicillins
Quinolones
Resistance
Sulfonamides
Superinfection
Tetracyclines
Urinary anti-infectives

Treatment of infection is complicated by the great variety of medications available and their differing modes of action (e.g., bacteriostatic versus bactericidal). The first step in treatment is identification of the causative organism and the specific medication to which it is sensitive. **Culture and sensitivity (C&S) tests** will be ordered, based on symptoms (e.g., wound, throat, urine, or blood). It is imperative to obtain the appropriate specimen before administering medication. Results of C&S tests will not be available for 24–48 h. In the meantime, depending on the clinical condition of the patient, the physician may order an empiric (best guess based on history) anti-infective regimen that would likely be active against the organisms encountered at a given site of infection (e.g., brain, lung, skin, etc.).

RESISTANCE

Sometimes organisms build up **resistance** to drugs that have been used too frequently, and then the drugs are no longer effective. This explains why antibiotics should not be used for the common cold, which is caused by viruses and not bacteria. Organisms can also become resistant if infections have been treated incompletely, as when the medication is discontinued before the required number of days to be fully effective.

More than 70% of bacteria that cause nosocomial (hospital-acquired) infections are resistant to at least one of the drugs most commonly used to treat those infections, according to the U.S. Centers for Disease Control and Prevention (CDC). Also of concern, infections due to resistant organisms that were seen only in hospital settings are now increasingly being seen in the community. Antimicrobial resistance is rising not only in prevalence but also across all classes of antibiotics.

An example of an organism resistant to most antibiotics is methicillin-resistant *Staphylococcus aureus* (MRSA). Vancomycin IV is one of a small number of drugs effective against MRSA. The CDC also reports outbreaks of tuberculosis resistant to standard drug therapy (see Antituberculosis Agents).

Some strains of enterococci have become resistant to most of the antibiotics, including vancomycin. Infections such as bacteremia, endocarditis, or urinary tract infections (UTIs), which are caused by vancomycin-resistant enterococci (VRE), can be very difficult to treat. Treatment options are limited and mortality rates are high.

Resistance to antiviral and antifungal agents is also an important clinical problem. Many strains of Type A influenza are now resistant to oseltamivir (Tamiflu). Individuals infected with human immunodeficiency virus (HIV) wage a constant battle with resistance because the virus is only suppressed, not eradicated; that is, it is hidden in the patient's immune system by ongoing antiretroviral treatment. Candida species resistant to fluconazole are a growing problem in many health care institutions as well due to widespread use of this antifungal agent. Anti-infective resistance is caused by many factors. Therefore, the strategies needed to combat the problem are also complex. Effective strategies include better patient and physician *education* on appropriate anti-infective use, accurate diagnosis, and targeted treatment of infections. Strict adherence to *preventive measures* such as routine handwashing/alcohol wiping between patient visits and rapid isolation of patients with resistant infections are also extremely important.

Selection of anti-infective drugs is based on several factors:

1. ***Site of the infection.*** This helps determine the initial empiric anti-infective regimen.
2. ***Status of hepatic and/or renal function.*** Lower doses or alternative drugs might be indicated with impairment.
3. ***Age of the patient.*** Some anti-infectives are more toxic in children or the elderly. Lower doses or alternative drugs might be indicated.
4. ***Pregnancy or lactation.*** Some anti-infectives can cross the placenta and cause damage to the developing fetus; for example,

tetracycline or streptomycin. Others can be carried in breast milk and can cause toxicity to the infant.

5. ***Likelihood of organisms developing resistance.*** Sometimes a combination of drugs is used to decrease the chance of developing resistance to a single drug. Examples of combination therapy include sulfamethoxazole and trimethoprim combined to treat urinary tract infections. Another example is the combination of three or more drugs to treat tuberculosis.
6. ***Known allergy to the anti-infective drug.*** In such cases, an alternative should be used.

ADVERSE REACTIONS

Adverse reactions to anti-infectives are divided into three categories:

1. ***Allergic hypersensitivity.*** Over response of the body to a specific substance. A *mild* reaction with only rash, urticaria (hives), or mild fever is usually treated with corticosteroids or antihistamines, and the medication is *discontinued.* Sometimes severe reactions occur with the first administration of a specific medication (e.g., penicillin), or they may follow a mild reaction. *Severe* reactions may be manifested as **anaphylaxis**, a sudden onset of dyspnea, chest constriction, shock, and collapse. Unless treated promptly with epinephrine, corticosteroids, and CPR (cardiopulmonary resuscitation), death may result.
2. ***Direct toxicity.*** Results in tissue damage, such as ototoxicity (hearing difficulties or dizziness), nephrotoxicity (kidney problems), hepatotoxicity (liver damage), blood dyscrasias (abnormalities in blood components), phlebitis, or phototoxicity. Sometimes the damage can be permanent, or it may be reversible when the medication is discontinued. The health care practitioner's responsibility involves assessment of physical condition and laboratory reports, and potential *discontinuance* of medication at the first sign of toxicity.
3. ***Indirect toxicity, or superinfection.*** Manifested as a new infection as a result of killing the normal flora in the intestines or mucous membranes, especially with broad-spectrum antibiotics and therefore allowing colonization of these areas with different resistant bacteria or fungi. Symptoms of superinfections can include diarrhea, vaginitis, stomatitis, or glossitis. Treatment consists of antifungal medications, including buttermilk or yogurt in the diet, or administering Lactinex (see Chapter 16) to help restore normal intestinal flora. Probiotics, available OTC in capsule form, are used prophylactically to prevent superinfections, especially severe colitis.

It would be impractical to list all of the anti-infective agents on the market. Therefore, only a few examples of the most frequently used drugs are listed in each category. The antibiotics are divided into therapeutic categories, including aminoglycosides, cephalosporins, macrolides, penicillins, quinolones, and

tetracyclines. In addition, antifungals, antituberculosis agents, sulfonamides, and **urinary anti-infectives** are also listed. Miscellaneous anti-infective agents, including some drugs used to treat opportunistic infections associated with AIDS (autoimmune deficiency syndrome), are included. Antiviral drugs, used to treat HIV (human immunodeficiency virus) and other viral infections, are also described.

We have omitted the amebicides, antihelmintics, and antimalarial drugs, as well as a detailed discussion on vaccines, but urge those in the public health or pediatric fields to investigate these drugs as appropriate to their practice.

VACCINES/IMMUNIZATIONS

Information regarding vaccines and immunizations changes from time to time and requirements may vary by state, territory, or country. Therefore, the most up-to-date information regarding vaccines, immunization recommendations, and requirements can be obtained by contacting the Centers for Disease Control and Prevention (CDC) and the National Immunization Program at http://www.cdc.gov/vaccines. The best source of up-to-date vaccine info is the CDC website, Advisory Committee on Immunization Practices (ACIP).You can also call the CDC Info Contact Center at 800-232-4636 or the National Immunization Hotline at 800-232-2522 (English) or 800-232-0233 (Spanish).

The CDC has information regarding the latest infection-control measures in place around the world. One recommendation of the CDC regarding influenza vaccine is relevant to your practice. The CDC recommends that all older individuals, and those at any age who are immune compromised or have a serious medical condition, be given the influenza vaccine in the last quarter of the year, annually. In addition, all health care practitioners who have contact with those at risk, as just mentioned, should also receive the flu vaccine. The CDC recently expanded the recommended ages for annual influenza vaccine to *all* children from 6 months to 18 years, instead of just children under 5. It is your responsibility to stress the importance of this prophylactic measure in helping to prevent serious, possibly fatal, complications from contracting virulent forms of influenza.

There has been much controversy about whether vaccines and autism are linked. The first purported link was with the measles-mumps-rubella (MMR) vaccine. It has also been speculated that thimerosal, a mercury-containing preservative long used in vaccines, is linked to increased rates of autism. In both cases, after reviewing available data and studies, the Immunization Safety Review Committee (ISRC) of the Institute of Medicine (IOM) has determined that evidence is insufficient to demonstrate a causal relationship between vaccines and autism.

AMINOGLYCOSIDES

Aminoglycosides, e.g., gentamycin in combination with other antibiotics, are used to treat many infections caused by *gram-negative* bacteria (e.g., *Escherichia coli* and *Pseudomonas*) as well as *gram-positive* bacteria (e.g., *Staphylococcus aureus*). Enterococci may be resistant to aminoglycosides.

Aminoglycosides are used in the *short-term* treatment of many serious infections (e.g., bacteria in the bloodstream causing very low blood pressure) *only* when other less toxic anti-infectives are ineffective or contraindicated. Examples of aminoglycosides include amikacin, gentamicin, and tobramycin. Because of poor absorption from the gastrointestinal (GI) tract, aminoglycosides are usually administered parenterally (i.e., IM or IV).

Serum levels (peak and trough) are often drawn to determine optimal dosing and lessen the risk of side effects. These levels measure the amount of drug in the blood at different times and are used to adjust subsequent doses and/or the frequency between doses. Peak serum levels are drawn one hour after the start of the infusion or IM injection of the third dose of aminoglycoside; trough levels are drawn 30 minutes before the next dose.

Serious side effects from aminoglycosides, especially in older adults, dehydrated patients, or those with renal or hearing impairment, can include:

- *Nephrotoxicity*, generally reversible upon discontinuation
- *Ototoxicity*, both auditory (hearing loss) and vestibular (vertigo), may be permanent
- Neuromuscular blockade, including respiratory paralysis
- CNS symptoms including headache, tremor, lethargy, numbness, seizures

Blurred vision, rash, or urticaria

Contraindications or extreme caution with aminoglycosides applies to patients with:

Tinnitus, vertigo, and high-frequency hearing loss

Reduced renal function

Dehydration

Pregnant or nursing women Infants or older adults

Interactions of aminoglycosides may occur with:

Other ototoxic drugs (e.g., amphotericin B, polymixin B, bacitracin, and vancomycin)

General anesthetics or neuromuscular blocking agents (e.g., succinylcholine), which can cause respiratory paralysis

Antiemetics—may mask symptoms of vestibular ototoxicity

PATIENT EDUCATION

Patients being treated with aminoglycosides should be instructed regarding:

Extreme importance of close medical supervision during therapy

Careful observation of intake and urinary output

Prompt reporting of any side effects, especially kidney or hearing problems

CEPHALOSPORINS

Cephalosporins are semisynthetic antibiotic derivatives produced by a fungus. They are related to the penicillins and *some* patients allergic to penicillin are also allergic to cephalosporins. In general, cephalosporins are broad-spectrum, active against many gram-positive and gram-negative bacteria. However, there are many different cephalosporins and they vary widely in their activity against specific bacteria.

Cephalosporins are classified as first, second, third, or fourth generation, according to the organisms susceptible to their activity. First-generation drugs, for example, cephalexin, are usually effective against gram-positive and some gram-negative organisms, such as those causing skin/soft tissue or urinary tract infections. Second-generation drugs, for example, cefaclor, are usually effective against many gram-positive and gram-negative organisms, such as many strains causing bacterial pneumonia. Third-generation drugs, for example, ceftriaxone, are usually effective against more gram-negative bacteria than the others and are sometimes used for sexually transmitted diseases (STD) such as chancroid or gonorrhea. Ceftazidime is extremely active against Psuedomonas aeruginosa. Cefepime (Maxipime), a parenteral cephalosporin with excellent activity against both gram-positive and gram-negative bacteria, is classified as a fourth-generation cephalosporin.

A C&S may be helpful to determine which cephalosporin is appropriate depending on the organism(s) recovered. Different drugs are used to treat different infections of the respiratory tract, skin, urinary tract, bones and joints, septicemias, some sexually transmitted diseases, and endocarditis. They are also used prophylactically, especially in high-risk patients, for many types of surgery.

Side effects of cephalosporins can include:

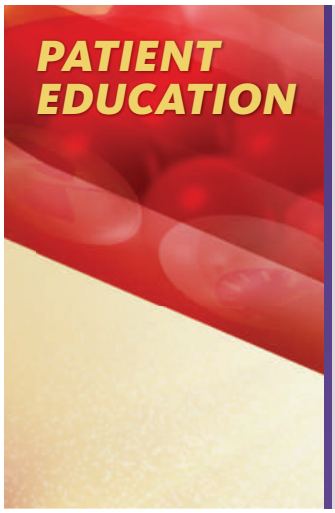
- Hypersensitivity, including rash, edema, or anaphylaxis (especially in those allergic to penicillin)
- Blood dyscrasias (e.g., increased bleeding time or transient leukopenia)
- Renal toxicity, especially in older patients
- Mild hepatic dysfunction
- Nausea, vomiting, and diarrhea
- Phlebitis with IV administration and pain at site of IM injection
- Respiratory distress
- Seizures

Contraindications or extreme caution with cephalosporins applies to:

- Known allergies, especially to penicillin (3%–7% cross-sensitivity; more so with first generation cephalosporins)
- Prolonged use possibly leading to superinfections or severe colitis

Interactions with cephalosporins can include:

- *Increased* effectiveness with probenecid
- Disulfiram-like reactions (flushing, tachycardia, shock) with alcohol ingestion and cefotetan



Patients being treated with cephalosporins should be instructed regarding:

- Possible allergic reactions
- Avoidance of alcohol
- Reporting any side effects to physician
- Including buttermilk or yogurt in diet to restore normal intestinal flora
- Taking without regard to meals but with food if stomach upset occurs
- Attention to signs of abnormal bleeding (checking stools and urine for blood)

MACROLIDES

Macrolides, such as erythromycin, clarithromycin, and azithromycin, are used in many infections of the respiratory tract and for skin conditions such as acne or for some sexually transmitted infections when the patient is allergic to penicillin. Erythromycins are considered among the least toxic antibiotics and are therefore preferred for treating susceptible organisms under conditions in which more toxic antibiotics might be dangerous (e.g., in patients with renal disease, pregnant patients, or small infants).

Gram-negative bacilli are generally resistant to the macrolides, and resistant strains of Group A *streptococc*i and *Streptococcus pneumoniae* are increasing in number.

Clarithromycin, in combination with amoxicillin and lansoprazole (Prevpac Kit), is also used to treat *Helicobacter pylori* in patients with duodenal ulcer. See Chapter 16 for further discussion. Unrelated to its antibacterial effect, erythromycin in low doses stimulates gastric emptying. Therefore, it is used in the treatment of gastroparesis and other GI motility disorders.

Side effects from macrolides of a serious nature are rare, and mild side effects, usually dose related, can include:

- Anorexia, nausea, vomiting, diarrhea, and cramps
- Urticaria and rash
- Superinfections
- Serious side effects can occur with some interactions. See below.

Contraindications or caution with macrolides applies to patients with:

- Liver dysfunction, GI disease
- Electrolyte imbalances

Interactions of macrolides (erythromycin and clarithromycin but *not* azithromycin) may occur with potentiation of the following drugs and possible toxicity:

- Carbamazepine (Tegretol)—ataxia, dizziness, drowsiness
- Cyclosporine (immunosuppressant with kidney/liver transplants)

Theophylline

Benzodiazepines—potentiation of sedative effects

Warfarin—may prolong prothrombin time and bleeding

Digoxin

Statins—leading to myopathy

Warning. Erythromycin can cause abnormal, potentially fatal, cardiac arrhythmias when combined with the following drugs, which increase its concentration in the blood:

Calcium channel blockers—verapamil or diltiazem

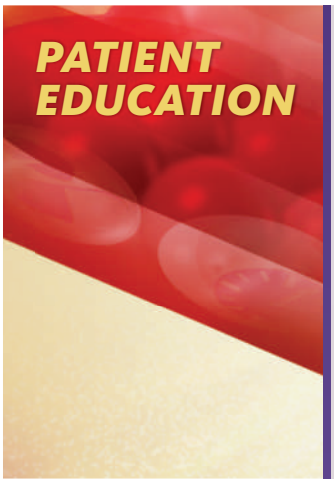
Antiarrythmic agents (see Chapter 25)

azole antifungals—i.e., fluconazole (Diflucan)

Quinolones

Always check the label, or ask a pharmacist, for any other dangerous interactions with erythromycin.

Note Azithromycin (Zithromax) is generally not associated with many of the drug interactions seen with the other macrolides just described.



Patients being treated with macrolides should be instructed regarding:

Common GI side effects to be expected

Importance of reporting side effects for possible dosage adjustment or prescription of medication for symptomatic relief

Taking medication with full glass of water one hour before or two hours after meals, unless stomach upset (some forms can be taken without regard to meals)

Including yogurt or buttermilk in diet may help regulate intestinal flora and reduce incidence of diarrhea

Not taking with other medications (see Interactions)

PENICILLINS

Penicillins are antibiotics produced from certain species of a fungus. They are used to treat many streptococcal and some staphylococcal and meningococcal infections, including respiratory and intestinal infections. Penicillin is the drug of choice for treatment of syphilis and is also used prophylactically to prevent recurrences of rheumatic fever. Amoxicillin is also used in combination with other drugs to treat *Helicobacter pylori* infection associated with *duodenal* ulcer disease (see discussion in previous section and in Chapter 16).

Some semisynthetic penicillins have a wider spectrum of activity and are called extended-spectrum penicillins, for example, piperacillin. These broad-spectrum penicillins are used in the treatment of infections due to organisms such as *Pseudomonas*.

Some organisms, including both gram-positive and gram-negative bacteria have become *resistant* to many forms of penicillin. Culture and sensitivity tests, when available, are essential to provide targeted therapy against the infecting organism.

Serious side effects of penicillins can include:

- Hypersensitivity reactions ranging from rash to fatal anaphylaxis
- Superinfections (especially with oral ampicillin)
- Nausea, vomiting, and diarrhea

Blood dyscrasias, which are reversible with discontinuance of drug

Renal and hepatic disorders (rare)

CNS effects, for example, confusion, anxiety, seizures (especially with penicillin G)

Contraindications or extreme caution with penicillins applies to patients with:

History of allergies, including asthma, eczema, or hay fever (anaphylaxis has been reported with parenteral, oral, or intradermal skin testing)

Treatment for severe reactions includes discontinuance of the drug, immediate administration of appropriate medications (e.g., epinephrine and corticosteroids), and maintenance of a patent airway. Administration of antihistamines with penicillin will *not* prevent hypersensitivity reactions.

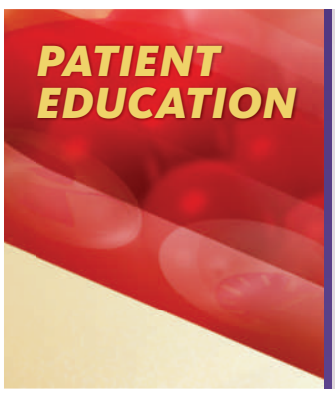
Interactions of penicillins include:

Potentiation of penicillin with probenecid, which may be desirable
Potentiation with anti-inflammatory drugs such as methotrexate and salicylates given concomitantly (at the same time); monitor for increased side effects

Antagonistic effect (delayed absorption) of oral penicillins when given with antacids or with food

Antagonistic effect of some other anti-infectives on penicillin

Penicillin V or ampicillin may inhibit the action of estrogen-containing oral contraceptives.



Patients being treated with penicillin should be instructed regarding:

Discontinuance of medication and *immediate* reporting of any hypersensitivity reactions (e.g., rash, swelling, or difficulty breathing)

Taking medication on time as prescribed on empty stomach, one hour before or two hours after meals, with full glass of water

Avoidance of antacids and alcohol

Effectiveness of estrogen contraceptives may be affected

See Table 17-1 for a summary of the aminoglycosides, cephalosporins, macrolides, and penicillins.

Table 17-1 Anti-infective Agents: Aminoglycosides, Cephalosporins, Macrolides, and Penicillins

GENERIC NAME	TRADE NAME	AVERAGE DOSAGE
Aminoglycosides		
amikacin	Amikin	IM, IV 15 mg per kg per day in 1–3 divided doses
gentamycin		IM, IV 3-6 mg per kg per day in 1–3 divided doses
tobramycin		IM, IV 3-6 mg per kg per day in 1–3 divided doses
Cephalosporins		
First-generation		
cephalexin	Keflex	PO Cap, liquid, tab 250–500 mg q6h
cefazolin		IM, IV 250 mg q8h to 2 g q8h
Second-generation		
cefaclor		PO 250–500 mg q8h, cap, liq.
cefuroxime	Ceftin	PO tab, liq. 125–500 mg q12h,
	Zinacef	IM, IV 750–1500 mg q8h-q6h
Third-generation		
cefdinir	Omnicef	PO cap, susp 300 mg q12h or 600 mg q24h
ceftazidime	Fortaz	IM, IV 1–2g q8-12h
ceftriaxone	Rocephin	IV, deep IM 250 mg–2 g daily
Fourth-generation		
cefepime	Maxipime	IV 500 mg–2 g q12h
		IM 500 mg–1g q12h (UTI only)
Macrolides		
erythromycin	Ery-Tab,	PO tab, cap 250 mg q6h–500 mg q12h
	EES, EryPed	PO tab, susp. 400–800 mg q6–12h
	Erythrocin	IV 15–20 mg per kg per day divided q6h
clarithromycin	Biaxin	PO tab, liq. 250–500 mg q12h
	Biaxin XL	PO tab 1000 mg daily
azithromycin	Zithromax	PO tab, susp. 500 mg × 1, then 250 mg daily
		IV 500 mg daily
Penicillins		
penicillin G	Bicillin L-A	Deep IM 600,000–2.4 million units
penicillin VK		PO tab, liq. 250–500 mg q6h
amoxicillin		PO caps, liq. 250 mg–1 g q8h; 875 mg q12h
ampicillin		PO caps, liq. 250–500 mg q6h
		IM, IV 1–2 g q4–6h
Extended-spectrum		
amoxicillin-clavulanate	Augmentin	PO tab, liq. 250–500 mg q8h, 875 mg q12h
	Augmentin ES	PO susp. 90 mg per kg in 2 divided doses (acute otitis media)
	Augmentin XR	PO tab 2000 mg q12h
piperacillin-tazobactam	Zosyn	IV 2.25–4.5 g q6–8h

Note: Average dose ranges are listed. In severe infections, higher doses may be indicated. Many other anti-infectives are available. Only a few are represented here. Pediatric doses are computed according to weight and condition of the child.

QUINOLONES

Quinolones, such as ciprofloxacin (Cipro) or levofloxacin (Levaquin), are used in adults for the treatment of some infections of the urinary tract, sinuses, lower respiratory tract, GI tract, skin, bones, and joints, and in treating gonorrhea. Since these antibiotics are useful for many different infections, some organisms are showing increased resistance to the quinolones. Therefore, these agents should be reserved for infections that require therapy with a fluoroquinolone such as *Pseudomonas* infections or when a patient is allergic to other antibiotics.

Resistance has developed in strains of *Pseudomonas aeruginosa* and *S. aureus*. Therefore, culture and sensitivity tests should be obtained to identify the causative organism *before initiating a quinolone*, and therapy adjusted if necessary.

Side effects of the quinolones can include:

- Nausea, vomiting, diarrhea, abdominal pain, colitis (especially older adult patients)
- CNS effects—headache, dizziness, confusion, irritability, seizures, anxiety

Crystalluria—may require drinking liberal quantities of fluids

- Superinfection—treat infection appropriately, may need to stop drug

Hypersensitivity reactions or rash—rare

- Phototoxicity—exposure to sunlight can cause severe sunburn
- Possible cartilage or tendon damage

Contraindications or caution with quinolones applies to:

Older adults, especially with GI disease or arteriosclerosis

Children or adolescents—*potential for cartilage damage*

Strenuous exercise during and several weeks after therapy—(*potential for tendon rupture*)

Pregnancy and lactation

Seizure disorders

Cardiac disease (may cause or contribute to cardiac arrhythmias)

Interactions of quinolones may occur with:

Theophylline—ciprofloxacin can potentiate serious or fatal central nervous system (CNS) effects, cardiac arrest, or respiratory failure

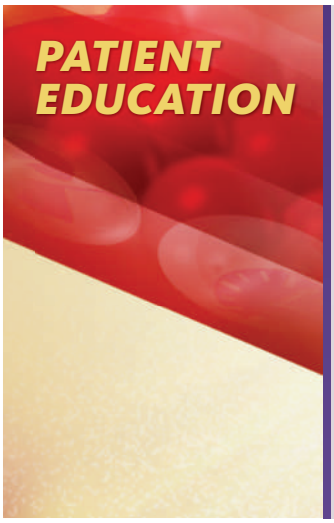
Probenicid—increased blood levels of Cipro

Antacids—decreased absorption

Coumadin—increased risk of bleeding

Preparations containing Fe, Mg, Zn, Ca—decrease absorption (do not give within two hours)

Sucralfate (Carafate)—contains aluminum ions, which decrease absorption



Patients taking quinolones should be instructed regarding:

- Not taking other medication without physician's approval
- Drinking liberal quantities of fluids
- Restricting caffeine intake—see CNS effects
- Avoiding excessive exposure to the sun
- Avoiding strenuous exercise during and several weeks after therapy (potential for cartilage or tendon damage)
- Reporting all side effects, especially rash or hypersensitivity signs
- Geriatric patients should follow preceding instructions, especially reporting GI effects or CNS effects (see Side Effects)

TETRACYCLINES

Tetracyclines are broad-spectrum antibiotics used in the treatment of infections caused by rickettsia, chlamydia, or some *uncommon* bacteria. Diseases such as Rocky Mountain spotted fever, atypical pneumonia, some sexually transmitted diseases and some severe cases of inflammatory acne are treated with tetracycline. Doxycycline can also be used to treat skin and skin structure infections caused by community-acquired MRSA. Tetracycline is also used to treat *H. pylori* infection associated with duodenal ulcer disease in combination with bismuth salicylate and metronidazole (Helidac Therapy Kit). See Chapter 16 for further discussion on this topic. However, some organisms are showing increasing resistance to the tetracyclines, and therefore they should be used only when other antibiotics are ineffective or contraindicated.

Side effects of tetracyclines can include:

- Nausea, vomiting, and diarrhea (frequently dose related)
- Superinfections such as vaginitis and stomatitis
- Photosensitivity, with exaggerated sunburn
- Discolored teeth in fetus or young children
- Retarded bone growth in fetus or young children
- Hepatic or renal toxicity (rare)
- CNS symptoms such as vertigo and cerebral edema
- Thrombophlebitis possible with IV therapy
- Allergic hypersensitivity reactions rare

Contraindications and warnings with tetracyclines include:

- Pregnancy, lactation, and children under age 8
- Patients exposed to direct sunlight
- Caution in patients with liver or GI disease
- Patients with renal disease (doxycycline preferred)

Interactions of tetracyclines may occur with the following antagonists (which decrease absorption):

Antacids, calcium supplements, or magnesium laxatives

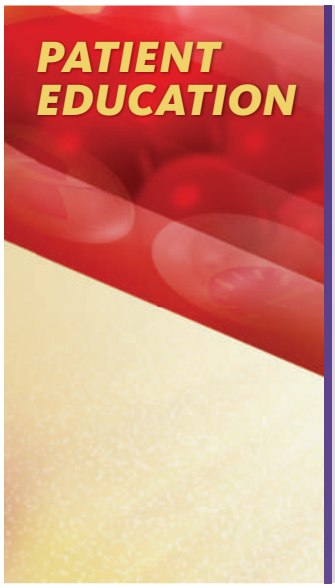
Iron preparations, zinc

Antidiarrhea agents containing kaolin, pectin, or bismuth

Dairy products (doxycycline and minocycline not significantly affected)

Oral contraceptives—breakthrough bleeding or pregnancy may occur

Tigecycline (Tygacil), a derivative of minocycline, is a newer IV antibiotic approved for the treatment of intra-abdominal and skin structure infections caused by several microorganisms, including MRSA. It should be reserved for more serious and resistant infections in order to maintain its full spectrum of activity.



Patients being treated with tetracyclines should be instructed regarding:

- Avoiding exposure to sunlight
- Avoiding this medication if pregnant or nursing or a child under 8 years of age
- Administration preferable on an empty stomach with full glass of water, one hour before or two hours after meals, unless there is gastric distress
- Avoiding iron, calcium, magnesium, and antidiarrheal agents or dairy foods within two hours of taking tetracyclines
- Not taking at bedtime to prevent irritation from esophageal reflux
- Discarding any expired drug—nephrotoxicity can result from taking outdated drug

ANTIFUNGALS

Antifungal agents are used to treat specific susceptible fungi. The medications are quite different in action and purpose, and are treated separately.

Amphotericin B

Amphotericin B is administered IV for the treatment of severe systemic, potentially fatal infections caused by susceptible fungi. It is sometimes considered the drug of choice to treat severe fungal infections resulting from immunosuppressive therapy (e.g., antineoplastic agents), or in patients with acquired immunodeficiency syndrome (AIDS), or those with severe illness (e.g., meningitis). *Severe side effects* are expected, and therefore close medical supervision (hospitalization) is usually required so that measures are available to provide symptomatic relief (e.g., antipyretics, antihistamines, and antiemetics).

Side effects of amphotericin B commonly include several of the following:

- Headache, chills, fever, hypotension, tachypnea
- Malaise, muscle and joint pain, and weakness
- Anorexia, nausea, vomiting, and cramps
- Nephrotoxicity—occurs to some degree in most patients

  Anemia
- Hypokalemia, hypomagnesemia

Because of the many severe side effects and certain dose-limiting toxicities associated with conventional amphotericin B, other formulations have been developed. One example is a lipid-based product (Abelcet) that increases the tolerability of the drug without compromising its antifungal effects. Because patient tolerance varies greatly, a test dose is advisable.

Fluconazole

Fluconazole is one of the most widely prescribed antifungal agents. It offers activity against many fungal pathogens without the serious toxicity of amphotericin B. Because of good patient tolerance and oral dosage, the drug is appropriate for patients requiring prolonged antifungal therapy. It is used in the treatment of oropharyngeal (thrush) and esophageal candidiasis and serious systemic candidal infections (e.g., urinary tract and blood stream infections). Patients with recurrent candidiasis, especially those who are immunodeficient, may require maintenance therapy to prevent relapse. A single oral dose of fluconazole is effective treatment for vaginal candidiasis.

Side effects of fluconazole can include:

- Moderate nausea, vomiting, abdominal pain, diarrhea

  Rash
- Hepatic abnormalities

  Dizziness and headache

Contraindications or extreme caution with fluconazole applies to:

Pregnant or nursing women

Hepatic or renal disease

Interactions of fluconazole may occur with:

Warfarin—increased prothrombin time could cause hemorrhage

Oral antidiabetic agents—hypoglycemia can result

Rifampin—can lead to clinical failure of fluconazole

Statins (except pravastatin)—increased risk of myopathy

Griseofulvin

Griseofulvin is administered PO in the treatment of *specific* fungi causing *tinea* infections (e.g., ringworm or athlete's foot) that do not respond to topical agents. Accurate diagnosis of the infecting organism is essential.

Side effects of griseofulvin can include:

- Headache—frequent initially
- Thirst, nausea, vomiting, and diarrhea
- Hypersensitivity reactions—rash, urticaria
- Photosensitivity
- Hepatic toxicity

Contraindications or warnings with griseofulvin include:

- Children under age 2
- Pregnancy—or women who may become pregnant while taking the drug
- Liver dysfunction
- Porphyria
- Penicillin hypersensitivity (possible cross-sensitivity)

Interactions of griseofulvin may occur with:

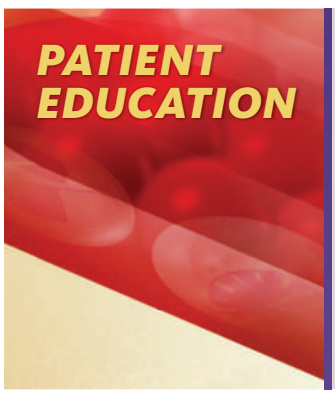
- Alcohol, causing flushing and tachycardia
- Phenobarbital, which is antagonistic to griseofulvin action (impairs absorption)
- Warfarin—decreased prothrombin time (decreased anticoagulant effect)
- Oral contraceptives—may decrease contraceptive efficacy

Nystatin

Nystatin is used to treat oral cavity candidiasis. It is also used as a fungicide in the topical treatment of skin and mucous membranes; for example, diaper area, mouth, or vagina (see Skin Medications).

Side effects of nystatin are rare but may include nausea, vomiting, and diarrhea with high oral doses occasionally.

Caution should be taken in the use of nystatin with pregnant or nursing women.



Patients on antifungal therapy should be instructed regarding:

- Taking the medication for prolonged periods as prescribed, even after symptoms have subsided
- Reporting relapses promptly to physician
- Reporting side effects immediately to the physician for possible dosage adjustment or symptomatic treatment
- Not taking any other medications at the same time without physician approval (see Interactions)

ANTITUBERCULOSIS AGENTS

Antituberculosis agents are administered for two purposes: (1) to treat asymptomatic infection (no evidence of clinical disease), for instance, after exposure to active tuberculosis and/or significantly positive PPD (purified protein

derivative) skin test; and (2) for treatment of active clinical tuberculosis and to prevent relapse.

For asymptomatic tuberculosis, the *treatment* consists of daily administration of isoniazid (INH) alone for 6–12 months to prevent development of the disease.

For patients who are intolerant of INH, or who are presumed to be infected with INH-resistant organisms, an alternative treatment consists of *rifampin with pyrazinamide.* Treatment of clinical tuberculosis is challenging for two reasons:

1. Increasing incidence of tuberculosis, particularly among certain high-risk populations (e.g., HIV-infected individuals, socioeconomically disadvantaged racial/ethnic minorities, homeless individuals)
2. Organisms have become resistant (multi-drug and extensive drug resistant) due to patient noncompliance or failure to complete the 6–24-month conventional treatment.

Therefore, the CDC recommends the following treatment regimen:

1. The American Thoracic Society (ATS) and the CDC currently recommend *short-course regimens* (i.e., at least 6 months) for the treatment of uncomplicated pulmonary tuberculosis in adults. According to the ATS, CDC, and American Academy of Pediatrics (AAP), short-course regimens are also suitable in children. Directly observed therapy (DOT) should be used for all regimens administered two or three times per week whenever possible to ensure compliance.
2. The initial regimen for the treatment of tuberculosis should include INH given once daily for two months (in combination with rifampin, pyrazinamide, and ethambutol), followed by isoniazid and rifampin given daily, twice weekly, or three times per week for an additional four months (and at least three months beyond culture conversion). If the likelihood of INH or rifampin resistance is low (i.e., 4%), an initial regimen of INH, rifampin, and pyrazinamide may be considered. HIV-positive patients should always receive induction therapy with four drugs by DOT. When drug susceptibility results are available, the regimen should be altered as appropriate. In addition, treatment may be extended to nine months or longer in HIV-infected patients, dependent upon clinical signs and symptoms or conversion of sputum cultures from positive to negative.

Although these drugs cross the placenta, they do not appear to have teratogenic effects. The CDC recommends that tuberculosis during pregnancy be treated initially with isoniazid, rifampin, and ethambutol for nine months. Streptomycin is not included because it may cause congenital ototoxicity. Since recommendations change due to resistant strains and newly developed information, consulting www.cdc.gov/mmwr for current CDC recommendations is advised.

Side effects of *INH and rifampin* are usually more pronounced in the first few weeks of therapy and can be treated symptomatically. Pyridoxine (vitamin B_6) is often given (25–50 mg PO daily) with INH to reduce the risk of CNS effects

and peripheral neuropathy. Dosage changes are sometimes required in cases of acute toxicity, but the medication must *not* be discontinued. Side effects can include:

- Nausea, vomiting, and diarrhea
- Dizziness, blurred vision, headache, and fatigue
- Numbness, weakness of extremities
- Hepatic toxicity—especially those over 35 and children (see Cautions)
- Body fluids colored red-orange with rifampin
- Hypersensitivity reaction, with flulike symptoms (sometimes with rifampin)

Contraindications or caution with INH and rifampin applies to:

Chronic liver disease or alcoholics, periodic laboratory tests required

Impaired renal function

Children's doses of INH and rifampin should be limited to 10 and 15 mg/kg, respectively, to decrease likelihood of hepatic toxicity.

Interactions with rifampin include:

Antagonism by oral hypoglycemics, corticosteroids, digitalis, anticoagulants, and *estrogen* (serum levels of these drugs are reduced when taking rifampin)

Decrease in the serum concentration of anti-retroviral protease inhibitors (PIs) which may result in HIV treatment failure

Interactions with INH include:

Potentiation by phenytoin (Dilantin); increased action (possible toxicity) when taken with isoniazid

Increase risk of hepatotoxicity with rifampin (versus each agent alone)

Alcohol, which increases possibility of liver toxicity with both INH and rifampin

Side effects of ethambutol can include:

- Optic neuritis—with visual problems (reversible if discontinued early)
- Dermatitis, pruritus, headache, malaise, fever, confusion, joint pain, GI symptoms, peripheral neuritis rarely

Cautions and contraindications with ethambutol include:

Visual testing should be performed before and during therapy

Impaired renal function—reduced doses indicated

Diabetes, especially diabetic retinopathy

Ocular defects

Children under 13—and only in children whose visual acuity can accurately be determined and monitored

Pregnancy—caution

Patients with gout (ethambutol can cause hyperuricemia)

Side effects of pyrazinamide can include:

- Hepatic toxicity
- Gout—increased uric acid
- Hypersensitivity
- GI disturbances

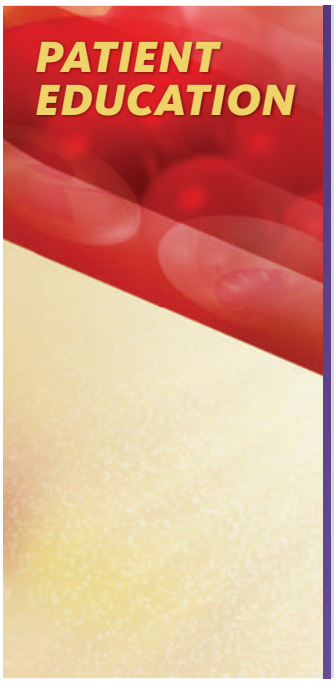
Contraindications and warnings with pyrazinamide include:

- Renal failure or history of gout
- Diabetes
- Severe hepatic disease or alcoholism
- Children—potential toxicity
- Pregnant or nursing women

Side effects of streptomycin, common to all aminoglycosides, include:

- Ototoxicity
- Nephrotoxicity

Streptomycin is administered by deep IM injection, alternating sites. Although not authorized by the manufacturer, it has been administered IV without adverse side effects (IV in at least 100 mL NS over 20–30 minutes).



Patients taking antituberculosis agents should be instructed regarding:

- Taking rifampin on empty stomach for maximum absorption, or with food if nauseated
- Taking prescribed medication for *lengthy required period of time* even though asymptomatic
- Reporting side effects for possible dosage adjustment or prescription of other palliative medications to relieve discomfort
- Importance of frequent medical and laboratory checks
- Red-orange color of urine, feces, sputum, sweat, and tears with use of rifampin
- Not wearing contact lens with rifampin
- Interactions with other drugs (e.g., *birth control pills may be ineffective*)
- Avoidance of alcohol
- Importance of visual testing periodically with ethambutol

See Table 17-2 for a summary of quinolones, tetracyclines, antifungal, and antituberculosis agents.

Table 17-2 Anti-infective Agents: Quinolones, Tetracyclines, Antifungals, and Antituberculosis Agents

GENERIC NAME	TRADE NAME	AVERAGE DOSAGE	COMMENTS
Quinolones			
ciprofloxacin	Cipro	PO 250–750 mg q12h; IV 200–400 mg q12h	Do C&S before Rx, cartilage/ tendon damage possible, phototoxicity
	Cipro XR	PO 500–1,000 mg per day (UTIs only)	
levofloxacin	Levaquin	PO, IV 250–750 mg q24h	
Tetracyclines			
tetracycline HCl		PO cap, tab, syrup 250–500 mg q6–12h	Phototoxicity, discolored teeth in infants and children
doxycycline	Vibramycin	PO cap, tab, susp., IV 100–200 mg daily divided doses	Phototoxicity, discolored teeth in infants and children
tigecycline	Tygacil	IV 100 mg x1, 50 mg q12h	
Antifungals			
amphotericin B	Abelcet, AmBisome	IV dose varies with condition and product formulation	Special IV precautions, protect from light
fluconazole	Diflucan	PO or IV 50–400 mg daily	Prolonged or maintenance doses frequently
griseofulvin	Gris-Peg	PO tab, 300–750 mg per day or 2–4 divided doses	Administer with fatty meal to increase absorption
nystatin		PO tab, susp. 500,000–1 million units 3–4 × per day, topical cream, oint., or powder	Continue treatment for 48 h after symptoms are resolved to prevent relapse
Antituberculosis Agents			
	Myambutol	PO 15–25 mg per kg per day (max 1,600 mg)	Preventive alone, or as treatment with other medications
isoniazid	INH	PO 5 mg per kg per day (max 300 mg) or 15 mg per kg 3 times per week	Always with other medications
pyrazinamide	PZA	PO 15–30 mg per kg per day (max 2 g)	Always with other medications
rifampin	Rifadin	PO 10 mg per kg per day (max 600 mg)	Initial phase with other drugs
streptomycin		IM (IV) 15 mg per kg per day (max 1 g)	With other medications initial phase

Note: Other anti-infectives are available. Only a few are represented here. Pediatric doses are computed according to weight and condition of child.

MISCELLANEOUS ANTI-INFECTIVES

Clindamycin

Clindamycin has a wider spectrum of activity than lincomycin, from which it is derived. It is used in the treatment of serious respiratory tract infections, septicemia, osteomyelitis, serious infections of the female pelvis caused by susceptible bacteria, and for *Pneumocystis jiroveci pneumonia* associated with AIDS (see AIDS section in this chapter). It is also used as a prophylactic regimen in dental procedures for penicillin-allergic patients. Clindamycin may be a viable therapeutic option for community acquired MRSA.

Side effects of clindamycin that frequently occur can include:

- Nausea, vomiting, diarrhea (drug should be discontinued if this develops), colitis
- Rash, pruritus, fever, and occasionally anaphylaxis
- Local effects—minimize by deep IM or frequent IV catheter change

Cautions of clindamycin include:

History of GI, hepatic, or renal disease

Older adults

Children

Pregnancy and lactation—contraindicated

Metronidazole

Metronidazole (Flagyl) is a synthetic antibacterial and antiprotozoal agent that is effective against protozoa such as *Trichomonas vaginalis* and against amebiasis and giardiasis. In addition, it is one of the most effective drugs available against anaerobic bacterial infections (intra-abdominal, skin, gynecological, septicemia, bone/joint, lower respiratory tract). Metronidazole is also useful in treating Crohn's disease, antibiotic-associated diarrhea, rosacea, and *H. pylori* infection (in combination with other drugs to avoid development of resistance). It is available in oral, parenteral, and topical formulations. Because of its mechanism of action, metronidazole is a highly effective antimicrobial. Resistance to metronidazole is almost nonexistent.

Side effects of Flagyl include:

- Abdominal pain, nausea/vomiting

  Anorexia, metallic taste, xerostomia
- Headache, dizziness, ataxia
- Flushing, rash, urticaria

  Peripheral neuropathy (rare) and seizures
- Dark urine (common but harmless)

Contraindications/precautions with Flagyl include:

Avoid alcohol during and 48 h after treatment (disulfiram-like reaction)

History of blood dyscrasias

Pregnancy (especially during first trimester) and lactation

Use in children (except for treatment of amebiasis)

CNS and hepatic disease

Vancomycin

Vancomycin is structurally unrelated to other available antibiotics. IV vancomycin is used in the treatment of potentially life-threatening infections caused by susceptible organisms that cannot be treated with other less toxic anti-infective agents. It is the drug of choice for methicillin-resistant *Staphylococcus aureus* (MRSA), treating gram-positive infections in penicillin-allergic patients, and some endocarditis. The CDC reports that enterococci cause about 1 out of every 8 infections in hospitals and that about 30% of these are *vancomycin-resistant enterococci (VRE)*. Use of vancomycin should be restricted to cases in which it is absolutely necessary, and it should rarely be used prophylactically.

Although vancomycin is poorly absorbed after oral administration, it is occasionally given orally to treat GI infections such as pseudomembranous colitis due to overgrowth of *C. difficile*. It is important to note that patients treated with IV vancomycin for systemic infections should not be switched to the oral form (a common practice with other antibiotics), because it is not effective by the oral route for that purpose.

Side effects of vancomycin can include:

- Ototoxicity or nephrotoxicity (occurred primarily with older impure formulations) with IV use—discontinue with tinnitus, may precede deafness
- *Local effects*—give only IV with care, can cause necrosis or thrombophlebitis
- Rash, anaphylaxis, vascular collapse (hypersensitivity reactions reported in 5%–10% of patients)

Pseudomembranous colitis due to *Clostridium difficile* infection (rare)

Caution for vancomycin with:

Older adults

Hearing impaired

Renal impairment—Serum drug levels are often drawn to determine optimal dosing to maximize efficacy against MRSA. Kidney function is also monitored frequently by serum creatinine and BUN to determine dosage adjustments

Contraindicated with pregnancy and lactation

AGENTS FOR VRE

Vancomycin has been used as "the last line of defense" against staphylococcal infections, as well as for certain streptococcal and enterococcal infections. However, in recent years, cases of vancomycin-resistant staphylococci (VRSA) and vancomycin-resistant enterococci (VRE) have become more prevalent across the globe. Also, drug-resistant infections, particularly those by

gram-positive pathogens, have spread from hospitals and nursing homes to communities.

Linezolid (Zyvox) is indicated for gram-positive infections and is approved for the treatment of bacterial pneumonia skin, skin structure infections, and MRSA and VRE infections, including those infections due to susceptible organisms that are complicated by bacteremia. Linezolid is effective in treating diabetic foot infections, which are among the most serious complications of diabetes (leading to amputation in severe cases) and are the leading cause of diabetes-related hospitalizations.

Linezolid, administered by IV infusion or orally, is a nonselective inhibitor of monoamine oxidase (MAO) that has implications for medication safety and drug interactions. Inappropriate use, leading to an increase in resistant organisms, is a concern, and treatment alternatives should be carefully considered before using linezolid in outpatient settings.

Side effects of Zyvox can include:

- Nausea, headache, diarrhea (stop medication and contact physician with blood in stool or abdominal pain)
- Myelosuppression (including anemia and thrombocytopenia)
- Lactic acidosis
- Pseudomembranous colitis

Contraindications or caution with Zyvox applies to:

Blood dyscrasias

Cardiac disease, hypertension

GI disease, hyperthyroidism

Pregnancy, lactation, infants

Interactions of Zyvox may occur with:

Beta-blockers (worsen bradycardia)

Radiographic contrast media (increased risk of seizures)

Antidepressants (e.g., SSRIs can cause serotonin syndrome)

Migraine medications (triptans)

Sympathomimetics such as phenylephrine, pseudoephedrine (hypertensive reaction)

Foods or beverages with high tyramine content (see discussion in Chapter 20)

Daptomycin (Cubicin) is the first in a new class of antibiotics called lipopeptides with a spectrum of activity similar to vancomycin. Daptomycin shows promise in treating VRE infections and endocarditis with associated bacteremia.

Side effects of Cubicin can include:

Constipation, nausea, injection site reactions, and headache

- Elevated levels of creatinine phosphokinase (CPK), leading to myopathy (monitor CPK levels weekly)

Contraindications or caution with Cubicin applies to:

Renal impairment—dosage adjustments required in severe disease

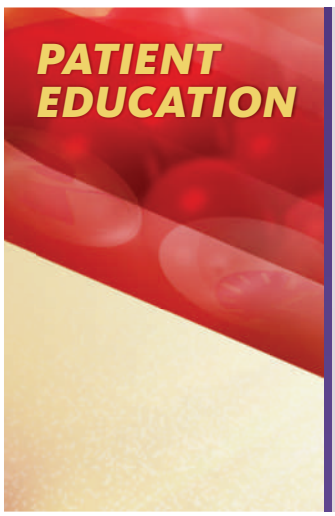
Pneumonia—daptomycin is inactivated by pulmonary surfactant and therefore is ineffective

See Table 17.3 for Miscellaneous Anti-infectives and Agents for VRE.

Table 17-3 Miscellaneous Anti-infectives and Agents for VRE

GENERIC NAME	TRADE NAME	AVERAGE DOSAGE	COMMENTS
Miscellaneous Anti-infectives			
clindamycin	Cleocin	PO 150–450 mg q6h, Peds 8–25 mg per kg per day divided doses, IM/IV 600 mg–2.7 g per day divided doses	
metronidazole	Flagyl	250–500 mg q8h–q6h IV, PO (max 4 g per 24 h)	
	Flagyl ER	PO 750 mg per day (for bacterial vaginosis)	
vancomycin	Vancocin	PO: 125–500 mg q6h × 7–10 days	For pseudomembranous colitis (IV route not effective)
		IV: 10–20 mg per kg IV q12–24h	IV dose varies according to age, weight, indication, renal function and serum drug monitoring
Agents for VRE			
daptomycin	Cubicin	IV 4–6 mg per kg q24h	Adjust dosage with severe renal impairment
linezolid	Zyvox	PO, IV 600 mg q12h	

Note: Other anti-infectives are available. Only a few are represented here. Pediatric doses are computed according to weight and condition of child.



Patients taking antibiotics should be instructed regarding:

Unless directed otherwise, taking all antibiotics with a full glass of water on empty stomach, at least one hour before meals or two hours after meals

Not taking with fruit juice

Not taking with antacids

Not taking with alcohol

If side effects occur, discontinuing medication and consulting the physician or pharmacist

Reporting rash, swelling, or breathing difficulty to the physician *immediately*

Taking antibiotics at prescribed times to maintain blood levels

Taking entire prescription *completely*; *not* discontinuing when symptoms of infection disappear

Not taking any other medications, prescriptions, or over-the-counter drugs at the same time as antibiotics without checking first with the physician or pharmacist regarding interactions

ANTIVIRALS

Acyclovir

The **antiviral** *acyclovir* is used predominantly in the treatment of herpes simplex, herpes zoster (shingles), and varicella zoster (chickenpox) infections. Acyclovir does not cure or prevent further occurrence of blisterlike lesions. Topical application appears effective only with initial infections in relieving discomfort and shortening healing time of lesions (see Skin Medications.) Oral treatment is most effective in initial treatment of herpes to relieve pain and to speed healing of lesions and is also used to treat recurrent infections in some patients. In immunocompromised patients and children, parenteral treatment is recommended.

Herpes zoster (shingles) *is best treated within 24 to 72 h of onset* of rash (blisterlike) or intense pain on the skin of one side of the trunk or head. Delayed treatment with an antiviral medication can lead to complications, especially in older adults, such as intense pain, post-herpetic neuralgia (PHN), lasting for weeks or months. PHN is treated with tricyclic antidepressants (e.g., imipramine) or anticonvulsants (e.g., gabapentin). (See Chapter 20, Adjuvant Analgesics.)

Valacyclovir (Valtrex) is a pro-drug that is converted to acyclovir as it is broken down within the body. The adverse reaction profile is the same as for acyclovir, but improved bioavailability means less frequent dosing for valacyclovir. Famciclovir (Famvir) has a similar spectrum of activity to acyclovir, but has a longer duration of action and can be dosed less frequently.

Side effects of acyclovir are not common, but can include:

Impaired renal function, especially with *rapid IV infusion*

- Lethargy, tremors, confusion, and headache, especially with older adults
- Rash, urticaria, pruritus and photosensitivity
- Nausea, vomiting, abdominal pain, and diarrhea

Contraindications or caution with acyclovir include:

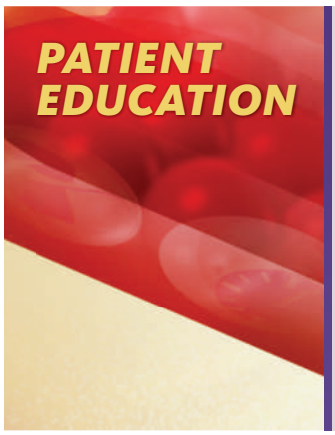
Children, breast feeding

Renal disease (adjust dosage)

Dehydration

Neurological abnormalities with high doses

Zostavax is a herpes zoster vaccine approved for the prevention of shingles in appropriate persons aged 60 to 80. The vaccine is administered in a single subcutaneous dose. It reportedly decreases the occurrence of herpes zoster by approximately 50% and prevents the development of PHN by two thirds.



Patients being treated with acyclovir should be instructed regarding:

- The fact that acyclovir is usually effective only with *initial* infection in relieving pain and shortening healing of lesions, but is *not* a cure and there can be recurrences of lesions
- Reporting side effects
- Taking medicine only as prescribed. Do not share drug with others
- Finish full course prescribed, even if feeling better
- Avoidance of sexual intercourse when visible genital herpes lesions are present and using protection at other times

Neuraminidase Inhibitors

Oseltamivir (Tamiflu) and zanamivir (Relenza) belong to a class of antivirals called *neuraminidase inhibitors* and are indicated for the treatment of uncomplicated acute illness due to influenza types A and B. Safety and efficacy for the prophylaxis of influenza infection in infants < 1yr (for Tamiflu) and children < 5yrs (for Relenza) are not yet established. Oseltamivir is given orally and zanamivir via inhalation; both will shorten the duration of illness about 1 day if taken *within 48 h of symptom onset.*

Since zanamivir is given via inhalation, its main side effect is airway irritation and bronchospasm, especially in patients with asthma and chronic obstructive pulmonary disease (COPD). In patients with susceptibility to bronchospasm, a bronchodilator can be concurrently administered (see Chapter 26 on respiratory drugs). Oseltamivir causes nausea, vomiting, and diarrhea in one out of four patients receiving it; these side effects can be lessened by taking the medication with food.

Ribavirin

A drug with the broadest spectrum of antiviral activity, *ribavirin*, is used via nasal and oral inhalation for the treatment of infants and children with respiratory syncytial virus (RSV) infections. It has also been used orally or parenterally in the treatment of other severe viral infections in adults, for example, Lassa fever, Hantavirus, and hepatitis C (in combination with interferon alfa).

Side effects of ribavirin can include:

- Respiratory complications
- Hypotension, cardiac arrest
- Anemia
- Rash, conjunctivitis

Contraindicated during pregnancy or lactation. Health care practitioners and visitors who are pregnant or lactating should be warned about the *serious risk of close contact with patients receiving ribavirin inhalation therapy*. Also contraindicated for older adults and those with cardiac disease.

Interactions of ribavirin with NRTIs (agents for HIV), depending on specific agent, can:

Antagonize antiviral action against HIV

Cause lactic acidosis

Cause hepatic failure

TREATMENT OF HUMAN IMMUNODEFICIENCY VIRUS/AIDS INFECTIONS

Treatment of HIV and AIDS infections is a highly specialized field. Those actively practicing in that field must be updated frequently on the many *new* medications and *frequently changing protocols*.

The following information is presented to give health care practitioners an overview of the complexity of HIV therapy. If you are not actively practicing in this area, you would not be expected to be familiar with all of the many drugs for HIV. (See Table 17-4.) However, all health care practitioners should be aware that there are numerous side effects and interactions specific to individualized medications. If you are caring for someone with HIV, it is imperative that you familiarize yourself with that particular individual's requirements by researching current information and consulting the pharmacist and/or infectious disease specialists. Additional resources are described following the section, which discusses drugs for HIV.

Acquired immunodeficiency syndrome (AIDS) is due to infection by the human immunodeficiency virus (HIV). Agents approved to treat HIV ("antiretrovirals") are classified by their mechanism of action and include: (1) protease inhibitors (PIs), (2) nucleoside reverse transcriptase inhibitors (NRTIs), (3) non-nucleoside reverse transcriptase inhibitors (NNRTIs), (4) fusion inhibitors (FIs), (5) integrase inhibitors, and (6) CCR5 antagonists.

The treatment of HIV infection consists of using highly active antiretroviral therapy (HAART) combinations of three or more antiretroviral (ARV) agents and is one of several factors that has led to a decline in the U.S. mortality rate of AIDS. The primary approach to therapy is disruption of the virus at different stages in its reproduction. Eradication of HIV infection *cannot* be achieved with currently available antiretroviral regimens. *The goals of HIV therapy are to achieve maximal and durable suppression of viral load, restore and/or preserve immunological function, improve quality of life, reduce HIV-related morbidity, prolong survival, and prevent vertical HIV transmission.*

The treatment of HIV-infected patients is complex due to the availability of numerous antiretroviral agents and the rapid growth of new information. A patient's clinical condition, readiness for lifelong therapy, CD4 count, and plasma viral load are essential parameters to be used in decisions to initiate or change therapies. Current guidelines for initial treatment of HIV infection recommend the use of two NRTIs with either a protease inhibitor or an NNRTI. Consult www.aidinfo.nih.gov for most current treatment information.

Antiretroviral Protease Inhibitors (PIs)

The first PI to be approved was saquinavir (Invirase), followed by more than eight other antiretroviral protease inhibitors. (See Table 17-4 for names of other PIs.)

Side effects can include:

All PIs are associated with GI intolerance, including nausea, vomiting, and diarrhea

Table 17-4 Antivirals and Drugs for HIV/AIDS

GENERIC NAME	TRADE NAME	DOSAGE
Antivirals		Take entire Rx even if feeling better.
for herpes infections		
acyclovir	Zovirax	PO 200–800 mg 5 × per daily q4h, IV 5 mg per kg q 8h
famciclovir	Famvir	PO 500 mg q8h
valacyclovir	Valtrex	PO 1,000 mg q8h
for influenza		
oseltamivir	Tamiflu	PO 75 mg BID for 5 days
zanamivir	Relenza	Inhale 10 mg q12h for 5 days
for RSV		
ribavirin	Virazole	Pwdr/sol–inhalation
	Copegus	Oral, dose varies
Example Drugs for HIV[a]		**Class Adverse Effects**
Protease inhibitors (PIs)		
atazanavir	Reyataz	GI intolerance, hyperglycemia
darunavir	Prezista	
Nucleoside reverse transcriptase inhibitors (NRTIs)[b]		
abacavir	Ziagen	Lactic acidosis, liver dysfunction
lamivudine/zidovudine	Combivir	
zidovudine	Retrovir	
Non-nucleoside reverse transcriptase inhibitors (NNRTIs)		
delavirdine	Rescriptor	Rash; many drug interactions
efavirenz	Sustiva	
Fusion inhibitors (FIs)		
enfuvirtide	Fuzeon	Adverse effects vary with drug
CCR5 Antagonists		
maraviroc	Selzentry	
Integrase Inhibitor		
raltegravir	Isentress	

[a]Other drugs and combinations are being used investigationally in the treatment of HIV- and AIDS-related diseases. Dosage varies with condition. *Check dosage very carefully.*
[b]*Other combination products available in this class are not listed.*

Taste alteration in patients receiving ritonavir, especially the liquid formulation

Fat redistribution, hyperlipidemia, and insulin resistance

Hyperglycemia, new-onset diabetes mellitus, diabetic ketoacidosis, and exacerbation of existing diabetes

Increased spontaneous bleeding episodes in hemophilia patients (joints, soft tissues, intracranial, and GI bleeding)

Indinavir may cause kidney stones (patients should drink at least 1.5 L/day of water to ensure adequate hydration and prevent kidney stones)

Interactions with PIs are many. Check with the pharmacist before administering with other drugs.

Dietary considerations with PIs:

Most PIs should be taken with food to reduce nausea and gastric irritation. Always check instructions regarding administration.

Nucleoside Reverse Transcriptase Inhibitors (NRTIs)

Zidovudine (ZDV, Retrovir) was the first agent to be approved for the treatment of HIV, followed by more than six other NRTIs. (See Table 17-4 for names of other NRTIs.) Combivir, a combination of zidovudine and lamivudine (there are currently four other combinations), allows patients to reduce the number of pills needed daily, which can be upward of 20 a day for certain drug combinations. Most NRTIs are dose adjusted in patients with renal dysfunction.

Side effects of NRTIs can include:

As a class, NRTIs have been associated with lactic acidosis and liver dysfunction (infrequently, but have a high mortality rate)

The major side effect of zidovudine is bone marrow suppression consisting of anemia and/or neutropenia

Didanosine has been associated with pancreatitis

Didanosine and stavudine are associated with peripheral neuropathy

Abacavir has been associated with hypersensitivity reactions that can be fatal. Prior to starting abacavir, it is recommended to obtain an HLA B5701 genetic test. If positive, abacavir should not be started because the patient will be at a higher risk of developing a life-threatening hypersensitivity reaction. Patients who develop signs or symptoms of abacavir hypersensitivity (which may include fever, rash, fatigue, nausea, vomiting, diarrhea, cough, and sore throat) should discontinue abacavir immediately.

Interactions of NRTIs include:

Alcohol

Antacids and iron preparations

Dietary considerations with NRTIs include:

Always check instructions regarding administration as some should be given ac and some pc.

Non-Nucleoside Reverse Transcriptase Inhibitors (NNRTIs)

Nevirapine (Viramune) was the first NNRTI to be approved, followed by three others (see Table 17-4 for names of other NNRTIs).

Adverse reactions with NNRTIs can include:

Hepatitis possible with some

Side effects of NNRTIs can include:

CNS symptoms may include dizziness, insomnia, and mental symptoms

Interactions with NNRTIs are many. Check with the pharmacist before administering with other drugs.

Dietary considerations with NNRTIs:

Always check instructions regarding administration as some should be given ac and some pc.

Fusion Inhibitors (FIs)

This class of antiretroviral agents, called fusion inhibitors, has been shown to block entry of HIV into cells, which may keep the virus from reproducing. Enfuvirtide (Fuzeon) was the first fusion inhibitor approved for treatment–experienced patients with ongoing HIV replication despite current ARV use. It is administered by subcutaneous injection twice daily.

Almost all patients develop local site reactions to enfuvirtide, usually consisting of mild or moderate pain, erythema, itching, induration, nodules, and cysts. It is important to remember to rotate injection sites.

CCR5 Antagonists

Maraviroc (Selzentry) is the first oral CCR5 antagonist and is used in conjunction with other ARVs. Hepatotoxicity has been reported and may be accompanied by signs/symptoms of a systemic allergic reaction. Do not use maraviroc with St. John's Wort as this combination can lead to treatment failure.

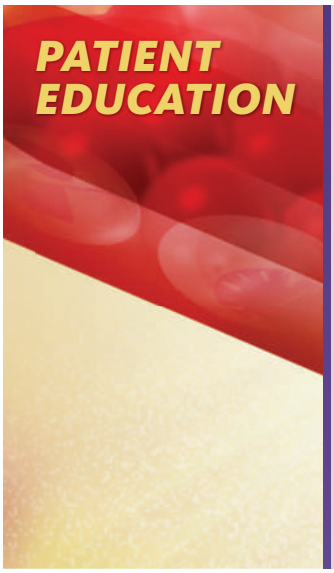
Integrase Inhibitor

Raltegravir (Isentress) is the first ARV in this class which is designed to slow the advancement of HIV infection by blocking the enzyme needed for viral replication. It is indicated for use in combination with other ARVs in treatment-experienced adults. Most common adverse effects are nausea, headache, diarrhea, and pyrexia. Rifampin can decrease plasma concentrations of raltegravir.

Although highly active antiretroviral therapy (HAART) is a significant advance in the treatment of HIV, it is still not a cure. Other factors such as high cost, complicated regimens, patient adherence, and interactions with other therapies may limit the utility of these regimens.

HIV INFORMATION AND RESOURCES

Current recommendations for the clinical use of antiretrovirals (ARVs) in the management of HIV-infected adults, adolescents, children, and infants may be found at HIV/AIDS Education and Resource Center at (800) 448-0440 or at www.aidsinfo.nih.gov. These guidelines are developed by the U.S. Department of Health and Human Services and the Henry J. Kaiser Family Foundation.



Patients taking antiretrovirals should be instructed regarding:

- No cure for HIV, and opportunistic infections may develop
- Taking the drug in an upright position with full glass of water
- Taking the drug exactly as prescribed; do not stop abruptly
- Taking into account dietary considerations
- Reporting any change in health status or side effects
- Not exceeding the prescribed dosage
- Not sharing the drug with others
- Not taking any other drugs unless prescribed, for example, acetaminophen contraindicated
- Medication does *not* reduce the risk of transmission of HIV to others through sexual contact or blood contamination.

Treatment of the Opportunistic Infections of AIDS

Opportunistic infections are those that occur because the immune system is compromised; for example, Kaposi's sarcoma, *Pneumocystis jiroveci* pneumonia, and toxoplasmosis.

- ***Interferons*** are antiviral drugs sometimes used in the palliative treatment of AIDS-related *Kaposi's sarcoma* in selected adults who meet certain criteria; that is, who are otherwise asymptomatic and not severely immunocompromised. Interferon has also been used in the treatment of chronic hepatitis and in some leukemias and other malignancies. *Adverse side effects are common* and varied, depending on dosage and condition treated (see Antineoplastic Drugs).
- Pneumocystis jirovecii pneumonia treatment:

Sulfamethoxazole (SMX) and trimethoprim (TMP) (oral or IV) for prevention in all HIV-infected children and in asymptomatic adults with CD41 T-cell counts less than 200; for *treatment* of adults and children (see Side Effects, Contraindications, and Interactions under Sulfonamides in this chapter).

Pentamidine aerosolized oral inhalation (antiprotozoal agent) for *prevention* in HIV-infected children and in adults with CD41 T-cell counts less than 200; for *treatment* of adults and children in patients whose infection does not respond to SMX-TMP or who cannot tolerate SMX-TMP because of allergies or adverse side effects.

Side effects of pentamidine can include:

Nephrotoxicity

Cough and bronchospasm

Electrolyte imbalance

Cautions: Health care personnel who administer pentamidine inhalation therapy to HIV-infected patients should be aware of the possibility of exposure to tuberculosis in cough-inducing procedures. Antituberculosis therapy should be initiated before pentamidine treatment in potentially infectious tuberculosis

patients. *Use of high-efficiency particulate air filter respirators by health care personnel in such settings is imperative, as well as appropriate isolation procedures.*

Caution (pentamidine) in pregnancy and lactation.

Clindamycin combined with primaquine (alternative treatment). See Side Effects and Cautions of clindamycin under Miscellaneous Anti-Infectives in this chapter.

- ***Toxoplasmosis treatments:***

Sulfamethoxazole and trimethoprim (Bactrim, Septra) or *pyrimethamine with sulfadoxine* (Fansidar). See Sulfonamides section for side effects of both of these combination drugs.

Clindamycin. See Side Effects and Cautions of clindamycin under Miscellaneous Anti-Infectives in this chapter.

- ***Cytomegalovirus retinitis treatment:***

Two antiviral agents used to treat this condition are foscarnet and ganciclovir.

Side effects of foscarnet are common and can be severe, including:

Nephrotoxicity

Nausea, vomiting, and diarrhea

Electrolyte imbalance and cardiac abnormalities

Coughing and dyspnea

Seizures

Blood dyscracias

Side effects of ganciclovir are frequent, but usually reversible, including:

Blood dyscrasias—neutropenia and thrombocytopenia

Headache, confusion, seizure

Renal effects

See Table 17-5 for a summary of drugs used to treat the opportunistic diseases of AIDS.

Table 17-5 Drugs for Opportunistic Diseases of AIDS

GENERIC NAME	TRADE NAME	AVERAGE DOSAGE
Sulfamethoxazole and trimethoprim	Bactrim, Septra	Adults or peds 15–20 mg per kg per day PO or IV div. doses
Clindamycin	Cleocin	1.2–3.6 g daily PO or IV div. doses
Pentamidine	NebuPent, Pentam	Aerosol inhalation, IM/slow IV infusion, dose varies
Interferon	Intron A	Dose varies • Always check current literature for dosage and side effects. • Other drugs and combinations are being used investigationally in the treatment of HIV- and AIDS-related diseases.

SULFONAMIDES

Sulfonamides are among the oldest anti-infectives. The increasing resistance of many bacteria has decreased the clinical usefulness of these agents. However, they are used most effectively in combinations with other drugs, for example, with trimethoprim (sulfamethoxazole and trimethoprim). In combinations such as these, resistance develops more slowly. Sulfamethoxazole and trimethoprim (Bactrim, Septra) is used for urinary tract infections (UTIs), especially acute, complicated UTIs; enteritis (e.g., travelers' diarrhea) and otitis media. In higher doses, it may also be considered as an oral alternative to vancomycin when treating MRSA infections. Sulfamethoxazole and trimethoprim is used in the treatment of *Pneumocystis jiroveci* pneumonia in AIDS patients or prevention of that disease in HIV-infected children (see treatment of HIV/AIDS in this chapter). This combination drug is also used in the treatment of toxoplasmosis in AIDS patients.

Side effects with sulfonamides are numerous and sometimes serious, especially with AIDS patients, and can include:

- Rash, pruritus, dermatitis, and photosensitivity
- Nausea, vomiting, and diarrhea
- High fever, headache, stomatitis, and conjunctivitis
- Blood dyscrasias
- Hepatic toxicity with jaundice
- Renal damage with crystalluria and hematuria
- Hypersensitivity reactions, which can be fatal

Contraindications or warnings with sulfonamides include:

- Impaired hepatic function
- Impaired renal function or urinary obstruction
- Blood dyscrasias
- Severe allergies or asthma (some studies suggest approximately 3% of the population is allergic to Sulfa drugs)
- Pregnancy or lactation

Interactions with sulfonamides include:

- Potentiation of anticoagulants and oral antidiabetics
- Antagonism of local anesthetics (e.g., procaine may inhibit antibacterial action of sulfa) Potentiation of phenytoin (Dilantin) (e.g., increasing serum drug concentrations)

PATIENT EDUCATION

Patients taking sulfonamides should be instructed regarding:

- Importance of drinking large amounts of fluid to prevent crystalluria
- Discontinuance of sulfa at first sign of rash

Reporting any side effects to physician *immediately*

Avoiding exposure to sunlight

Ingestion of sulfa with food, which delays, but does not reduce, absorption of the drug

URINARY ANTI-INFECTIVES

Urinary anti-infectives are usually bacteriostatic instead of bactericidal in action. Nitrofurantoin (Furadantin and Macrodantin) is most commonly used for initial or recurrent urinary tract infections caused by susceptible organisms. This medication is a recommended oral treatment option for cystitis (bladder infection) in women not men because tissue concentrations are generally lower resulting in inadequate treatment of occult prostatitis. Due to the achievement of lower tissue concentrations, nitrofurantoin is not routinely used to treat pyelonephritis in men or women. Treatment must continue for an adequate period of time to be effective and minimize recurrence of infection.

Side effects of nitrofurantoin can include:

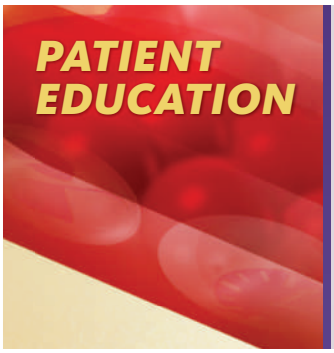
- Nausea and vomiting, which are less frequent if taken with milk or food
- Numbness and weakness of lower extremities
- Headache, dizziness, and weakness of muscles
- Respiratory distress with prolonged use
- Brown urine
- Anemia

Contraindications or caution with Furadantin and Macrodantin applies to:

- Renal or hepatic impairment
- Anemia
- Diabetes
- Electrolyte abnormalities
- Asthma
- Pregnancy and lactation
- Children under one month of age

Interactions of nitrofurantoin (antagonistic) with:

- Probenecid and magnesium
- Antacids containing magnesium decreasing the effectiveness of these drugs
- Quinolones



Patients taking nitrofurantoin should be instructed regarding:

- Importance of taking medication for required number of days
  Reporting side effects
- Taking medication with milk or food to reduce incidence of nausea and vomiting
- Avoiding antacids
- Discoloration of the urine, which can stain underpants

See Table 17-6 for a summary of the sulfonamides and urinary anti-infectives.

Table 17-6 Sulfonamides and Urinary Anti-infectives

GENERIC NAME	TRADE NAME	DOSAGE
Sulfonamides		
Sulfamethoxazole (smx) and trimethoprim (tmp)	Septra, Bactrim	Tab, suspension, IV 160 mg (tmp) q12h or 6–10 mg per kg per day in div. doses
Urinary Anti-infective		
nitrofurantoin	Macrodantin, Furadantin	Cap, suspension 50–100 mg 4 × per day
trimethoprim		100 mg tab q12–24h

Other anti-infective agents in all of these categories discussed in this chapter are available. This is a representative sample of drugs most commonly in use. Research is ongoing with these and other new drugs, and the FDA has developed procedures to expedite the review and approval of certain new drugs. FDA's fast track drug development programs are designed to facilitate the development and expedite the review of drug and biological products that are intended to treat serious or life-threatening conditions and that demonstrate the potential to address unmet medical needs.

CASE STUDY – A

Anti-infective Drugs

Marguerite Madre, a 19-year-old pregnant woman, allergic to penicillin, calls her physician and requests some tetracycline for her acne and some Keflex for a "sore throat." The following information would be useful to her.

1. Tetracycline is contraindicated under all of the following circumstances EXCEPT
   a. Pregnancy
   b. Children under age 8
   c. Working indoors
   d. Nursing a baby
2. Sometimes organisms develop resistance to drugs. The following practices could lead to resistance EXCEPT
   a. Too frequent antibiotic use
   b. Combination antibiotics
   c. Antibiotic for minor URI
   d. Stopping drug after two days
3. If she has fever, in addition to the sore throat, or trouble swallowing, the physician might order a throat culture to determine:
   a. Causative organisms
   b. Possible allergies
   c. Drug interactions
   d. Drug toxicity
4. Those allergic to penicillin might also be sensitive to cephalosporins. The following are signs of allergic reaction EXCEPT
   a. Rash
   b. Hives
   c. Trouble breathing
   d. Vomiting
5. Cephalosporins can cause superinfections manifested by all of the following EXCEPT
   a. Diarrhea
   b. Vomiting
   c. Sore mouth
   d. Vaginitis

CASE STUDY – B

Anti-infective Drugs

Tom Brown, a 35-year-old prison guard, has a skin test read as positive for tuberculosis infection. He has a cough. Active disease is confirmed by sputum test. The following information will be important to him.

1. He will need to take medicines for a minimum of
   a. 1 month
   b. 3 months
   c. 6 months
   d. 2 years
2. Family members will be treated prophylactically with which one of the following medications?
   a. Rifampin
   b. Isoniazid
   c. Ethambutol
   d. Streptomycin
3. While taking the antituberculosis drugs, which one of the following should be avoided?
   a. Milk
   b. Orange juice
   c. Alcohol
   d. Sunlight
4. He will take at least four drugs initially, including all of the following EXCEPT
   a. Isoniazid
   b. Rifampin
   c. Pyrazinamide
   d. Zidovudine
5. Side effects of INH and rifampin are more pronounced at first and can include all of the following EXCEPT
   a. Diarrhea
   b. Dizziness
   c. Hearing problems
   d. Nausea and vomiting

CHAPTER REVIEW QUIZ

Match the medication in the first column with the condition in the second column that it treats. Conditions may be used more than once.

	Medication	Condition
1. _____	nitrofurantoin (Macrodantin)	**a.** Herpes zoster and herpes simplex
2. _____	nystatin	**b.** MRSA and VRE
3. _____	fluconazole (Diflucan)	**c.** Urinary tract infections
4. _____	linezolid (Zyvox)	**d.** Tuberculosis
5. _____	Ethambutol	**e.** Acne
6. _____	Valacyclovir	**f.** Fungus
7. _____	Erythromycin	**g.** Influenza A

Choose the correct answer.

8. The goals of HIV therapy include all of the following EXCEPT:
- **a.** Restore immune function
- **b.** Improve quality of life
- **c.** Eradicate the virus
- **d.** Reduce morbidity

9. All of the following are possible side effects of sulfonamides EXCEPT:
- **a.** Kidney stones
- **b.** Hypersensitivity
- **c.** Photosensitivity
- **d.** Confusion

10. Which statement is not true of aminoglycosides, for example gentamycin?
- **a.** Usually given PO
- **b.** Use with caution in the elderly
- **c.** Can cause vertigo
- **d.** Can cause deafness

11. Which statement is not true of clarithromycin, a macrolide?
- **a.** Can cause superinfections
- **b.** Used to treat *H. pylori*
- **c.** useful for hospital-acquired infections
- **d.** Few interactions

12. The following statements are true of penicillin interactions EXCEPT?
- **a.** Potentiated with probenecid
- **b.** Penicillin inhibits contraceptives
- **c.** Potentiated with food
- **d.** Potentiated with NSAIDs

13. The quinolones, for example Cipro, can have all of the following side effects EXCEPT:
- **a.** Tendon rupture
- **b.** Sunburn
- **c.** Constipation
- **d.** Confusion

14. The following statements are true of tetracyclines EXCEPT:
- **a.** Discolor children's teeth
- **b.** Accelerate bone growth
- **c.** Used to treat acne
- **d.** Used to treat *H. pylori*

15. Interactions of INH and rifampin with specific other drugs can have the following specific results EXCEPT:
- **a.** Ineffective birth control
- **b.** Lower effect with hypoglycemics
- **c.** Optic neuritis
- **d.** Hepatic toxicity

16. The following statements are true of metronidazole (Flagyl) therapy EXCEPT:
- **a.** For *Trichomonas vaginalis*
- **b.** In combination for *H. pylori.*
- **c.** Avoid alcohol
- **d.** Causes constipation

17. The following statements apply to vancomycin therapy EXCEPT:
- **a.** Kidney side effect
- **b.** Used routinely for prophylaxis
- **c.** Deafness possible
- **d.** VRE possible

18. The following statements apply to treating herpes zoster (shingles) with acyclovir EXCEPT:
- **a.** Start within 72 h
- **b.** Relieves discomfort
- **c.** Shortens healing
- **d.** Prevents recurrence

Go to your StudyWARE™ CD-ROM and have fun learning as you play games and answer case study-related questions to help reinforce key concepts you learned in this chapter.

Go to your Study Guide and complete the review questions for this chapter

Chapter 18

Eye Medications

Objectives

Upon completion of this chapter, the learner should be able to

1. Demonstrate the administration technique for instillation of ophthalmic medication to reduce systemic absorption
2. List the five categories of ophthalmic medication
3. Identify side effects, contraindications, and interactions for each category of ophthalmic medication
4. Explain appropriate patient education necessary for each category of eye medication
5. Define the Key Terms and Concepts

Key Terms and Concepts

Antiglaucoma agents
Anti-infective
Anti-inflammatory
Beta-adrenergic blocker
Carbonic anhydrase inhibitors
Cycloplegic
Intraocular pressure
Miotics
Mydriatics

Medications for the eye can be classified into five categories: anti-infectives, anti-inflammatory agents, antiglaucoma agents, mydriatics, and local anesthetics.

ANTI-INFECTIVES

Many **anti-infective** ophthalmic topical ointments and solutions are available for treatment of superficial infections of the eye caused by susceptible organisms. In general, ointments are preferable to drops in children and patients with poor adherence, while drops are preferred in adults since ointments will cause blurring of vision for 20 minutes after instillation. It is important to determine the causative organism so that the appropriate medication is used. Ophthalmic antibiotic preparations (singly and/or in combination) include macrolides, bacitracin, sulfonamides, bacitracin-polymixin, and others. Fluoroquinolones are generally not first-line therapy due to concerns over resistance and cost. Aminoglycosides are avoided due to toxicity to the corneal epithelium. When treating infections, if there is no improvement in two to three days, suspect microbial resistance, inappropriate choice of drug, or incorrect diagnosis.

In general, topical therapy should not exceed 10 days. Prolonged use may result in overgrowth of nonsusceptible organisms including fungi. Always check the latest literature regarding resistant organisms and check the patient's history regarding allergies. See Chapter 17 for further details on anti-infective agents, resistance, and allergies.

PATIENT EDUCATION

Patients being treated with anti-infective ophthalmic preparations should be instructed regarding:

- Using only as directed; check dosage for frequency
- Careful instillation into the lower conjunctival sac to avoid contamination of the tip of the dropper or ointment tube (see Figure 18-1)
- Possible hypersensitivity reactions in patients with allergies of any kind
- Discontinuance of the medication and reporting immediately to a physician any signs of sensitivity (e.g., burning and itching)
- Careful handwashing to prevent spread of infection to other eye or other persons
- Not using eye makeup or not wearing contact lenses while treating eye infections
- When using more than one ophthalmic product at the same time, space them at least 5 minutes apart (to ensure maximum absorption) and administer the more viscous preparation (i.e., ointment, suspension) *last*.

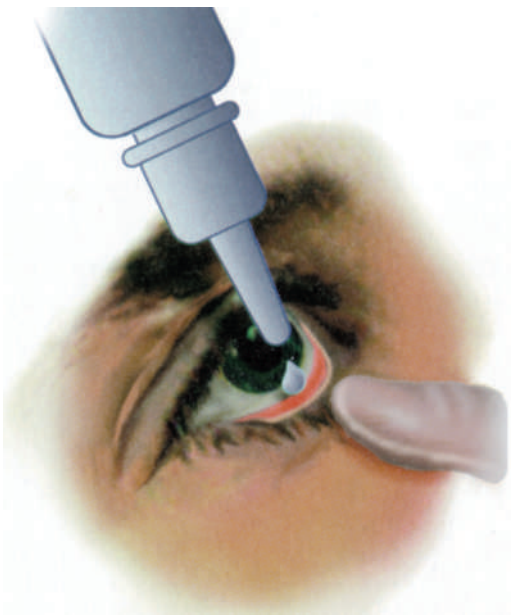
StudyWARE™ CONNECTION

See It In Action! Go to the StudyWARE™ CD-ROM to view a video on Administering Eye Medications.

Side effects of anti-infectives can include hypersensitivity reactions such as conjunctivitis, local burning, stinging, blurred vision, rash, and urticaria in allergic persons.

Contraindications or extreme caution for anti-infectives apply to:

- Anyone allergic to the drug
- Viral and fungal diseases of the ocular structure



Delmar/Cengage Learning

FIGURE 18-1 Instilling eye medication. Gently press the lower lid down and have the patient look upward. Opthalmic solution is dropped inside the lower eyelid.

Interactions may occur with prolonged use of corticosteroids, which can result in secondary ocular infections caused by suppression of immune response.

Antiviral ophthalmic preparations, used topically in the treatment of herpes simplex, keratitis, or conjunctivitis include trifluridine (Viroptic) ophthalmic solution. Dose is 1 drop to the lower conjunctival sac of the infected eye up to nine times daily at two-hour intervals while awake.

ANTI-INFLAMMATORY AGENTS

Anti-inflammatory ophthalmic agents are used to relieve inflammation of the eye or conjunctiva in allergic reactions, burns, postoperatively, or irritation from foreign substances.

Corticosteroids

Various topical forms of the corticosteroids are also useful in the *acute* stages of eye injury to prevent scarring but are not used for extended periods because of the danger of masking the symptoms of infection or slowing the healing process. In general, ophthalmic corticosteroids should only be prescribed by ophthamologists since they may cause sight-threatening complications when used inappropriately. Application of ophthalmic corticosteroids topically does not generally cause systemic effects. However, systemic absorption can be minimized by gentle pressure on the inner canthus of the eye following instillation of corticosteroid ophthalmic drops or ointment (see Figure 18-2).

Side effects of corticosteroids can include:

- Increased intraocular pressure (depends on dose, frequency, and length of treatment)

Delmar/Cengage Learning

FIGURE 18-2 Gentle pressure on the inner canthus following administration of ophthalmic medications. Systemic absorption is thus minimized with medications such as corticosteroids, miotics, and mydriatics.

- Reduced resistance to bacteria, virus, or fungus
- Delayed healing of corneal wounds, thinning of cornea, corneal ulceration
- Stinging, burning, or ocular pain
- Cataracts

Contraindications or extreme caution with corticosteroids applies to:

Acute bacterial, viral, or fungal infections

Primary open-angle glaucoma

Pregnancy

Prolonged use

Ophthalmic corticosteroids are also available in combination with antibiotics (i.e., TobraDex—tobramycin & dexamethasone; Blephamide—sulfacetamide & prednisolone). They are used to treat steroid-responsive inflammatory ocular conditions in which a corticosteroid is indicated and in which bacterial infection or risk of infection exists.

Nonsteroidal Anti-inflammatory Drugs (NSAIDs)

NSAIDs such as flurbiprofen (Ocufen) and ketorolac (Acular) ophthalmic drops are used to treat postoperative inflammation following cataract surgery. NSAIDs are not generally first-line agents for other eye conditions with inflammation, but are an alternative to corticosteroids if a contraindication exists.

Caution applies to those who may be allergic to aspirin and other NSAIDs.

Ophthalmic Immunologic Agent

Topical cyclosporine (Restasis) increases tear production in patients whose tear production is presumed to be suppressed due to ocular inflammation. It is an immunosuppressive agent for organ transplant rejection prophylaxis when administered systemically. However, the risk of systemic toxicity is minimal when given topically. Topical cyclosporine has demonstrated long-term efficacy and safety in the treatment of dry eye disease (other treatments are not recommended for long-term use).

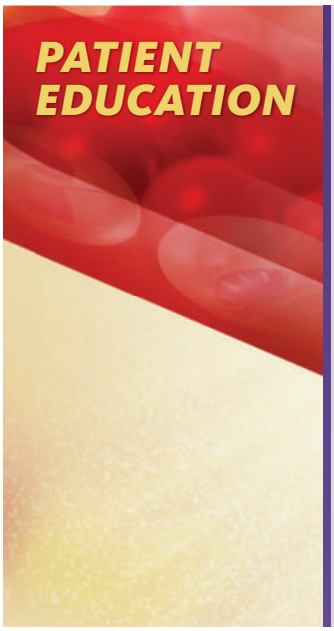
Contraindications or caution applies to patients with active ocular infections; topical cyclosporine has not been studied in patients with a history of herpes keratitis.

Side effects of topical cyclosporine which are mild and transient include ocular burning, stinging and blurred vision.

Antihistamines/Decongestants

Ophthalmic administration of antihistamines blocks histamine receptors in the conjunctiva, relieving ocular pruritis associated allergic conjunctivitis. Ophthalmic administration of decongestants causes vasoconstriction of blood

vessels, thereby providing relief from minor eye irritation. The two classes of drugs are also used in combination (i.e., Naphcon-A, Visine-A). See Chapter 26 on antihistamines for more information.



Patients being treated with anti-inflammatory ophthalmic drugs should be instructed regarding:

- Patients should avoid rubbing their eyes since this can worsen the condition
- Following directions carefully regarding time and amount
- Lowered resistance to infection—do not use long term
- Administration (i.e., pressure on tear duct at inner corner to reduce systemic absorption) (see Figure 18-2 and the video on your StudyWARE™)
- Avoid wearing contact lenses if eyes are red
- Remove lenses prior to using product; contacts may be reinserted for most products if eyes are not red
- Not using leftover drug for new eye inflammation—discard drug when no longer needed

See Table 18-1 for a summary of anti-inflammatory ophthalmic drugs.

Table 18-1 Anti-inflammatory Ophthalmic Drugs

GENERIC NAME	TRADE NAME	DOSAGE
Corticosteroids		
fluorometholone	FML	Oint, susp; varies with condition
prednisolone	Omnipred, Pred Forte	Sol, susp; varies with condition
	Many combinations with antibiotics	Oint, sol, susp; varies with condition
dexamethasone	Maxidex	Sol, susp; varies with condtion
	Many combinations with antibiotics	Oint, sol, susp; varies with condition
Nonsteroidal Anti-inflammatory Drugs		
flurbiprofen	Ocufen	Sol; varies with condition
ketorolac	Acular, Acular LS	Sol; varies with condition
Immunologic Agent		
cyclosporine	Restasis	emulsion 0.05%; 1 gtt q12h

Note: percent and dose ordered **carefully!** Follow directions. Do not use for longer than prescribed.
This is a representative sample; many other products available.

ANTIGLAUCOMA AGENTS

Glaucoma is an abnormal condition of the eye in which there is increased intraocular pressure (IOP) due to obstruction of the outflow of aqueous humor. This causes the optic nerve to deteriorate. There are two main types of glaucoma:

1. ***Acute (angle-closure) glaucoma.*** Characterized by a sudden onset of pain, blurred vision, and a dilated pupil, which is considered a medical emergency. If untreated, blindness can result in a few hours or days. Treatment consists of miotics (e.g., pilocarpine), osmotic agents (e.g., mannitol) (see Diuretics, Chapter 15), carbonic anhydrase inhibitors (e.g., Diamox), and surgery to open a pathway for release of aqueous humor.
2. ***Chronic (open-angle) glaucoma.*** Much more common, often bilateral, and develops slowly over a period of years with few symptoms except a gradual loss of peripheral vision and possibly blurred vision. Halos around lights and central blindness are late manifestations. *Treatment* consists of miotics, carbonic anhydrase inhibitors, and a local beta-adrenergic blocker, such as timolol (Timoptic) eye drops.

The first step in glaucoma therapy is to ensure the patient abstains from medications that may exacerbate glaucoma (i.e., potent corticosteroids, anticholinergics, and antihistamines). **Antiglaucoma** drugs, given to lower **intraocular pressure**, can be divided into five main categories based on their mode of action:

1. ***Carbonic anhydrase inhibitors,*** for example, Diamox. Act by decreasing the formation of aqueous humor and have a diuretic effect.
2. ***Miotics,*** for example, pilocarpine. Act by increasing the aqueous humor outflow.
3. ***Beta-adrenergic blockers,*** for example, timolol. Act by decreasing rate of aqueous humor production.
4. ***Alpha agonists,*** for example brimonidine (Alphagan-P). Decrease production of aqueous humor and increased outflow.
5. ***Prostaglandin analogs,*** for example latanoprost (Xalatan). Act by increasing aqueous outflow.

Drugs in different categories are sometimes given concomitantly. Combination products are sometimes available as well, for example, timolol combined with dorzolamide (Cosopt).

Carbonic Anhydrase Inhibitors (CAIs)

Acetazolamide (Diamox)

Carbonic anhydrase inhibitors such as acetazolamide (Diamox) reduce the formation of hydrogen and bicarbonate ions and have a diuretic effect. Oral acetazolamide (Diamox) has largely been replaced by newer topical preparations which have fewer side effects but is occasionally used in the treatment of open-angle glaucoma or short-term preoperatively to reduce intraocular pressure in angle-closure glaucoma, and is given with miotics or epinephrine products.

Side effects of CAIs, infrequent and usually dose related, can include:

- Nausea, vomiting, diarrhea, and constipation
- Thirst, taste alteration; frequent urination
- Drowsiness, fatigue, confusion, and seizures
- Numbness, muscular weakness, and tingling with high doses
- Blood dyscrasias; electrolyte imbalance
- Hepatic and renal disorders
- Photosensitivity (avoid excessive sunlight exposure)

Contraindications or caution with CAIs applies to:

- Chronic obstructive pulmonary disease (COPD)
- Diabetes
- Electrolyte, hematological, hepatic, pulmonary, and renal disorders
- Sulfonamide hypersensitivity
- Pregnancy and lactation

Interactions with CAIs are frequent because of increasing or decreasing excretion of other drugs and can include:

- Decreased effects of lithium, phenobarbital, and oral antidiabetics
- Increased effects of procainamide, quinidine, amphetamines, and other diuretics
- Hypokalemia with thiazides and corticosteroids

Dorzolamide (Trusopt)

Dorzolamide is a CAI that is applied topically to treat open-angle glaucoma. It is used as an adjunct to beta blockers.

Side effects of dorzolamide can include:

- Burning or stinging
- Bitter taste

Caution applies to:

- Those with sulfonamide hypersensitivity

PATIENT EDUCATION

Patients being treated with carbonic anhydrase inhibitors should be instructed regarding:

- Reporting side effects and response to the physician for appropriate dosage regulation
- Importance of follow-up with the physician

Miotics

Miotics are medications that cause the pupil to contract. Miotics reduce intraocular pressure by increasing the aqueous humor outflow. They act by contracting the ciliary muscle. Miotics (e.g., pilocarpine) are used in the treatment of open-angle glaucoma (considered third-line therapy due to side effects) or in short-term treatment of angle-closure glaucoma before surgery. Pilocarpine is also used after ophthalmic examinations in glaucoma patients to *constrict the pupil* and counteract the *mydriatic* (pupil-dilating) effect. Miotics are usually administered with acetazolamide, dipivefrin, and/or timolol. Because of its increased duration of effect and less frequent administration, pilocarpine hydrochloride gel may provide some advantages over ophthalmic solutions, especially long term with noncompliant patients.

Pilocarpine has cholinergic action and side effects. (See Chapter 13, Cholinergics.)

Side effects of pilocarpine, usually dose related, can include:

- Blurred vision and myopia
- Twitching, stinging, and burning
- Ocular pain and headache
- Photophobia and poor vision in dim light

Aggravation of inflammatory processes of the anterior chamber of the eye

Systemic effects with frequent or prolonged use or high doses of pilocarpine, especially in children, can include:

- Nausea, vomiting, and diarrhea
- Increased lacrimation, salivation, and sweating
- Hypotension, bradycardia
- Bronchospasm

Contraindications or caution with pilocarpine applies to:

Angle-closure glaucoma *with acute inflammation*

History of retinal detachment or retinal degeneration

Acute inflammatory processes

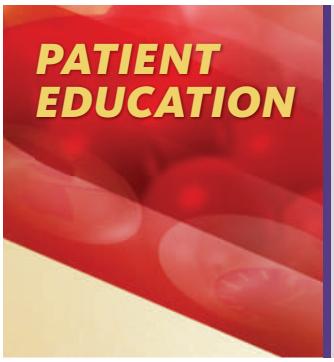
Soft contact lenses in place

Corneal abrasion

Interactions of pilocarpine may occur with:

Topical NSAIDs, which reduce effectiveness

Topical atropine and phenylephrine, which reduce effectiveness



Patients being treated with miotics should be instructed regarding:

- Following directions carefully regarding time and amount
- Administration by closing tear duct after instillation (see Figure 18-2)
- Reporting side effects to the physician for possible dosage adjustment
- Administration at bedtime to reduce side effects
- Not driving at night

Beta-Adrenergic Blockers

Timolol (Timoptic)

Timolol is a **beta-adrenergic blocker** that remains the gold standard against which all new glaucoma treatments are compared. It is used topically to lower intraocular pressure in open-angle glaucoma. Other beta-blockers are also used topically to reduce IOP by decreasing the rate of aqueous humor production.

Side effects of beta-blockers are infrequent but may include:

- Ocular irritation, conjunctivitis, or diplopia
- Transient blurred vision with the gel formulation
- Aggravation of *preexisting* cardiovascular or pulmonary disorders, which may cause bradycardia, hypotension, dizziness, and bronchospasm

Contraindications or extreme caution with beta-blockers applies to:

- Bradycardia and heart block
- Patients receiving oral beta-blocker drugs
- Asthma and chronic obstructive pulmonary disease (COPD)
- Children, pregnancy, and lactation
- Diabetes and hyperthyroidism
- Closed-angle glaucoma

Interactions of beta-blockers may occur with:

- Other antiglaucoma drugs to help lower IOP
- Oral beta-blockers to increase chances of hypotension, bradycardia, and heart block

Betaxolol (Betoptic-S)

Betaxolol is a *cardioselective* beta-blocker that can be used with caution in patients with bronchospastic pulmonary disease since it does not affect the pulmonary receptors.

PATIENT EDUCATION

Patients being treated with beta-adrenergic blockers should be instructed regarding:

- Administration by closing tear duct after instillation to reduce systemic effects (see Figure 18-2)
- Caution in patients with cardiac or pulmonary disorders or who are taking oral beta-blockers
- Importance of regular eye examinations
- Continuous use of medications for glaucoma; *do not discontinue abruptly*
- When administering more than one ophthalmic medication, allowing time interval (at least five minutes) between medications

Alpha Agonist

Brimonidine (Alphagan-P) is a selective alpha-agonist that decreases formation and increases outflow of aqueous humor with minimal effects on cardiovascular or pulmonary hemodynamics. It is an alternative for those for whom topical beta-blocker therapy is contraindicated.

Side effects of alpha agonists can include:

- Conjunctival redness, itchiness, stinging
- Dizziness, dry mouth and headache.

PATIENT EDUCATION

Patients being treated with sympathomimetics should be instructed regarding reporting side effects to the physician immediately.

Prostaglandin Analogs

Latanoprost (Xalatan), travoprost (Travatan), and others, are prostaglandin analogs that cause the greatest reduction in IOP by increasing the outflow of aqueous humor. They may be used concomitantly with other topical ophthalmic drugs to lower IOP (administer the drugs at least five minutes apart).

Side effects of prostaglandin analogs include:

- Blurred vision, burning, and stinging
- Slow, gradual change in the color of the iris (resultant color change may be permanent)
- Change in length, thickness, and pigmentation of eyelashes
- Systemic effects rarely, including upper respiratory tract infection, muscle and joint pain

Contraindications or extreme caution with prostaglandin analogs applies to:

Contact lens wearers

Hepatic and renal disease

Pregnancy, lactation, use in children

Drug interaction of prostaglandin analogs with eye drops containing the preservative thimerosal (precipitation occurs). If such drugs are used, administer with an interval of at least five minutes between applications. There are no other clinical significant drug interactions.

More frequent administration of prostaglandin analogs than the dosage indicated in Table 18-2 may actually decrease their IOP lowering effect. Refrigerate unopened bottle of Xalatan; once opened the container may be stored at room temperature for six weeks. Travatan does not require refrigeration.

Inform patients about the possibility of iris color change (increase of the brown pigment).

Contact physician immediately if ocular reactions develop.

Prostaglandin analogs contain a preservative that may be absorbed by contact lenses. Remove lenses prior to administration of the drug and wait 15 min before reinserting.

See Table 18-2 for a summary of antiglaucoma agents.

Table 18-2 Antiglaucoma Agents

GENERIC NAME	TRADE NAME	DOSAGE
Carbonic Anhydrase Inhibitors		
acetazolamide	Diamox	Cap, tab, IV, 250–500 mg 4 × per day (max 1 g per day)
dorzolamide	Trusopt	Ophthalmic sol, 1 gtt* TID
Miotics[a]		
pilocarpine HCl	Isopto Carpine	Ophthalmic sol. 0.5–6%[b], dose varies
pilocarpine gel	Pilopine HS	Ophthalmic gel 4% at bedtime
Beta-Adrenergic Blockers		
timolol	Timoptic	Ophthalmic sol. 0.25–0.5% 1 gtt BID
	Timoptic-XE	Ophthalmic gel 0.25–0.5% 1 gtt QD
timolol with dorzolamide	Cosopt	Ophthalmic sol, 1 gtt BID
betaxolol		Ophthalmic sol. 0.5%, 1–2 gtts BID
	Betoptic-S	Ophthalmic susp 0.25% 1 gtt BID

Table 18-2 Antiglaucoma Agents—*continued*

GENERIC NAME	TRADE NAME	DOSAGE
Alpha Agonist		
brimonidine	Alphagan-P	Ophthalmic sol. 0.1%, 0.15%, 0.2%; 1 gtt TID (8 h apart)
Prostaglandin Analogs		
latanoprost	Xalatan	Ophthalmic sol. 0.005%, 1 gtt at bedtime
travoprost	Travatan, Travatan-Z	Ophthalmic sol. 0.004%, 1 gtt at bedtime

[a]Constrict the pupil.
[b]Wide variation in strengths available. Check carefully for correct percentage.
*gtt = drop
Other antiglaucoma agents and combination drugs are available. This is a representative list.

MYDRIATICS

Mydriatics (e.g., atropine) are used topically to *dilate the pupil* for ophthalmic examinations. Atropine also acts as a **cycloplegic** (paralyzes the muscles of accommodation). It is the drug of choice in eye examinations for children. However, other mydriatics, for example cyclopentolate, are more often used for adults because of faster action and faster recovery time.

Side effects of mydriatics, more likely in older adult patients, may include:

- ! Increased IOP
- Local irritation, burning sensation transient
- ! Blurred vision common
- Flushing, dryness of skin, and fever
- Confusion (caution in older adults)

Contraindications for mydriatics apply to:

- Angle-closure glaucoma
- Infants

Phenylephrine is a sympathomimetic that produces mydriasis without cycloplegia. Side effects and contraindications are similar to those of epinephrine.

Patients being treated with mydriatics should be instructed regarding:

- Administration by closing tear duct after instillation (see Figure 18-2)
- Aseptic technique to prevent contamination of medicine
- Blurred vision and sensitivity to light to be expected (wear dark glasses or stay out of bright light)

See Table 18-3 for a summary of the mydriatics.

Table 18-3 Mydriatics and Local Anesthetics for the Eye

GENERIC NAME	TRADE NAME	DOSAGE	COMMENTS
Mydriatics[a]			
atropine	Isopto Atropine	Oint, sol 1%	Administered 60 min before exam
cyclopentolate	Cyclogyl	Ophthalmic sol, 0.5–2%[b]	Check carefully for percent
phenylephrine	AK-Dilate	Ophthalmic sol, 2.5%, 10%[b]	
Local Anesthetics			
tetracaine	TetraVisc	Sol, 0.5%	Apply eye patch
proparacaine	Alcaine	Sol, 0.5%	Apply eye patch

[a]Dilate the pupil.
[b]Wide variations in strengths available. Check carefully for correct percentage!

LOCAL ANESTHETICS

Local ophthalmic anesthetics, such as tetracaine *(TetraVisc)*, are applied topically to the eye for minor surgical procedures, removal of foreign bodies, or painful injury.

Side effects of local anesthetics are rare, except with prolonged use but may include *hypersensitivity* (transient stinging), reactions such as *anaphylaxis in those allergic to the "-caine" local anesthetics* (ester type).

Contraindicated for prolonged use because of the danger of corneal erosions.

PATIENT EDUCATION

Patients given local ophthalmic anesthetics should be instructed regarding:

- Necessity of wearing an eye patch after use of tetracaine because of loss of blink reflex
- Avoidance of touching or rubbing the eye until the anesthesia has worn off

PATIENT EDUCATION

Patients taking ophthalmic medications should be instructed regarding:

- Making certain the correct medication and correct percent solution are used as prescribed
- It is critical to continue glaucoma treatment for a lifetime and have regular eye exams to prevent future vision damage

Proper aseptic technique to prevent contamination of the other eye, the dropper, or the ointment tube

Instillation of the *correct number of drops* or amount of ointment into the conjunctival sac (see Figure 18-1)

Closing the eye gently so as not to squeeze the medication out

Applying gentle pressure to inner canthus after instillation to minimize systemic effects (see Figure 18-2)

Use of an eyecup as an aid to administration is discouraged due to risk of contamination.

Monitor expiration dates closely—do not use outdated medication.

CASE STUDY – A

Eye Medications

Ida Williams, age 35, has been using corticosteroid eye drops for one week for "bloodshot eyes." She now has a purulent drainage from the left eye. She needs the following information.

1. Corticosteroid ophthalmic drops are used to treat all of the following EXCEPT
   a. Inflammation
   b. Allergies
   c. Infection
   d. Burns

2. Eye infections can be treated with all of the following EXCEPT
   a. Viroptic
   b. Prednisolone
   c. Gentamycin
   d. Polymixin B

3. The choice of antibiotic product would include consideration of the following EXCEPT
   a. Allergies
   b. Resistance
   c. Sensitivity of organism
   d. Age of the patient

4. Side effects of corticosteroid products with extended use could include the following EXCEPT
   a. Increased IOP
   b. Stinging
   c. Premature healing
   d. Fungal infections

5. Administration of antibiotic drops would include the following instruction EXCEPT
   a. Wash hands first
   b. Instill in inner canthus
   c. Avoid contaminating tip
   d. Discontinue with itching

CASE STUDY – B

Eye Medications

Saul Glossman, age 70, has been diagnosed with open-angle glaucoma. He will need the following information.

1. Treatment could include all of the following EXCEPT
- a. Isopto Carpine
- b. Timoptic
- c. Atropine
- d. Trusopt

2. The purpose of antiglaucoma drugs can include all of the following EXCEPT
- a. Reduce IOP
- b. Dilate pupil
- c. Reduce aqueous formation
- d. Increase aqueous outflow

3. The following statements are true of Diamox EXCEPT
- a. Diuretic effect
- b. Given PO
- c. Reduces IOP
- d. Given alone

4. Side effects of pilocarpine could include all of the following EXCEPT
- a. Photophobia
- b. Headache
- c. Urinary retention
- d. Blurred vision

5. Side effects of Timoptic can include all of the following EXCEPT
- a. Palpitations
- b. Bronchospasm
- c. Hypotension
- d. Dizziness

CHAPTER REVIEW QUIZ

Match the medication in the first column with the condition in the second column that it is used to treat. Conditions may be used more than once.

Medication		Condition
1. _____	Cosopt	**a.** To dilate pupils
2. _____	Acular	**b.** Glaucoma
3. _____	tetracaine	**c.** Allergic reaction of eyes
4. _____	Atropine	**d.** Postoperative inflammation
5. _____	Prednisolone	**e.** Eye injury pain
6. _____	Pilocarpine	
7. _____	Timoptic	
8. _____	Diamox	
9. _____	Travatan	
10. _____	phenylephrine	

Choose the correct answer.

11. When using more than one ophthalmic product at the same time, the following rules apply EXCEPT:
    a. Give five minutes apart
    b. Give drops before ointment
    c. Give one with highest % last
    d. Close the tear duct after instillation
12. Patients being treated with anti-infective eye preparations should be given the following instructions EXCEPT:
    a. Do not use makeup
    b. Discontinue if burning occurs
    c. Do not wear contact lenses
    d. Use eyecup for administration
13. Corticosteroid ophthalmic products could cause all of the following EXCEPT:
    a. Ocular pain
    b. Inflammation
    c. Thinning of cornea
    d. Corneal ulceration
14. The following statements are true of carbonic anhydrase inhibitors, for example Diamox, EXCEPT:
    a. Used to treat glaucoma
    b. For diabetic retinopathy
    c. Have diuretic effect
    d. Combined with miotics

15. The following statements are true of prostaglandin agonists, for example Xalatan, EXCEPT:

a. Contain thimerosal preservative
b. Increase aqueous humor outflow
c. Can change eye color
d. Can affect eyelashes

Go to your StudyWARE™ CD-ROM and have fun learning as you play games and answer case study-related questions to help reinforce key concepts you learned in this chapter.

Go to your Study Guide and complete the review questions for this chapter.

Chapter 19

Analgesics, Sedatives, and Hypnotics

Objectives

Upon completion of this chapter, the learner should be able to

1. Compare and contrast the purpose and action of nonopioid, opioid, and adjuvant analgesics, sedatives, and hypnotics
2. List the side effects of the major analgesics, sedatives, and hypnotics
3. Describe the necessary information for patient education regarding interactions and cautions
4. Explain the contraindications to administration of the CNS depressants in this chapter
5. Define the Key Terms and concepts

Key Terms and Concepts

Adjuvant
Analgesics
Antipyretic
Coanalgesic
Dependence
Endogenous
Endorphins
Hypnotics
Opioids
Paradoxical
Placebo effect
Sedatives
Subjective
Tinnitus
Tolerance

Analgesics, sedatives, and hypnotics depress central nervous system (CNS) action to varying degrees. Some drugs can be classified into more than one category, depending on the dosage. Analgesics are given to relieve pain. Sedatives are given to calm, soothe, or produce sedation. Hypnotics are given to produce sleep.

ANALGESICS

The most common reason patients seek out medical care is pain. Pain is **subjective** (i.e., it can be experienced or perceived only by the individual subject). Health care practitioners can assess a patient's pain by asking the patient to describe the pain, its location, and assessing pain severity by using validated pain assessment scales. Pain has both psychological and physiological components. Some persons have a higher pain threshold than others because of conditioning, ethnic background, sensitivity, or physiological factors (e.g., endorphin release).

Endorphins are **endogenous** analgesics produced within the body as a reaction to severe pain or intense exercise (e.g., "runner's high"). Endorphins block the transmission of pain. Endorphin release may be responsible for a **placebo effect**: relief from pain as the result of suggestion without the administration of an analgesic.

Opioid Analgesics

Analgesics can be classified as opioid, nonopioid, and adjuvant. Opioids are classified as full or pure agonists, partial agonists, or mixed agonist-antagonists depending on the specific receptors they bind to and their activity at the receptor. Full agonists are commonly used because their action is similar to that of opium in altering the perception of pain, and they do not have a ceiling to their analgesic effects, that is, medication level at which there is no enhanced analgesia. These opioids (e.g., morphine, hydromorphone, meperidine, oxycodone, and fentanyl) will not reverse analgesia like the other classes (e.g., pentazocine, butorphanol, and nalbuphine).

Opioids are controlled substances in the United States and include both the natural opium alkaloids, such as morphine and codeine, and the synthetics, such as meperidine (Demerol) and propoxyphene (Darvon). On July 7, 2009, the Food and Drug Administration (FDA) implemented actions to reduce the risk of overdose in people who use pain medications, such as Darvon and Darvocet. These medications contain the drug propoxyphene, which is linked to death from overdoses. Because of the drug's potential risks, the agency is requiring manufacturers to provide more information to help physicians and patients decide whether propoxyphene is the appropriate pain treatment and is requiring manufacturers of propoxyphene-containing products to strengthen the label's boxed warning to emphasize the risk for overdose when using these products.

Tramadol (Ultram), a weak opiate agonist, is currently not classified as a controlled substance on the Federal level. Opioids tend to cause **tolerance** (i.e., a larger dose of opioid is needed to achieve the same level of analgesia) and physiological **dependence** (i.e., physical adaptation of the body to the opioid and withdrawal symptoms after abrupt drug discontinuation) with chronic use.

Addiction or psychological dependence is usually not a problem for patients who require opioids for pain management. The majority of people stop taking opioids when their pain stops. Because of tolerance, the potential for developing dependence, and the potential for developing undesirable side effects, opioids are not used for extended periods except to relieve chronic pain, for example, cancer pain, terminal illness, and in selected patients with nonmalignant pain who do not benefit from other pain relief methods. Adequate pain control is important for the terminally ill. Dependence is irrelevant for dying patients and should not be a consideration. More effective pain control can be achieved by combining opioids with nonopioid and adjuvant drugs. Analgesics should be given to terminally ill patients with constant ***around-the-clock*** pain, with additional "as needed" doses, for breakthrough pain, and dosages adjusted to achieve pain relief with an acceptable level of side effects. Around-the-clock dosing prevents pain from developing.

Chronic pain therapy, for example, for back pain, sometimes includes the addition of a tricyclic antidepressant or anticonvulsant to the analgesic regimen. These drugs that enhance analgesic effects are called *adjuvant* analgesics and are explained later in this chapter. This addition can reduce the needed dosage of opioids.

Side effects of opioids can include:

- Sedation
- Confusion, euphoria, restlessness, and agitation
- Headache and dizziness
- Hypotension and bradycardia
- Urinary retention; sexual dysfunction
- Nausea/vomiting (usually resolves within a few days), and constipation (frequently requires treatment)
- Respiratory depression (appropriate dose titration reduces risk)
- Physical and/or emotional dependence; tolerance
- Blurred vision
- Seizures with large doses
- Flushing, rash, and pruritus (opiate agonists cause histamine release except tramadol)

Contraindications or extreme caution with opioids applies to:

- Head injury (i.e., conditions associated with increased intracranial pressure)
- Cardiac disease, hypotension
- CNS depression
- GI, Hepatic, renal, and thyroid disease
- Chronic obstructive pulmonary disease (COPD), asthma
- Pregnancy, lactation, and pediatrics
- Older adults, patients, and debilitated
- Driving or operating machinery; may impair mental or physical abilities
- Addiction prone, suicidal, and alcoholic
- Opiate agonist hypersensitivity
- Abrupt drug discontinuation in patients taking opioids chronically

Interactions include potentiation of effect of opioids with all CNS depressants, including:

- Psychotropics
- Alcohol
- Sedatives and hypnotics
- Muscle relaxants
- Antihistamines
- Antiemetics
- Antiarrhythmics or antihypertensives

Preoperatively, an opioid like fentanyl (Sublimaze), is usually administered parenterally before the start of anesthesia, according to directions of the anesthesiologist. Meperidine is not recommended for routine use due to a metabolite that may accumulate and cause seizures in patients with kidney disease. Morphine or hydromorphone are commonly used to manage moderate to severe pain due to their longer duration of effect and potency. Hydromorphone is 4 to 8 times more potent than morphine so caution is necessary to avoid medication errors.

Opioid agonists are available in various strengths, as concentrated oral solutions and in combination products. Carefully note product/strength to be administered.

Tramadol

Tramadol (Ultram) is a centrally acting synthetic analog of codeine with a dual mechanism of action. It produces analgesia by weak inhibition of norepinephrine and serotonin reuptake and is an opioid receptor agonist. Tramadol has less potential for abuse or respiratory depression (although both may occur).

Note By inhibiting reuptake, the substance (such as serotonin) will be around longer and therefore have a greater effect.

Side effects and ***precautions*** of tramadol are similar to the opioids listed above.

Interactions of tramadol with:

Monoamine oxidase inhibitors (MAOIs) or neuroleptics—may increase seizure risk

Carbamazepine (Tegretol) antagonizes tramadol action

Selective serotonin reuptake inhibitors (SSRIs) (especially Paxil, Zoloft)—may cause serotonin syndrome and increase seizure risk

See Table 19-1 for a summary of the opioid analgesics.

The **opioid antagonist** naloxone (Narcan) is used in the treatment of opioid overdoses and in the operating room, delivery room, and newborn nursery for opiate-induced respiratory depression.

Naltrexone, a pure opioid antagonist, and buprenorphine, a partial opioid antagonist, are used in the treatment of opioid dependence (see Chapter 20).

Nonopioid Analgesics

Nonopioid analgesics, many of which are available without prescription as over-the-counter (OTC) medications, are very popular. Therefore, it is extremely important that the health care practitioner be informed and responsible for patient education in this very important area of public health. The lay public needs to become aware of the dangers of self-medication, overdosage, side effects, and interactions, as well as the grave danger of poisoning to children and older adults by inappropriate use of these readily available drugs.

Table 19-1 Opioid Analgesics*

GENERIC NAME	TRADE NAME	DOSAGE	USES/COMMENTS
butorphanol	Stadol	1–4 mg IM, or 0.5–2 mg IV, or 1 mg (one spray) nasal spray q3–4h PRN	Moderate to severe acute, pain (e.g., migraine)
codeine	codeine[a]	15–60 mg PO/IM q4h PRN; subcu q4h PRN; PO 10–20 mg q4–6h PRN	Mild to moderate acute, chronic, and cancer pain; antitussive
fentanyl citrate	Actiq (loz.), Fentora (buccal) Sublimaze Duragesic	PO 200–400 mcg q4–6h PRN; or 25–100 mcg slow IV/IM Transdermal q72h	Moderate to severe acute, chronic, or cancer pain *Not* for acute pain
hydrocodone with acetaminophen *(not available singly)*	Lorcet[b] Lortab Vicodin	PO 5–10 mg or 5–10 mL (liquid) q4–6h PRN	Moderate acute, chronic, cancer pain, or antitussive; max 4 g acetaminophen per day
hydromorphone	Dilaudid	PO 1–4 mg q3–4h PRN IM, IV, subcu 1–2 mg q3–4h PRN R 3 mg q6–8h PRN	Moderate to severe acute, chronic, or cancer pain
meperidine	Demerol	50–150 mg PO/IM/subcu, q3–4h PRN	Moderate to severe acute pain, not for chronic pain, not for older adults
methadone	Dolophine	2.5–10 mg IM/subcu/PO initially q3–4h PRN; maint. 5–20 mg PO q6–8h PRN	Severe acute, chronic, and cancer pain; also for narcotic withdrawal
morphine sulphate			
immediate release	morphine	PO 10–30 mg or R 10–20 mg q4h PRN; IV 2.5–15 mg over 4–5 min.; IM/subcu 2.5–20 mg q4h PRN	Moderate to severe acute, chronic, or cancer pain
extended release	MS Contin (tab)	PO, R 15–100 mg q8–12h	Don't crush! OD can be fatal
	Avinza (cap)	PO 30 mg q24h (initially, titrate to response)	May open caps and sprinkle contents on applesauce; can give Kadian contents via a gastrostomy tube
	Kadian (cap)	PO 10 mg BID or 20 mg QD (initially, titrate to response)	

(*continued*)

Table 19-1 Opioid Analgesics*—*continued*

GENERIC NAME	TRADE NAME	DOSAGE	USES/COMMENTS
oxycodone			
controlled release	Oxycontin	PO 10–80 mg SR q8–12h	Serious abuse potential, overdose can be fatal; Do not crush.
immediate release	Roxicodone	PO 5–10mg or 5–10 mL (soln) q6h PRN	Moderate to severe acute, chronic, or cancer pain
with aspirin	Percodan[c]	PO 1–2 tabs q4–6h PRN	Max 12 tabs per 24 hours
with acetaminophen	Percocet, Tylox	PO 1–2 tabs/caps q4–6h PRN	Max 4 g acetaminophen per day
Pentazocine	Talwin	30 mg IV/IM q3–4h PRN	Moderate to severe pain; not for older adults; naloxone added to prevent abuse
with naloxone	Talwin-NX	PO 50–100 mg q3–4h PRN	
propoxyphene HCL	Darvon	PO 65–100 mg q4h PRN	Mild to moderate acute, chronic, or cancer pain; not for older adults
with acetaminophen	Darvocet[d]	PO 1–2 tabs q4h prn (max 4 g acetaminophen per day)	
Tramadol	Ultram	PO 50–100 mg q4–6h PRN, max 400 mg daily	Weak opioid analgesic, not controlled Federally
with acetaminophen	Ultram ER	PO 100–300 mg daily	Do not crush
	Ultracet	PO 2 tabs q4–6h PRN	Max 8 tabs per day

***Combination Opioid Products** (Check for allergies, especially aspirin combinations.)

[a]Tylenol with Codeine tabs contain 300 mg acetaminophen plus codeine:

#2 tab 15 mg codeine, #3 tab 30 mg, #4 tab 60 mg (max acetaminophen dose 4 g per day).

Tylenol with codeine elixir: 120 mg acetaminophen and 12 mg codeine per 5 mL.

[b]Lortab, or Vicodin tabs: 500 mg acetaminophen and 5 mg hydrocodone.

Lorcet Plus tabs: 650 mg acetaminophen and 7.5 mg hydrocodone.

Lorcet tabs: 650 mg acetaminophen and 10 mg hydrocodone.

Vicodan ES tabs: 750 mg acetaminophen and 7.5 mg hydrocodone.

Vicodin HP tabs: 660 mg acetaminophen and 10 mg hydrocodone.

Lortab elixir: 167 mg acetaminophen and 2.5 mg hydrocodone per 5 mL.

[c]Percodan or Endodan tabs: 325 mg aspirin and 5 mg oxycodone.

Percocet, Roxicet, or Endocet: 325 mg acetaminophen and 5 mg oxycodone. (other strengths available)

Tylox: 500 mg acetaminophen and 5 mg oxycodone.

[d]Darvocet-N 50: 325 mg acetaminophen and 50 mg propoxyphene.

Darvocet-N 100: 650 mg acetaminophen and 100 mg propoxyphene.

Darvocet-A 500: 500 mg acetaminophen and 100 mg propoxyphene.

The nonopioids are given for the purposes of relieving mild to moderate pain, fever, and anti-inflammatory conditions, for example, arthritis. This group of analgesics is also used as a **coanalgesic** in severe acute or chronic pain requiring opioids. The salicylates (aspirin, salsalate, choline magnesium trisalicylate) are most commonly used for their *analgesic* and **antipyretic**

properties, as well as for their anti-inflammatory action. Other anti-inflammatory drugs, for example, ibuprofen, are also used for their analgesic properties. The nonsteroidal anti-inflammatory drugs (NSAIDs) are discussed in Chapter 21.

Acetaminophen has analgesic and antipyretic properties but very little effect on inflammation. Aspirin and acetaminophen are frequently combined with opioids (see Table 19-1) or with other drugs for more effective analgesic action. See Table 19-2 for a representative sample of nonopioid analgesics and antipyretics. There are many other combination analgesic products available OTC. Patients should be instructed to check all ingredients in these combination products because of potentially serious adverse side effects, for example, aspirin allergy or acetaminophen contraindications.

Table 19-2 Nonopioid Analgesics and Antipyretics

GENERIC NAME	TRADE NAME	DOSAGE	COMMENTS
acetylsalicylic acid[a] (ASA, aspirin)	Ecotrin, Ascriptin, Bufferin	325-650 mg PO or rectal supp q4h PRN; larger doses for arthritis	Give with milk or food; may cause Reye's syndrome in children and teenagers
Acetaminophen	Tylenol, Panadol	325–650 mg PO or rectal supp q4h PRN (max 4 g per day)	No anti-inflammatory action; less effective than ASA for soft tissue pain
combinations[b]			
ASA and caffeine	Anacin	2 tabs PO q6h PRN, max 8 per day	
ASA and meprobamate	Equagesic	1–2 tabs PO 3–4 × per day	Used to treat pain accompanied by anxiety and/or tension
ASA, acetaminophen, and caffeine	Excedrin	2 tabs/caps PO q6h PRN, max 8 per day	Also for pain of migraine headaches
butalbital, caffeine, with acetaminophen with aspirin	Esgic, Fioricet Fiorinal	1–2 tabs/caps PO q4h PRN, max 6 per day	For tension headache/ migraine

[a]Other nonsteroidal anti-inflammatory drugs with analgesic action are listed in Table 21-2.
[b]Representative sample.

Salicylates and Other NSAIDS

Salicylate analgesic and anti-inflammatory actions are associated primarily with preventing the formation of prostaglandins and the subsequent inflammatory response prostaglandins help to induce. The salicylates, for example, aspirin (ASA) and other NSAIDs, are also discussed in Chapter 21.

Side effects of salicylates and other NSAIDs, especially with prolonged use and/or high dosages, can include:

- Prolonged bleeding time
- Bleeding and frequent bruising
- Gastric distress, ulceration, and bleeding (which may be silent)
- **Tinnitus** (ringing or roaring in the ears) and hearing loss with overdose

Hepatic dysfunction

Renal insufficiency, decreased urine output with sodium and water retention, renal failure

Drowsiness, dizziness, headache, sweating, euphoria, depression

Rash

- Coma, respiratory failure, or anaphylaxis, which can result from hypersensitivity or overdosage, especially with children (watch for aspirin allergy)
- Gastrointestinal (GI) symptoms, which can be minimized by administration with food, milk, or by using an aspirin buffered with antacids or in enteric-coated form

Poisoning—keep out of reach of children (especially flavored children's aspirin)

Contraindications for salicylates and other NSAIDs include:

GI ulcer and bleeding

Bleeding disorders in patients taking anticoagulants

Asthma

Children younger than 15 with influenza-like illness (because of the danger of Reye's syndrome)

Pregnancy

Lactation

Vitamin K deficiency

Allergy to ASA

Caution in use of salicylates and other NSAIDs with the following:

Anemia

Hepatic disease

Renal disease

Hodgkin's disease

Pre/postoperatively (discontinue five to seven days before elective surgery)

Interactions of salicylates may also occur with NSAIDs and the following:

Alcohol (may increase potential for ulceration and bleeding)

Anticoagulants (potentiation)

Corticosteroids (gastric ulcer)

Antacids in high doses (decreased effect)

NSAIDs (decreased effect, increased GI side effects)

Do not give salicylates and NSAIDs together. (unless approved by physician)

Insulin or oral antidiabetic agents (increased effects); may interfere with certain urinary glucose tests

Methotrexate (increased effects)

Probenecid (decreased effects)

Antihypertensives: angiotensin-converting enzyme (ACE) inhibitors, beta-blockers and diuretics (decreased effects)

Carbonic anhydrase inhibitors (toxic effects)—for example, Diamox

Acetaminophen

Acetaminophen (Tylenol) is used extensively in the treatment of mild to moderate pain and fever. It has very little effect on inflammation. However, acetaminophen has fewer adverse side effects than the salicylates (e.g., does not cause gastric irritation or precipitate bleeding). Therefore, it is sometimes used only for its analgesic properties in treating the chronic pain of arthritis so that the salicylate dosage may be reduced to safer levels with fewer side effects in these patients.

Side effects of acetaminophen are rare, but large doses can cause:

- Severe liver toxicity
- Renal insufficiency (decreased urine output)

Rash or urticaria

Blood dyscrasias

Caution must be used with frequent acetaminophen use and alcohol ingestion because of potential liver damage. Caution also with pregnancy and breast-feeding.

Contraindicated with hypersensitivity to acetaminophen or any component of the combination product.

Note

Acetaminophen (Tylenol) is frequently combined with opioid analgesics when stronger pain relief is required. Some examples of such combinations include Tylenol #3, Lorcet, Lortab, Vicodin, Tylox, Percocet, Roxicet, and Darvocet. For examples of other opioid combinations, and for information regarding the proportion of the ingredients in each product, see Table 19-1 and the Combination Opioid Products footnote, below the table. Remember, all opioids (except tramadol) are Federally controlled substances.

See Table 19-2 for a summary of the nonopioid analgesics and antipyretics.

Adjuvant Analgesics

These drugs were originally intended for treatment of conditions other than pain. **Adjuvant** analgesics may enhance analgesic effect with opioids and nonopioids, produce analgesia alone, or reduce the side effects of analgesics. Two classes commonly used for analgesia include anticonvulsants and specific classes of antidepressants. Lidocaine is available topically in a patch (Lidoderm) and may be especially effective to treat nerve pain and other types of localized pain while avoiding the adverse effects of oral or parenterally administered medications. See Table 19-3 for a summary of adjuvant analgesics.

Table 19-3 Adjuvant Analgesics and Local Anesthetic

GENERIC NAME	TRADE NAME	DOSAGE[a]	COMMENTS
Antidepressants			
Tricyclics			
amitriptyline	(Elavil)*	PO 10– 150 mg at bedtime	Use with caution in the older adult
nortriptyline	Pamelor	PO 10–150 mg at bedtime	
imipramine	Tofranil	PO 10–150 mg at bedtime	
SNRIs[b]			
duloxetine	Cymbalta	PO 60–120 mg daily	Also used for fibromyalgia
venlafaxine	Effexor	PO 75–225 mg daily	
Anticonvulsants			
carbamazepine	Tegretol	PO 200–600 mg BID PO	Especially for trigeminal neuralgia; monitor serum levels periodically
gabapentin	Neurontin	600–3600 mg per day div. doses 3–4 × per day	For nerve pain, especially postherpetic neuralgia
lamotrigine	Lamictal	PO 25–200 mg BID	Slow titration to avoid rash
pregabalin	Lyrica	150–600 mg per day 2–3 div. doses	Slow titration to avoid rash for diabetic neuropathy and postherpetic neuralgia
Local Anesthetic			
Lidocaine	Lidoderm	1–3 Patches 5% daily (may be cut into smaller sizes)	For postherpetic neuralgia (on 12 h/off 12 h)

*Brand name no longer marketed, but name is still commonly used.

[a]***Note:*** All adjuvants should be started at the lower end of the dosage range and titrated upward in small increments weekly according to clinical response.

[b]Serotonin norepinephrine reuptake inhibitors.

Tricyclic Antidepressants

Tricyclic antidepressants are used in the treatment of nerve pain associated with herpes, arthritis, diabetes, and cancer, migraine or tension headaches, insomnia, and depression. Often, the patient will describe the pain as "burning." Tricyclic antidepressant actions are associated with increasing available norepinephrine and serotonin, which blocks pain transmission. Drugs used commonly for pain include amitriptyline, imipramine, and nortriptyline. Allow two to three weeks to see therapeutic effects.

Side effects of tricyclic antidepressants can include:

- Dry mouth, urinary retention, delirium, constipation
- Sedation (take at bedtime)
- Orthostatic hypotension
- Tachyarrhythmias

  Heart block in cardiac patients

The degree of side effects varies with each antidepressant. Side effects may be additive with opioids (e.g., increased constipation, hypotension, sedation, etc.).

Caution with tricyclics if used with prostatic hypertrophy, urinary retention, increased intraocular pressure, and glaucoma.

Contraindications for tricyclics include hypersensitivity and recovery phase of myocardial infarction.

Serotonin Norepinephrine Reuptake Inhibitors (SNRIs)

Duloxetine (Cymbalta) and venlafaxine (Effexor) are antidepressants that inhibit the reuptake of both serotonin and norepinephrine. They do not affect histamine or muscarinic receptors like the tricyclics, thus anticholinergic side effects are not present. The SNRI antidepressants are used to treat diabetic neuropathy and fibromyalgia.

Side effects of SNRIs include sleep disturbance, headache, nausea, stomach pain, diarrhea, constipation, dizziness, and sweating. Venlafaxne has the potential to increase blood pressure and heart rate.

Contraindications/Precautions include narrow-angle glaucoma, hepatic or renal impairment, abrupt discontinuation, and substantial alcohol use.

Interactions with SNRIs and MAOIs or SSRIs may result in a serotonin syndrome which is characterized by a rapid development of hyperthermia, hypertension, rigidity, autonomic instability, and mental status changes that can include coma and delirium.

Anticonvulsants

Anticonvulsants (i.e., Neurontin and Tegretol), like tricyclic antidepressants, are commonly used for the management of nerve pain associated with neuralgia, herpes zoster (shingles), and cancer. Anticonvulsant therapy is implemented

when the patient describes the pain as "sharp," "shooting," "shock-like pain," or "lightning-like." Gabapentin (Neurontin) is generally considered a first-line *anticonvulsant* for neuropathic pain therapy, followed by carbamazepine (Tegretol) and lamotrigine (Lamictal).

Pregabalin (Lyrica), a compound that is chemically and structurally similar to gabapentin, is the newest second-generation anticonvulsant approved by the FDA for use in diabetic neuropathy and postherpetic neuralgia. Pregabalin has been designated as a Schedule V controlled substance because of its potential for abuse and dependence.

Side effects of anticonvulsants can include the following:

- Sedation, dizziness, and confusion
- Nausea, vomiting, constipation, and anorexia
- Ataxia and unsteadiness

Hepatitis (not Lyrica)

Rash, Stevens-Johnson syndrome (Lamictal—start low, slow titration upward)

- Bone marrow suppression

Nystagmus, diplopia (double vision), and blurred vision

Gingivitis (gabapentin)

Weight gain and peripheral edema (pregabalin)

Caution with anticonvulsants if used with allergies, hepatitis, cardiac disease, and renal disease.

CAUTION Do not confuse *Lamictal* (anticonvulsant) with *Lamisil* (antifungal).

Contraindications with anticonvulsants include:

Hypersensitivity

Psychiatric conditions (increased risk of suicidal ideation and behavior)

Pregnancy

SA (sinoatrial) and AV (atrioventricular) block (Tegretol)

Hemolytic disorders (Tegretol)

Abrupt discontinuation

Interactions of anticonvulsants occur with:

Alcohol (decreased effects)

Antacids (decreased effects) (Neurontin)

Antineoplastics (decreased effects) (Tegretol)

CNS depressants (decreased effects) (Tegretol)

Folic acid (decreased effects) (Lamictal)

ACE inhibitors and Lyrica (increased risk of angioedema)

Antiretrovirals (increased or decreased effects) with Lamictal and Tegretol

LOCAL ANESTHETIC

The lidocaine patch (Lidoderm) is approved for the management of postherpetic neuralgia, although it can provide significant analgesia in other forms of neuropathic pain, including diabetic neuropathy and musculoskeletal pain such as osteoarthritis and low back pain. Topical lidocaine provides pain relief through a peripheral effect and generally has little if any central action. The penetration of topical lidocaine into intact skin is sufficient to produce an analgesic effect, but less than the amount necessary to produce anesthesia.

The lidocaine patch must be applied to intact skin. Patches may be cut into smaller sizes with scissors before removal of the release liner. To reduce the potential for serious adverse effects, patches are worn only once for up to 12 h within a 24-h period, then removed.

Side effects of the lidocaine patch, local in nature, are generally mild and transient, and include:

- Erythema, edema and hives
- Allergic reactions

Precautions and contraindications for the lidocaine patch include:

Sensitivity to local anesthetics

Hepatic disease

Nonintact skin

Pregnancy, breast-feeding, and pediatric use

Handling and disposal to prevent access by children or pets

Drug interactions of the lidocaine patch with:

Antiarrhythmic drugs such as mexiletene

Local anesthetics

Note

Sometimes a local vasoconstricting agent such as epinephrine is given in conjunction with a local anesthetic injection such as lidocaine to further help localize the effect and thereby prolong the duration of effect.

Antimigraine Agents

Migraine is the most common neurovascular headache and may include nausea, vomiting, and sensitivity to light or noise. Migraines (and most other forms of headache) respond best when treated early. Simple analgesics (see Table 19-2),

NSAIDs (see Chapter 21) and opioid analgesics can be effective, especially if they are taken at the initial sign of migraine.

Serotonin Receptor Agonists (SRAs)

For those patients unresponsive to the aforementioned treatments, serotonin agonists were developed based on the observation that serotonin levels decrease, while vasodilation and inflammation of blood vessels in the brain increase, as the migraine symptoms worsen during an attack. SRAs are also effective in treating the nausea and vomiting associated with migraines because serotonin receptors are also found in the GI tract.

The first "triptan" approved was sumatriptan (Imitrex), followed by six others. SRAs are indicated for the acute treatment of migraines in adults and have no therapeutic value for the prophylactic management of migraine headaches. Nasal spray formulations may be useful if the patient has nausea and vomiting or cannot swallow tablets.

Side effects of SRAs include:

- Malaise, fatigue, dizziness, drowsiness
- Nausea, vomiting, diarrhea
- Asthenia, tingling, paresthesias, flushing
- Pain or pressure in the chest, neck, or jaw
- Arrhythmias, angina, palpitations, myocardial infarction, cardiac arrest

Contraindications and precautions with SRAs include:

- Patients with cerebrovascular or cardiovascular disease; uncontrolled hypertension
- Peripheral vascular disease
- Hepatic or renal disease (dose adjustments may be needed)
- Use in older adults (who are more likely to have decreased hepatic function and more pronounced blood pressure increases and are at risk for coronary artery disease)
- Pregnancy, lactation, use in children

Drug interactions of SRAs with:

- Ergot alkaloids (i.e., methylergonovine)—additive vasopastic effects
- MAOIs elevate plasma levels of most triptans (do not use within two weeks of discontinuing use of the MAOI)
- Most antidepressants potentiate the effects of serotonin (including SSRIs and tricyclics) and may result in serotonin syndrome (mental status changes, diaphoresis, tremor, hyperreflexia, and fever) when used in combination
- Macrolide antibiotics, antiretroviral protease inhibitors, and "azole" antifungals with eletriptan (increased plasma levels)—do not use within at least 72 h of each other.
- See Table 19-4 for information on antimigraine agents.

Table 19-4 Antimigraine Agents

GENERIC NAME	TRADE NAME	DOSAGE FORMS	INITIAL DOSE ADULT	REPEAT TIME (HOURS)	DAILY MAXIMUM DOSE (MG)
eletriptan	Relpax	Tablet	20–40 mg	2	80
rizatriptan	Maxalt	Tablet	5–10 mg	2	30
	Maxalt-MLT	OD tablet	5–10 mg	2	30
sumatriptan	Imitrex	subcu	6 mg	1	12
		Nasal	5–20 mg	2	40
		Tablet	25–100 mg	2	200
zolmitriptam	Zomig	Tablet	2.5–5 mg	2	10
		Nasal	5 mg	2	10

OD, orally disintegrating tablet.
Note: Representative sample; other products are available.

SEDATIVES AND HYPNOTICS

Sedatives and **hypnotics** are medications used to promote sedation in smaller doses and promote sleep in larger doses. The sedative-hypnotics discussed in this section are classified as benzodiazepines (BZDs) and nonbenzodiazepines (non-BZDs). Some psychotropic drugs like trazodone (see Chapter 22) and some antihistamines (see Chapter 26 and below) are also used as sedative-hypnotics.

! *Antihistamines*, for example, diphenhydramine (Benadryl, Unisom, Sominex) have an extended half-life, remaining in the system longer. Because of slower metabolism and impaired circulation, the older or debilitated patient is particularly susceptible to *side effects*, such as dizziness, hypotension, confusion, and decreased coordination. These effects can continue for a longer time, resulting in "morning-after" problems. Therefore, antihistamines are not as effective as other available sedative-hypnotics.

None of these medications should be used for extended periods of time except under close medical supervision, as in the treatment of epilepsy, because of the potential for psychological and physical dependence. In addition, these medications depress the REM (rapid eye movement, or dream) phase of sleep, and withdrawal after prolonged use can result in a severe rebound effect with nightmares and hallucinations. Abrupt withdrawal of hypnotics, even after short-term therapy, for example, one week, may result in rebound insomnia. Therefore, gradual reduction of dosage is indicated.

Before starting pharmacological treatment, patients should be encouraged to use more natural methods of combating insomnia. These include exercise during the day, avoiding daytime naps, avoiding heavy meals and activating medications near bedtime, warm milk, back rubs, soft music, and other calming influences. Additionally, avoidance of caffeine and alcohol should be stressed. Alcohol may help to initiate sleep but results in early awakening.

Barbiturates are rarely used now as sedative-hypnotics because of the many serious, potentially dangerous *side effects*, especially *CNS depression*. Phenobarbital is still used in the treatment of seizure disorders (see Chapter 22). However, there are many other safer and more effective hypnotics available. Therefore, the use of barbiturates for sedation is restricted to specific, limited circumstances in which the patient can be closely monitored (i.e., Brevital for general anesthesia induction and maintenance).

Benzodiazepines and Nonbenzodiazepines

Benzodiazepines (BZDs) like temazepam (Restoril) and nonbenzodiazepines (non-BZDs) like zolpidem (Ambien) have supplanted barbiturates as sedative-hypnotics and have less potential for abuse. However, withdrawal effects are observed after long-term use and *respiratory depression* (when taken with alcohol) can be potentially fatal. As mentioned earlier, the cause of insomnia should be established and underlying factors treated before a hypnotic is prescribed. Only short-term use (7–10 days) is recommended for most agents. Like BZDs, non-BZDs are classified as controlled substances due to the possibility of physical and psychological dependence.

Side effects of all the sedative-hypnotics can include:

- Daytime sedation, confusion, and headache—hangover effect
- Increased risk of falls (especially in older adults or with long-acting hypnotics)
- Dependence/withdrawal symptoms
- Amnesia, hallucinations, and bizarre behavior may occur more often with triazolam (Halcion) than with other benzodiazepines
- Sleep walking and engaging in complex tasks (i.e., "sleep eating"; "sleep driving")

Contraindications and warnings for all the sedative-hypnotics include:

Hypersensitivity

Severe liver impairment

Coadministration of ketoconazole or itraconazole with triazolam

Severe renal impairment

Porphyria (with BZDs)

Abrupt discontinuation
Older adults
Patients
Debilitated
Addiction prone
Renal impairment
Liver impairment
Depressed and mentally unstable
Suicidal individuals
Pregnancy and lactation
Children
COPD and sleep apnea

Interactions of all the sedative hypnotics with the following drugs can be dangerous and potentially fatal:

Psychotropic drugs
Alcohol
Muscle relaxants
Antiemetics
Antihistamines
Analgesics

Melatonin Receptor Agonist

Ramelteon (Rozerem) is the first FDA-approved prescription medication that acts on melatonin receptors, mimicking the actions of melatonin to trigger sleep onset. As a result of this mechanism of action, dependence and abuse potential are eliminated, and ramelteon is not classified as a controlled substance.

Ramelteon works quickly, generally inducing sleep in less than 1 hour. There have been no studies comparing the effectiveness of ramelteon against other hypnotics or even against melatonin supplements (see Table 11-3 for information regarding melatonin). Dose reductions are not required in older adults, however, ramelteon should be used with caution in hepatically impaired patients.

The use of ramelteon is contraindicated with fluvoxamine (Luvox) which inhibits the metabolism of ramelteon. Do not use ramelteon with melatonin due to potential for additive sedative effects.

See Table 19-5 for a summary of the sedatives and hypnotics.

The website www.pain-topics.org is a very good noncommercial resource for healthcare professionals and their patients, providing open access to clinical news, information, research, and education for evidence-based pain-management practices.

Table 19-5 **Sedatives and Hypnotics (Use Hypnotics Short Term Only)**

GENERIC NAME	TRADE NAME	DOSAGE	COMMENTS
Benzodiazepines			
temazepam	Restoril	7.5–30 mg PO at bedtime	Intermediate onset, duration
triazolam	Halcion	0.125–0.25 mg PO at bedtime	Can cause amnesia, hallucinations, bizarre behavior, rapid onset, short duration
Non-benzodiazepines			
eszopiclone	Lunesta	PO 1–3 mg at bedtime	Rapid onset; not limited to short term use
zolpidem	Ambien	5–10 mg PO at bedtime	Rapid induction 30 min; short half-life (less than 3 h)
	Ambien CR	PO 6.25–12.5 mg at bedtime	Not limited to short term use
zaleplon	Sonata	PO 5–10 mg at bedtime	Rapid onset, very short half-life
Melatonin Receptor Agonist			
ramelteon	Rozerem	PO 5–10 mg within 30 min. of bedtime	Not limited to short term use; not a controlled substance

PATIENT EDUCATION

Patients taking analgesics, sedatives, or hypnotics should be instructed regarding:

- Potential for physical and psychological dependence and tolerance with opioids, sedatives, and hypnotics
- Taking only limited doses for short periods of time, *except* to relieve pain in terminal illness (in terminal cases, analgesics should be given on a regular basis around the clock to prevent or control pain)
- Caution with interactions; *not* taking any medications (except under close medical supervision) that potentiate CNS depression (e.g., psychotropics, *alcohol*, muscle relaxants, antihistamines, antiemetics, cardiac medications, and antihypertensives)
- Serious potential side effects with prolonged use or overdose of opioids, sedatives, and hypnotics (e.g., oversedation, dizziness, headache, confusion, agitation, nausea, constipation, urinary retention, and *potentially fatal* respiratory depression, bradycardia, or hypotension)

Tolerance with prolonged use, with increasingly larger doses required to achieve the same effect

Potential for overdose of sedatives or hypnotics and **paradoxical** reactions with older adults (e.g., confusion, agitation, hallucinations, and hyperexcitability)

Withdrawal after prolonged use of sedatives and hypnotics possibly leading to rebound effects with nightmares, hallucinations, or insomnia

Mental alertness and physical coordination impairment causing accidents or falls

Caution regarding OTC analgesic combinations and checking ingredients on the label; being aware of possible side effects with those containing aspirin (e.g., gastric distress or bleeding)

Not discontinuing abruptly

CASE STUDY – A

Analgesics

Sarah Saloom, a 45-year-old terminal cancer patient, is discharged from the hospital to her home with hospice care. Her husband is concerned that she be pain-free, but worries that she will become "addicted" to her pain medicines. He needs the following information.

1. Opioids, for example, morphine, are given regularly with all of the following conditions EXCEPT
   a. Cancer pain
   b. Arthritis pain
   c. Short-term acute pain
   d. Terminally ill

2. Morphine is frequently combined with other drugs to enhance pain relief. Which one would NOT potentiate effect?
   a. Ibuprofen
   b. Tofranil
   c. Narcan
   d. Neurontin

3. Analgesics are *most* effective for terminally ill patients when given
   a. As necessary
   b. During waking hours
   c. Before meals
   d. Around-the-clock

4. Side effects of opioids can include all of the following EXCEPT
   a. Dizziness
   b. Diarrhea
   c. Nausea
   d. Confusion

5. Opioids are frequently given with nonopioids for better analgesic action. Which one is NOT considered a coanalgesic?
   a. Acetaminophen
   b. Aspirin
   c. Amitriptyline
   d. Ambien

CASE STUDY – B

Hypnotics

Freda Stone, a 70-year-old patient with arthritis pain, has been taking Restoril for sleep for years. She wants to change to Halcion now. She needs the following information.

1. Which statement is generally true of most hypnotics?
- a. Rapid elimination usual
- b. Safe for older adults
- c. Effective long term
- d. Side effects common

2. Halcion can have all of the following side effects EXCEPT
- a. Amnesia
- b. Hallucinations
- c. Palpitations
- d. Bizarre behavior

3. Which of the following would be LEAST susceptible to ill effects?
- a. Children
- b. Debilitated
- c. Obese
- d. Older adults

4. Common side effects of many hypnotics can include all of the following EXCEPT
- a. Dizziness
- b. Diuresis
- c. Confusion
- d. Hangover

5. Hypnotic interactions can be potentially dangerous with all of the following EXCEPT
- a. Alcohol
- b. Antidepressants
- c. Analgesics
- d. Antacids

CHAPTER REVIEW QUIZ

Match the medication in the first column with the classification in the second column. Classifications may be used more than once.

	Medication	Condition
1. _____	amitripytline	**a.** Antitussive
2. _____	Vicodin	**b.** Opioid antagonist
3. _____	Imitrek	**c.** Opioid analgesic with aspirin
4. _____	methadone	**d.** Tricyclic antidepressant (adjuvant)
5. _____	Percodan	**e.** Opioid analgesic with acetaminophen
6. _____	Duragesic	**f.** Nonopioid analgesic (not controlled)
7. _____	fentanyl	**g.** Anticonvulsant (adjuvant analgesic)
8. _____	codeine	**h.** Synthetic analgesic for acute pain
9. _____	Narcan	**i.** Opioid analgesic and narcotic withdrawal
10. _____	Tegretol	**j.** Transdermal analgesic for chronic pain
		k. Anti-migraine

Choose the correct answer.

11. Diphenhydramine (Benadryl, Unisom) can cause all of the following side effects EXCEPT:
    a. Dizziness **c.** Confusion
    b. Hypertension **d.** Decreased coordination
12. The following statements are true of barbiturates, for example, phenobarbital, EXCEPT:
    a. Interact with alcohol **c.** CNS depressant
    b. Extended half-life **d.** Insomnia remedy
13. The following statements are true of opioids containing acetaminophen, for example, Tylox, EXCEPT:
    a. Antipyretic **c.** Analgesic
    b. Anti-inflammatory **d.** Many interactions
14. Tricyclic antidepressants, used as adjuvant analgesics, can have the following side effects EXCEPT:
    a. Urinary frequency **c.** Constipation
    b. Tachycardia **d.** Dry mouth

15. Anticonvulsants, for example, Neurontin, are used for nerve pain associated with the following conditions, EXCEPT:

a. Neuralgia
b. Cancer
c. Shingles
d. Polymyalgia

Go to your StudyWARE™ CD-ROM and have fun learning as you play games and answer case study-related questions to help reinforce key concepts you learned in this chapter.

Go to your Study Guide and complete the review questions for this chapter.

Chapter 20

Psychotropic Medications, Alcohol, and Drug Abuse

Objectives

Upon completion of this chapter, the learner should be able to

1. Categorize the most commonly used psychotropic medications according to the following five classifications: CNS stimulants, antidepressants, anxiolytics, antimanic, and antipsychotic medications
2. List the purpose, action, side effects, interactions, and contraindications for psychotropic medications in common use
3. Describe the physiological effects of prolonged alcohol use
4. Explain treatment of acute and chronic alcoholism
5. Compare and contrast drug addiction and habituation
6. Describe the effects of three commonly used illegal drugs
7. List the responsibilities of the health care practitioner in combating drug abuse
8. Define the Key Terms and Concepts

Key Terms and Concepts

Addiction
Antidepressant
Antipsychotic
Anxiolytics
Ataxia
Atypical antipsychotics
Bipolar disorders
Chemical dependency
Extrapyramidal
Heterocyclic
Neurotransmitters
Psychotropic
SNRIs
SSRIs
Tardive dyskinesia
Tricyclics

Psychotropic refers to any substance that acts on the mind. Psychotropic medications are drugs that can exert a therapeutic effect on a person's mental processes, emotions, or behavior. Drugs used for other purposes can have psychotropic effects. Examples of other medications that affect mental functioning are anesthetics, analgesics, sedatives, hypnotics, and antiemetics, which are discussed in other chapters.

Psychotropic medications can be classified according to the purpose for administration. The five classes are CNS stimulants, antidepressants, anxiolytics, antimanic, and antipsychotic medications.

Psychotropic medications are frequently prescribed concurrently with psychotherapy or professional counseling.

CNS STIMULANTS

CNS (central nervous system) stimulant medications are given for the purpose of promoting CNS functioning. One drug in this category, caffeine citrate, has been used in the treatment of neonatal apnea to stimulate the central nervous system's respiratory drive.

Prolonged, high intake of caffeine in any form may produce tolerance, habituation, and psychological dependence. Physical signs of withdrawal such as headaches, irritation, nervousness, anxiety, and dizziness may occur upon abrupt discontinuation of the stimulant.

Since caffeine crosses the placenta and is also distributed into the milk of nursing women, most clinicians recommend that those who are pregnant or nursing avoid or limit their consumption of foods, beverages, and drugs containing caffeine; for example, over-the-counter (OTC) analgesics or decongestants.

Other CNS stimulant drugs include controlled substances, such as the amphetamines (e.g., Adderall) and methylphenidate (Ritalin), which are used to treat attention-deficit hyperactivity disorder (ADHD) in children over age 6, and for narcolepsy. Ritalin is also occasionally used in the treatment of senile apathy and major depression refractory to other therapies. The use of amphetamines to reduce appetite in the treatment of obesity is not recommended because tolerance develops rapidly and physical or psychic dependence may develop within a few weeks. *These drugs have a high potential for abuse and should be used only under medical supervision for diagnosed medical disorders.* However, when these drugs are used appropriately, as ordered by the physician, abuse potential and dependence appear to be minimal.

Side effects of the controlled CNS stimulants can include:

- Nervousness, insomnia, irritability, seizures, or psychosis from overdose
- Tachycardia, palpitations, hypertension, and cardiac arrhythmias
- Dizziness, headache, and blurred vision (dilated pupils with photophobia)
- Gastrointestinal (GI) disturbances, including anorexia, nausea, vomiting, abdominal pain, and dry mouth
- Habituation and dependence possible with prolonged use

An FDA review of reports of serious cardiovascular adverse events in patients taking usual doses of ADHD products revealed reports of sudden death in patients with underlying serious heart problems or defects, and reports of stroke and heart attack in adults with certain risk factors. FDA recommends that children, adolescents, or adults who are being considered for treatment with ADHD drug products work with their physician or other health care professionals to develop a treatment plan that includes a careful health history and evaluation of current status, particularly for cardiovascular and psychiatric problems (including assessment for a family history of such problems).

Contraindications or caution with CNS stimulants applies to:

- Treatment for obesity (never more than three to six weeks)—without diet and exercise modifications, weight gain resumes after discontinuation of medication
- Patients with anxiety or agitation

History of drug dependence, alcoholism, or eating disorders

Hyperthyroidism

Cardiovascular disorders

Closed-angle glaucoma (not modafinil)

Pregnant or nursing women

Abrupt withdrawal, depression results

Use with monoamine oxidase inhibitors (MAOI) may cause hypertensive crisis

Caution with sustained release preparations differing designations (CD, ER, LA, SR) and their respective dosing requirements (see Table 20-1).

Pediatric precautions: Prolonged administration of CNS stimulants to children with ADHD has been reported to cause at least a temporary suppression of normal weight and/or height patterns in some patients, and therefore close monitoring is required. Growth rebound has been observed after discontinuation, and attainment of normal adult weight and height do not appear to be compromised. CNS stimulants, including amphetamines, have been reported to exacerbate motor and vocal tics and Tourette's disorder, and clinical evaluation for these disorders in children and their families should precede use of the drugs. Children should also be observed carefully for development of tics while receiving these drugs.

There is some evidence that medication use only during school days may be tried in children with controlled ADHD, but only if no significant behavior or social difficulties are noted. Once controlled, dosage reduction or interruption may be possible during weekends, holidays, or vacations.

Abuse of amphetamines: Signs and symptoms of chronic amphetamine abuse and acute toxicity are discussed later in this chapter in the section entitled Drug Abuse. Treatment of acute toxicity is also described in that section.

Daytrana is a transdermal system that contains methylphenidate in a multipolymeric adhesive matrix (making the drug difficult to extract) that is difficult to reapply once taken off. Vyvanse is a prodrug that is converted to dextroamphetamine in the GI tract. Both products have potential for a lower risk of abuse than other formulations.

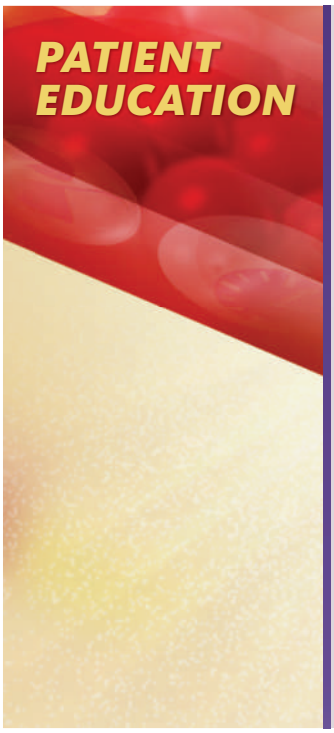
Modafinil (Provigil) is a psychostimulant medication approved for narcolepsy, sleep apnea, and shift-work sleep disorder in adults and adolescents (>16 years old). The potential for abuse and dependence appears to be lower than that for the amphetamines and methylphenidate. Modafinil is effective in treating ADHD in children and adolescents (but not adults), but was not approved by the FDA for this purpose due to serious side effects that developed with the doses used in clinical trials. It has also not been demonstrated to promote weight loss.

Side effects of modafinil (Provigil) for approved indications are infrequent. Only about 1% of people complain of mild headache and nausea.

Cautions for the use of modafinil include: Possible causes of fatigue and sleepiness should be determined before stimulant medicines are prescribed

to increase wakefulness. Without adequate investigation, some common disorders, such as diabetes and sleep apnea, might go undiagnosed.

Reducing the necessary amount of restorative sleep for prolonged periods of time can result in mental and physical problems, especially neurological and cardiovascular effects.



- Patients receiving controlled CNS stimulants should be warned about the potential side effects utilizing the Patient Medication Guide that is given out each time these products are dispensed.
- They should be cautioned about the potential for abuse and should take them only according to physician's orders.
- Medication should be taken early in the day to reduce insomnia.
- Abrupt withdrawal may result in depression, irritability, fatigue, agitation, and disturbed sleep.
- Parents of children receiving amphetamines and methylphenidate should watch for signs of tics, gastric disturbance, insomnia, weight loss, or nervousness, and report to the physician.
- Patients should be warned particularly about potential for dangerous cardiovascular side effects.
- Do not chew or crush sustained release products.
- Those taking modafinil should be cautioned about the necessity for regular sleep in sufficient amounts to restore mental and physiological functioning to an optimal level.

SELECTIVE NOREPINEPHRINE REUPTAKE INHIBITOR (SNRI)

Atomoxetine (Strattera) is a selective norepinephrine reuptake inhibitor (SNRI) and the first *nonstimulant, noncontrolled* drug approved for attention-deficit hyperactivity disorder (ADHD). Atomoxetine, structurally related to fluoxetine, does not have a potential for abuse and has been shown to be safe and effective in adolescents and children more than six years old and adults with ADHD.

Side effects of SNRIs include:

- Dry mouth, reduced appetite, fatigue
- Nausea, vomiting, constipation, dyspepsia
- Urinary hesitation/retention
- Increased risk of suicidal tendencies in children and adolescents ("black box" warning)

Contraindications and Cautions for SNRIs include:

- Narrow-angle glaucoma
- Cerebrovascular, heart, or hepatic disease
- Possible growth disturbance during treatment

Interactions of SNRIs with:

Methylphenidate (combination has not been studied)

Beta-agonists, vasopressor agents, quinidine

Fluoxetine, paroxetine, venlafaxine, MAOIs

See Table 20-1 for a summary of the CNS stimulants and non-stimulant medication for ADHD.

Table 20-1 Central Nervous System Stimulant and Nonstimulant Medications

GENERIC NAME	TRADE NAME	DOSAGE	COMMENTS
Stimulants			
caffeine citrate	Cafcit	PO 10–20 mg per kg X1, then 5 mg per kg per day	For neonatal apnea; Caution: Do *not* use caffeine and sodium benzoate
amphetamine mixtures	Adderall	PO 2.5–30 mg daily–in 1–3 divided doses per day (4–6 hours apart)	For narcolepsy, ADHD **(Attention-deficit/ hyperactivity disorder)** (>3 yrs old)
	Adderall XR	PO 5–30 mg daily	(>6 yrs old)
lisdexamfetamine	Vyvanse	PO 30–70 mg q A.M.	For ADHD >6 yrs old
methylphenidate	Ritalin	PO 2.5–20 mg BID-TID ac	For narcolepsy, ADHD (>6 yr)
	Ritalin SR, Metadate ER	10–60 mg div. doses (Note 8-h duration of action)	ER tabs, For ADHD, senile apathy, refractory depression
	Medadate CD, Ritalin LA	PO 20–60 mg q A.M.	ER (extended release) caps for once-daily treatment of ADHD
	Concerta	PO 18–54 mg q A.M.	Tablet shell is excreted intact
	Daytrana Patch	10–30 mg daily to hip (2 hrs before needed affect)	Remove patch after 9 hours
modafinil	Provigil	PO 100–400 mg daily	For narcolepsy, sleep apnea, and shift-work sleep disorder (>16 yr)
Non-Stimulant			
atomoxetine	Strattera	PO 10–50 mg QD-BID	Only noncontrolled, nonstimulant for ADHD (>6 yrs old)

ANTIDEPRESSANTS

Depression is frequently described as a chemical imbalance. In many depressed patients, certain chemicals in the brain may be in short supply. Chemicals in the brain, like dopamine, serotonin, and norepinephrine are known as **neurotransmitters**. Substances that travel across the synapse (contact point of two neurons) transmit messages between nerve cells. If these neurotransmitters are reabsorbed by one nerve ending before they have had a chance to make contact with the next nerve cell, they cannot perform their function. In depression, there may be a shortage of the neurotransmitters dopamine, serotonin, or norepinephrine.

Antidepressant medications, sometimes called mood elevators, are used primarily to treat patients with various types of depression. The five categories in general use are the tricyclic antidepressants, the MAOIs, the selective serotonin reuptake inhibitors (**SSRIs**), the selective norepinephrine reuptake inhibitors (**SNRIs**), and the heterocyclic antidepressants. Although symptoms may be relieved in the first month, it is generally advisable to counsel patients to continue antidepressant therapy for six to twelve months to prevent relapse.

The FDA has directed manufacturers of *all* antidepressants to include a Black Box warning that antidepressants increased the risk of suicidal thinking and behavior in short-term studies in children and adolescents with manic depressive disorder and other psychiatric disorders. There were no suicides in any of these studies. Anyone considering the use of antidepressants in a child, adolescent, or young adult must balance this risk with the clinical need. Patients should be observed closely for behaviors associated with these drugs (e.g., anxiety, agitation, panic attacks, insomnia, irritability, hostility, impulsivity, severe restlessness, hypomania, and mania) and communicate same with the prescribing health care provider.

Tricyclics

The mechanism of antidepressant action of the **tricyclics** involves potentiation of norepinephrine and serotonin activity by blocking their reuptake presynaptically. Their pharmacology also includes strong *anticholinergic* activity that is responsible for many of the side effects seen. Tricyclics are lethal in overdose (cardiac conduction abnormalities/ dysrhythmias).

The tricyclics have delayed action, elevating the mood and increasing alertness after two to four weeks. They are frequently given at bedtime because of a mild sedative effect. They should be used with caution (if at all) in the older adult because of the strong sedative and anticholinergic properties of this drug class and the increased risk of falls. Tricyclics may be more effective than SSRIs in some severe depression and are used as an adjunct in neuropathic pain control (see Chapter 19, Analgesics, Sedatives, and Hypnotics).

Side effects of the tricyclics, such as imipramine (Tofranil), are anticholinergic in action and can include:

- Dryness of the mouth
- Increased appetite and weight gain

- Drowsiness and dizziness
- Blurred vision
- Constipation and urinary retention, especially with benign prostatic hypertrophy (BPH)
- Postural hypotension, cardiac arrhythmias, and palpitation
- Confusion, especially in older adults

Contraindications or extreme caution with tricyclics applies to:

- Cardiac, renal, GI, and liver disorders
- Older adults
- Glaucoma
- Obesity
- Seizure disorder
- Pregnancy and lactation
- Concomitant use with MAOIs
- SSRIs—increase tricyclic blood levels

Interactions of tricyclics can include:

- Certain antiarrhythmics, some quinolones (QT prolongation)
- Clonidine—causing hypertensive crisis
- CNS drugs and alcohol

Monoamine Oxidase Inhibitors (MAOIs)

MAOIs were discovered as part of research with isoniazid (INH), an antitubercular drug. The mechanism of antidepressant action of MAOIs involve increasing the concentrations of serotonin, norepinephrine, and dopamine in the neuronal synapse by inhibiting the MAO enzyme.

The MAOIs, for example phenelzine (Nardil), are rarely used today because of potential serious side effects and numerous food, herbal, and drug interactions. They cannot be given until two weeks after tricyclics and other interacting drugs have been discontinued. These agents are typically reserved for refractory or atypical depression or those associated with panic disorder or phobias.

Side effects of MAO inhibitors are adrenergic in action and can include:

- Nervousness, agitation, and insomnia
- Headache
- Stiff neck
- Hypertension or hypertensive crisis (can be fatal)
- Tachycardia, palpitation, and chest pain
- Nausea, vomiting, and diarrhea
- Blurred vision

Contraindications and warnings for MAOIs apply to:

- Patients with cerebrovascular, heart, liver, and renal disease
- Children under 16 yr

Pregnancy and lactation

Abrupt discontinuation

Interactions of the MAOIs with some drugs, foods, and herbal supplements can cause *hypertensive crisis*, manifested by severe headache, palpitation, sweating, chest pain, possible intracranial hemorrhage, and even death. Interactions may occur with:

Adrenergic drugs and levodopa

SSRIs and SNRIs, resulting in seizures, fever, hypertension, and confusion ("serotonin syndrome")

CNS depressants, resulting in circulatory collapse

Foods containing tryamine, tryptamine, or tryptophan, such as yogurt, sour cream, all cheeses, liver (especially chicken), pickled herring, figs, raisins, bananas, pineapple, avocados, broad beans (Chinese pea pods), meat tenderizers, alcoholic beverages (especially red wine and beer), and all fermented or aged foods (e.g., corned beef, salami, and pepperoni)

EMSAM (selegilene) is a selective MAOI (type-B) administered as a transdermal patch indicated for treatment of major depressive disorder in adults. Blockade of this enzyme reduces the metabolism of dopamine, but not that of norepinephrine or serotonin. Transdermal administration allows for lower doses and direct absorption into the bloodstream, reducing the likelihood of a dietary tyramine induced hypertensive crisis (see Chapter 22, Anticonvulsants and Antiparkinsonian Drugs, for interactions and contraindications).

Selective Serotonin Reuptake Inhibitors (SSRIs)

SSRIs are considered to be the first-line medications for treatment of depression. They are preferred because of fewer side effects, greater safety in cases of overdose, and increased patient compliance.

The antidepressants in this category selectively block the reabsorption of the neurotransmitter serotonin, thus helping to restore the brain's chemical balance. Drugs in this class include fluoxetine (Prozac) and sertraline (Zoloft). Therapy may be required for several months or longer. Symptomatic relief may require one to four weeks and there is prolonged elimination of the drug. SSRIs do not significantly effect cognition in older adults.

Side effects of the SSRIs may include:

Sexual dysfunction

Nausea, anorexia

Diarrhea, sweating

Insomnia, anxiety, nervousness, tremor, drowsiness, fatigue, dizziness, headache

Other side effects have been reported in less than 1% to 3% of patients receiving them.

Caution with SSRIs applies to patients with the following conditions:

Liver or renal impairment

Suicide prone

Diabetes

Bipolar disorders—may precipitate manic attacks

Underweight, eating disorders

Pregnancy, lactation

Interactions of SSRIs possible with:

Other CNS drugs—lower doses of tricyclics may be needed; monitor for toxicity

MAOIs—never take concurrently

Certain analgesics (tramadol), antiemetics (metoclopramide), antimigraines ("triptans"), antibiotics (linezolid), and OTC products (St. John's wort, tryptophan) which can result in serotonin syndrome

Selective Norepinephrine Reuptake Inhibitors (SNRIs)

Duloxetine (Cymbalta) and venlafaxine (Effexor) are antidepressants that inhibit the reuptake of both serotonin and norepinephrine. Refer to Chapter 19 for details on these 2 agents.

Desvenlafaxine (Pristiq), also an SNRI, is the major metabolite of venlafaxine and is pharmacologically equiactive and equipotent to its parent compound. It is indicated for the treatment of major depressive disorder. The drug-related problems, warnings, and precautions associated with the use of desvenlafaxine are generally similar to those of other SNRIs.

Heterocyclic Antidepressants

The second-generation **heterocyclic** antidepressants are comparable in efficacy to the first-generation tricyclic antidepressants, but have differing effects on dopamine, norepinephrine, and serotonin, and distinctly different adverse effect profiles. Bupropion (Wellbutrin) is considered an *activating antidepressant* (like the SSRIs) and can be useful in cases of severe depression characterized by extreme fatigue, lethargy, and psychomotor retardation. It is also useful in helping to reduce relapse rates in persons who are quitting smoking (see Zyban in Chapter 26) and those patients who experience sexual dysfunction with other antidepressants.

Mirtazapine (Remeron) is a *calming antidepressant* that can be useful in treating agitated depression, mixed anxiety and depression, and fibromyalgia. A common side effect of mitrazapine is weight gain, which can be helpful in patients with a poor appetite. Trazodone (Desyrel) is highly sedating and is used in low doses as a hypnotic. It can be useful in higher doses in older adult patients for agitation secondary to dementia and to treat activation side effects caused by the SSRIs.

Side effects of heterocyclic antidepressants can include:

- Drowsiness—common (except bupropion)
- Insomnia, restlessness, agitation, anxiety (with bupropion)
- Dry mouth, nausea, dizziness, confusion
- Priapism or impotence—discontinue the drug (trazodone)
- Weight gain (mirtazapine, trazodone)

Interactions of heterocyclics with:

Other CNS depressants, including alcohol, may potentiate sedation (mirtazapine, trazodone) or increase the risk of seizures (bupropion).

MAOIs—never take concurrently

Food may decrease incidence of light-headedness.

Caution with heterocyclics applies to:

Suicide prone

Seizure disorder

Cardiac or liver disorders

See Table 20-2 for a summary of the antidepressant agents.

ANTIMANIC AGENTS

Lithium

Lithium salts are antimanic agents, not recommended for depression alone. **Bipolar disorders** (manic-depressive) are treated *long term* with lithium salts. A maintenance dose is established by monitoring blood levels. Serum levels are checked initially and every few months thereafter to maintain a level of 0.8–1.5 mEq/mL. Patients must be monitored and alerted for signs of toxicity.

Side effects of lithium can include:

- GI distress (usual initially and resolves)—take medicine with meals
- Cardiac arrhythmias and hypotension
- Thirst and polyuria (dehydration may cause acute toxicity)
- Tremors—can be treated with propranolol
- Thyroid problems

Signs of lithium toxicity can include:

- Drowsiness, confusion, blurred vision, and photophobia
- Tremors, muscle weakness, seizures, coma, and cardiovascular collapse

Caution with lithium must be used with:

Seizure disorders, Parkinsonism

Cardiovascular and kidney disorders

Older adults and debilitated patients

Thyroid disease

Table 20-2 Antidepressants

GENERIC NAME	TRADE NAME	DOSAGE	COMMENTS
Tricyclics			
amitriptyline	(Elavil)*	PO 50–300 mg daily	All of these drugs interact with CNS drugs. Give at bedtime.
desipramine	Norpramin	PO 75–300 mg daily	Less sedation, anticholinergic S.E., and orthostatic hypotension
doxepin	Sinequan,	PO 50–300 mg daily	Also used topically for eczema (Prudoxin)
imipramine	Tofranil	PO 75–300 mg daily	Also effective for enuresis
nortriptyline	Pamelor	PO 25–150 mg daily	Older adults and adolescent patients need lower dose
MAOIs			
isocarboxazid	Marplan	PO 20–60 mg daily in div. doses	All of these drugs interact with many foods and other drugs, resulting in serious reactions
phenelzine	Nardil	PO 45–90 mg daily in div. doses	
tranylcypromine	Parnate	PO 60 mg daily in div. doses	
SSRIs			
citalopram	Celexa	PO 20–60 mg daily	Take A.M. or P.M. with or without food
escitalopram	Lexapro	PO 10–20 mg daily	May be better tolerated than Celexa
fluoxetine	Prozac	PO 10–80 mg daily	Delayed response, long half-life; take A.M.
Paroxetine	Paxil	PO 10–60 mg daily	Older adults 1/2 dose; take in A.M.
	Paxil CR	PO 12.5–62.5 mg daily	Do not give with antacids
sertraline	Zoloft	PO 25–200 mg daily	Take in A.M.
SNRIs			
desvenlafaxine	Pristiq	PO 50–400 mg daily	Do not chew or crush
duloxetine	Cymbalta	PO 40–60 mg daily	Also used for neuropathy
venlafaxine	Effexor	PO 75–375 mg div. doses	Take PC to lessen nausea
	Effexor-XR	PO 37.5–225 mg daily	Do not chew or crush, swallow whole
Heterocyclics			
bupropion	Wellbutrin	PO 100–150 mg BID–TID	Take early in the day; space doses at least 6 hrs apart to minimize seizure risk
	Wellbutrin SR	PO 150–200 mg daily–BID	space doses at least 8 hrs apart
	Wellbutrin XL	PO 150–400 mg	give once daily in the A.M.
mirtazapine	Remeron	PO 15–45 mg daily	Take at bedtime, sedation common
trazodone		PO 25–100 mg at bedtime for insomnia PO 150–600 mg in div. doses for depression	Take PC to decrease dizziness and nausea; if drowsiness occurs, may give large portion of dose at bedtime

*Brand name no longer marketed, but name is still commonly used.

Interactions of lithium with CNS drugs, diuretics, nonsteroidal anti-inflammatory drugs (NSAIDs), angiotensin-converting enzyme (ACE) inhibitors, and sodium salts.

The anticonvulsants valproate (Depakote, Depakene) and carbamazepine (Tegretol) are also used for mood stabilization in bipolar illness (see Chapter 22, Anticonvulsants, for details on these drugs).

Symbyax, a combination of the atypical antipsychotic olanzapine and the SSRI fluoxetine, is the first FDA-approved combination product for the depressive phase of bipolar disorder. In addition, the atypical antipsychotics aripiprazole, olanzapine, quetiapine, risperidone, and ziprasidone are now approved to treat the manic phase of bipolar disorder. Refer to the discussion of these agents in this chapter for further details.

See Table 20-3 for a summary of antimanic agents.

Table 20-3 Antimanic Agents

ANTIMANIC AGENTS			
lithium	Lithobid, Eskalith	900–1,800 mg div. doses	0.8–1.5 mEq per mL (desired serum level)
carbamazepine	Tegretol, Tegretol XR	PO 400–1,600 mg in div. doses	4–12 mcg per mL (desired serum level)
valproate	Depakote, Depakene	PO 20–60 mg per kg per day (div. doses)	50–100 mcg per mL (desired serum level)
	Depakote ER	PO 250–1,000 mg per day	For migraine prophylaxis
olanzapine/ fluoxetine	Symbyax	PO q P.M. (various strengths)	For bipolar depression

ANXIOLYTICS

Antianxiety medications (e.g., benzodiazepines) are sometimes referred to as **anxiolytics** or minor tranquilizers. They are useful for the short-term treatment of (1) anxiety disorders, (2) some psychosomatic disorders and insomnia, (3) alcohol withdrawal, and (4) nausea and vomiting. Benzodiazepines, such as Valium, are also used as muscle relaxants, anticonvulsants, or preoperatively. Anxiolytics, when given in small doses, can reduce anxiety and promote relaxation without causing sedation. Larger doses are sometimes

prescribed at bedtime for their sedative effect. Minor tranquilizers should not be taken for prolonged periods of time because *tolerance, and physical and psychological dependence, may develop. Sudden withdrawal after prolonged use may result in seizures, agitation, psychosis, insomnia, and gastric distress.*

Compounds with a long half-life, such as diazepam (Valium), should be avoided in older adults. Oxazepam (Serax) and lorazepam (Ativan) have medium to short half-lives and inactive metabolites, and are less prone to accumulation in older adult patients or those with liver disease.

Side effects of the benzodiazepines may include:

- Depression, hallucinations, confusion, agitation, bizarre behavior, amnesia
- Drowsiness, lethargy, and headache
- **Ataxia** and tremor (Note: they are used to treat some types of EP reactions)
- Rash and itching
- Sensitivity to sunlight

Contraindications or extreme caution with benzodiazepines applies to:

Mental depression

Suicidal tendencies

Depressed vital signs

Pregnancy, lactation, and children

Liver and kidney dysfunction

Older adults and debilitated patients (paradoxical reactions), prolonged elimination time

Persons operating machinery

Interactions of benzodiazepines with potentiation of effect may occur with:

CNS depressants (e.g., analgesics, anesthetics, sedative hypnotics, other muscle relaxants, antihistamines, and alcohol)

Anti-retroviral protease inhibitors, erythromycin, ketoconazole, itraconazole, diltiazem, and verapamil

Phenytoin (potentiation of phenytoin by raising serum concentration)

Grapefruit juice can potentiate the effects of alprazolam and diazepam and should not be taken concurrently.

Midazolam (brand name Versed, no longer marketed) is a potent benzodiazepine. It is used preoperatively to relieve anxiety and provide sedation, light anesthesia, and amnesia of operative events. Because of its more rapid onset of sedative effects and more pronounced amnestic effects during the first hour following administration, it is considered the drug of choice for short surgical procedures. Midazolam is usually administered IV and the duration of amnesia is about one hour. It has also been used orally for preoperative sedation and to relieve anxiety with good results.

Midazolam may be used alone or in combination with an opioid such as fentanyl for painful procedures (e.g., endoscopy and cardiac catheterization with or without intervention). Midazolam is also used IV for induction of general anesthesia, along with an opioid. This potent sedative requires individualized dosage with adjustment for age, weight, clinical condition, and procedure.

Side effects of midazolam can include:

- *Depressed respiration* with large doses, especially in older adults and those with COPD (chronic obstructive pulmonary disease)
- Paradoxical reactions (agitation or involuntary movements) occur occasionally
- Nausea and vomiting occasionally

Cautions with midazolam:

- Watch for apnea, hypoxia, and/or cardiac arrest
- Respiratory status should be monitored continuously during parenteral use
- Facilities and equipment for respiratory and cardiovascular support should be readily available
- Vital signs should be monitored carefully for changes in blood pressure or decrease in heart rate
- Patients with electrolyte imbalance, renal impairment, and congestive heart failure, and children are at increased risk of complications

Contraindicated in pregnancy and those with narrow-angle glaucoma

Interactions of midazolam which can potentiate possibility of respiratory depression apply to:

- CNS depressants
- Cimetidine (Tagamet) and ranitidine (Zantac)
- Anti-retroviral protease inhibitors, erythromycin, ketoconazole, itraconazole, diltiazem, and verapamil

Other anxiolytics, not related to the benzodiazepines, include buspirone (BuSpar). Unlike the benzodiazepines, it has no anticonvulsant or muscle relaxant activity, does not substantially impair psychomotor function, and has little sedative effect. Limited evidence suggests that buspirone may be more effective for cognitive and interpersonal problems, including anger and hostility associated with anxiety, whereas the benzodiazepines may be more effective for somatic symptoms of anxiety.

Buspirone has a slower onset of action than most anxiolytics (two to four weeks for optimum effect). Therefore, it is ineffective on a PRN basis. It has little potential for tolerance or dependence and has been used without unusual adverse effects or decreased efficiency for as long as a year.

Side effects of buspirone (fewer and less severe) may include:

- Dizziness, drowsiness, and headache
- GI effects (e.g., nausea)

Caution with buspirone applies to renal and hepatic impairment.

Another short-term anxiolytic, chemically different from the benzodiazepines, is hydroxyzine (Vistaril). It is an antihistamine (H_1-blocker) structurally related to meclizine (Antivert).

Side effects of hydroxyzine generally anticholinergic in nature may include:

Drowsiness, ataxia, dizziness

Urinary retention, mydriasis

Caution with hydroxyzine applies to:

GI, hepatic, respiratory, and urinary disorders

Closed angle glaucoma

Older adults and in pregnancy (especially first trimester)

See Table 20-4 for a summary of antianxiety medications.

Table 20-4 Antianxiety Medications (Anxiolytics)

GENERIC	TRADE NAME	DOSAGE	COMMENTS
Benzodiazepines (short-term use only)			
alprazolam	Xanax	PO 0.125–0.5 mg BID–TID	Abrupt withdrawal may cause severe side effects
	Xanax XR	PO 0.5–6 mg q A.M.	For panic disorder
chlordiazepoxide	Librium	PO 5–25 mg TID or 4 × per day	Larger doses with severe anxiety or ethanol withdrawal
clorazepate	Tranxene	PO 7.5 –60 mg daily div. doses	For older adult patients no more than 15 mg daily
diazepam	Valium Diastat	PO 2–10 mg TID, IV R 0.2 mg per kg	Do not mix in syringe with other medications, also used as muscle relaxant or IV in status epilepticus; R for refractory seizures
lorazepam	Ativan	PO, IM, or IV 2–3 mg daily div. doses	For older adults who are agitated
midazolam	(Versed)*	PO, IM, IV dose varies with useage	Used preoperatively for short-term procedures
oxazepam	(Serax)*	PO 10–15 mg TID or 4 × per day	For older adults who are agitated
Other Anxiolytics			
buspirone	Buspar	PO 15–60 mg daily div doses	Slow onset of action, may be used long term
hydroxyzine	Vistaril	PO 25–100 mg 4 × per day or 25–100 mg deep IM	Also used as an antiemetic, antipruritic, or preoperative

*Brand name no longer marketed, but name is still commonly used.

ANTIPSYCHOTIC MEDICATIONS/MAJOR TRANQUILIZERS

Antipsychotic medications, or major tranquilizers, such as haloperidol (Haldol), are sometimes called neuroleptics. They are useful in two major areas:

Relieving symptoms of psychoses including delusion, hallucinations, agitation, and combativeness

Relieving nausea and vomiting; for example, prochlorperazine (Compazine) (see Chapter 16)

Many of the typical antipsychotics are classified chemically as phenothiazines; for example, chlorpromazine (Thorazine). Dosage can be regulated to modify disturbed behavior and relieve severe anxiety in many cases without profound impairment of consciousness. These agents work by blocking dopamine receptors, resulting in unbalanced cholinergic activity, which causes frequent **extrapyramidal** side effects (EPS) and **tardive dyskinesia** (TD).

Another class of antipsychotics, the **atypical antipsychotics**, for example risperidone, are chemically different from the phenothiazines, blocking both serotonin and dopamine receptors. This mechanism results in less potential for adverse effects, especially EPS and TD.

Although helpful in treating behavioral and psychological symptoms of dementia, typical or atypical antipsychotic drugs are not FDA-approved ("Black Box" warning) for the treatment of patients with dementia-related psychosis. Cerebrovascular adverse events (strokes, transient ischemic attacks, and cerebrovascular accidents), including fatalities, have been reported in older adults with dementia-related psychosis (Alzheimer's, vascular and mixed) being treated with antipsychotics. Since there is no FDA-approved medication for the treatment of dementia-related psychosis, other management options (behavioral/environmental modifications, recreational activities, etc.) should be considered by health care providers.

Side effects of typical antipsychotics differ based upon the potency of the agent. Low-potency agents including chlorpromazine and thioridazine are more likely to produce sedation, hypotension, and anticholinergic effects. High-potency agents, including haloperidol, fluphenazine, thiothixine, and trifluoroperazine are more likely to produce extrapyramidal reactions.

Side effects of all antipsychotics may include:

Postural hypotension, tachycardia, bradycardia, and vertigo

Anticholinergic effects (see Chapter 13 ANS drugs): dry mouth, constipation, urinary retention, blurred vision, fever, confusion, restlessness, agitation, and headache

Jaundice, rash, photosensitivity or hypersensitivity reactions

Increased risk of hyperglycemia, diabetes, and elevated cholesterol with the atypicals

Extrapyramidal reactions (EPS), severe CNS adverse effects, include:

- Parkinsonian symptoms, for example, tremors, drooling, dysphagia—more common in older adults

- *Tardive dyskinesia* (TD) (involuntary, and may be irreversible, movements such as tics)—more common in older adults, especially females
- Dystonic reactions (spasms of the head, neck, or tongue)—more frequent in children
- Akathisia (motor restlessness)—more common in children

Note

Parkinsonian symptoms and tardive dyskinesia may become permanent and irreversible. Therefore, patients receiving antipsychotic agents should be assessed frequently for these conditions. Dosage should not be terminated abruptly in those receiving high doses for prolonged periods of time.

Treatment of parkinsonian symptoms includes concomitant administration of an anticholinergic antiparkinsonian agent; for example, Artane or Cogentin (see Chapter 22). *Prophylactic administration of these drugs will not prevent extrapyramidal symptoms. These drugs will not alleviate symptoms of TD and can make them worse.* Dystonic reactions usually appear early in therapy and usually subside rapidly when the antipsychotic drug is discontinued. Trihexyphenidyl (Artane), benztropine (Cogentin), or diphenhydramine (Benadryl) are used to treat dystonic reactions. Patients receiving antipsychotic medication should be assessed for TD at the start of treatment and at least every six months with the Abnormal Involuntary Movement Scale (AIMS) (see Figure 20-1 and Figure 20-2) or Dyskinesia Identification System: Condensed User Scale (DISCUS) available from www.med-pass.com and other websites.

Contraindications for antipsychotics include:

Seizure disorders

Parkinsonian syndrome

Cerebrovascular disease

Severe depression

Pregnancy

Blood dyscrasias

Caution with antipsychotics applies to older adults, children, hepatic, cardiovascular, renal disease, prostatic hypertrophy, and diabetes.

Interactions of the antipsychotics may include:

Potentiation with CNS depressants, anticholinergics, antihypertensives

Drugs that prolong QT interval and increase the risk of life-threatening cardiac arrhythmias (antiarrhythmic agents, dolasetron, certain quinolones) with phenothiazines and ziprasidone

Antagonism with anticonvulsants (seizure activity may increase)

See Table 20-5 for a summary of the antipsychotic medications. See Figure 20-3 for a summary of psychotropic drugs.

INSTRUCTIONS: Complete Examination Procedure (reverse side) before making ratings.

Code: 0 = None, 1 = Minimal, may be extreme normal, 2 = Mild, 3 = Moderate, 4 = Severe

		(CIRCLE ONE)
FACIAL AND ORAL MOVEMENTS:	**1. Muscles of Facial Expression** e.g., movements of forehead, eyebrows, periorbital area, cheeks; include frowning, blinking, smiling, grimacing	0 1 2 3 4
	2. Lips and Perioral Areas e.g., puckering, pouting, smacking	0 1 2 3 4
	3. Jaw e.g., biting, clenching, mouth opening, lateral movement	0 1 2 3 4
	4. Tongue Rate only increase in movement both in and out of mouth, NOT inability to sustain movement	0 1 2 3 4
EXTREMITY MOVEMENTS:	**5. Upper (arms, wrists, hands, fingers)** Include choreic movements (i.e., rapid, objectively purposeless, irregular, spontaneous), athetoid movements (i.e., slow, irregular, complex, serpentine). Do NOT include tremor (i.e., repetitive, regular, rhythmic)	0 1 2 3 4
	6. Lower (legs, knees, ankles, toes) e.g., lateral knee movement, foot tapping, heel dropping, foot squirming, inversion and eversion of foot	0 1 2 3 4
TRUNK MOVEMENTS:	**7. Neck, shoulder, hips** e.g., rocking, twisting, squirming, pelvic gyrations	0 1 2 3 4
GLOBAL JUDGEMENTS:	**8. Severity of abnormal movements**	0 1 2 3 4
	9. Incapacitation due to abnormal movements	0 1 2 3 4
	10. Patient's awareness of abnormal movements Rate only patient's report	No awareness 0 Aware, no distress 1 Aware, mild distress 2 Aware, moderate distress 3 Aware, severe distress 4
		No = 0 Yes = 1
DENTAL STATUS:	**11. Current problems with teeth and/or dentures**	No = 0 Yes = 1
	12. Does patient usually wear dentures?	

It is always preferable to perform the entire AIMS Examination. This establishes consistent testing conditions and allows test results to be compared. Nonambulatory residents may be observed informally for abnormal involuntary movements while in bed or in a wheelchair. Uncooperative residents should be observed during normal activities.

You must check one of these boxes:
- ☐ Full examination conducted and scored
- ☐ Scores from informal observations—Resident was:
  - ☐ Not ambulatory—observed in ☐ bed ☐ wheelchair
  - ☐ Not cooperative

RATER	DATE:	PATIENT	Resident #

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FIGURE 20-1 **Abnormal Involuntary Movement Scale (AIMS). This test, or a comparable one, is performed every three to six months with all patients receiving antipsychotic medication to identify any signs of tardive dyskinesia.**

AIMS EXAMINATION PROCEDURE

Either before or after completing the examination procedure observe the patient unobtrusively, at rest (e.g., in waiting room).

The chair to be used in this examination should be a hard, firm one without arms.

1. Ask patient whether there is anything in his/her mouth (i.e., gum, candy, etc.) and if there is, to remove it.
2. Ask patient about the current condition of his/her teeth. Ask patient if he/she wears dentures. Do teeth or dentures bother patient now?
3. Ask patient whether he/she notices any movements in mouth, face, hands, or feet. If yes, ask to describe and to what extent they currently bother patient or interfere with his/her activities.
4. Have patient sit in chair with hands on knees, legs slightly apart, and feet flat on floor. (Look at entire body for movements while in this position.)
5. Ask patient to sit with hands hanging unsupported. If male, between legs, if female and wearing a dress, hanging over knees. (Observe hands and other body areas.)
6. Ask patient to open mouth. (Observe tongue at rest within mouth.) Do this twice.
7. Ask patient to protrude the tongue. (Observe abnormalities of tongue movement.)
8. ♦ Ask patient to tap thumb, with each finger, as rapidly as possible for 10–15 seconds; separately with right hand, then with left hand. (Observe facial and leg movements.)
9. Flex and extend patient's left and right arms (one at a time). (Note any rigidity and rate on DOTES.)
10. Ask patient to stand up. (Observe in profile. Observe all body areas again, hips included.)
11. ♦ Ask patient to extend both arms outstretched in front with palms down. (Observe trunk, legs, and mouth.)
12. ♦ Have patient walk a few paces, turn, and walk back to the chair. (Observe hands and gait.) Do this twice.

♦ Activated movement, some practitioners score these movements differently.

INTERPRETATION OF THE AIMS SCORE

- Individuals with no single score exceeding 1 are at very low risk of having a movement disorder.
- A score of 2 in only one of the seven body areas is borderline and the patient should be monitored closely.
- A patient with score of 2 in two or more of the seven body areas should be referred for a complete neurological examination.
- A score of 3 or 4 in only one body area warrants referring the patient for a complete neurological examination.

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FIGURE 20-2 **Abnormal Involuntary Movement Scale (AIMS). Examination procedure.**

Table 20-5 Antipsychotic Medications/Major Tranquilizers

GENERIC NAME	TRADE NAME	DOSAGE[a]	COMMENTS
Typical (*These drugs frequently cause EPS with long-term use. Monitor closely.*)			
Phenothiazines			
chlorpromazine	(Thorazine)*	PO 30–800 mg 1–4 doses daily, also deep IM, or IV	Primarily for agitation; also for nausea and vomiting and severe behaviour problems
fluphenazine	(Prolixin)*	IM, PO 0.5–40 mg daily div. doses	For older adults, reduce dose to ½ or ¼
perphenazine	(Trilafon)*	PO 4–64 mg daily div. doses	For psychosis, nausea, and vomiting in adults
prochlorperazine	(Compazine)*	PO, IM, IV 5–10 mg PR 25 mg BID	For agitation; primarily for nausea and vomiting in adults
thioridazine	(Mellaril)*	PO 50–800 mg daily div 2–4 × per d	For psychoneurosis, agitation, or combativeness
trifluoperazine	(Stelazine)*	PO 1–20 mg BID	For schizophrenia and short-term for non-psychotic disorders
Others			
haloperidol	Haldol	PO 0.5–30 mg daily div 2–3× daily	For agitation, especially with schizophrenia and delusions in older adults
	Haldol decanoate IM	IM 50–300 mg q 4 wk	
thiothixene	Navane	PO 2–60 mg daily div 2–3× daily	For chronic schizophrenic or behavioural management of withdrawn patients
Atypical			
aripiprazole	Abilify	PO 2–30 mg daily IM 9.75mg	For schizophrenia; adjunct treatment for depression
clozapine	Clozaril Fazaclo ODT	PO 12.5–900 mg (div. doses)	Monitor WBC, agranulocytosis risk
olanzapine	Zyprexa	PO 5–20 mg daily	Reduce dose by ½ for older adults
	Zyprexa Zydis	IM 10 mg (max. dose 30 mg per day)	For acute agitation orally-disintegrating tablet

Table 20-5 Antipsychotic—*continued*

GENERIC NAME	TRADE NAME	DOSAGE[a]	COMMENTS
paliperidone	Invega	PO 3–12 mg once daily	For schizophrenia; do not crush
quetiapine	Seroquel Seroquel XR	PO 50–800 mg daily (div. doses)	Monitor for orthostatic hypotension Also for depression assoc. with bipolar
risperidone	Risperdal	PO 1–4 mg BID	Reduce dose by ½ for older adults
	Risperdal Consta	IM 25–50 mg q2wk	For schizophrenia
ziprasidone	Geodon	PO 20–80 mg BID with food	Greater risk of cardiac disorders
		IM 10–20 mg q2–4h (max. dose 40 mg per day)	For acute psychosis/ agitation

*Brand name no longer marketed, but name is still commonly used.

[a]Varies with condition (divided doses).

There is no "ideal" antipsychotic medication. Both conventional and atypical antipsychotic medications are associated with significant adverse drug reactions. However, research indicates a chemical component in many forms of mental illness. By altering abnormal levels of certain chemicals in the brain, such as serotonin, norepinephrine, or dopamine, many patients with mental or emotional illness have been helped. Psychiatric hospitalization has decreased since the advent of antipsychotic medications.

PATIENT EDUCATION

Patients taking antipsychotic medications should be instructed regarding (utilize patient Medication Guides where available):

- Potential for psychological and/or physical dependence with prolonged use
- Caution in taking medication only in prescribed dosage and for limited period of time under medical supervision to reduce possibility of serious side effects from overdose or prolonged use
- Reporting adverse side effects to physician at once (e.g., dizziness, blurred vision, nervousness, palpitations and other cardiac symptoms, urinary retention, GI symptoms, adverse mental changes, and extrapyramidal reactions)
- Avoiding chemical abuse (e.g., alcohol or drugs) and obtaining professional treatment when these conditions exist

Possible severe withdrawal reactions (e.g., seizures) after prolonged use of psychotropic medications (withdrawal should never be abrupt, and medical supervision is indicated for prolonged administration of any of the psychotropic drugs)

Caution with interactions; *not* taking any other medications (except under close medical supervision) that can potentiate CNS depression (e.g., analgesics, *alcohol*, muscle relaxants, antihistamines, antiemetics, cardiac medications, or antihypertensives)

Not taking grapefruit juice with the benzodiazepines, especially alprazolam and diazepam

Older adult patients are more at risk for the side effects mentioned above because of slowed metabolism and cardiovascular, kidney, liver, and visual impairment. They should be issued the following cautions:

Rise slowly because of potential for hypotension.

Avoid operating machinery or driving while taking these drugs. Report to the physician immediately any side effects, especially dizziness, confusion, sleep disturbances, or weakness.

Avoid taking any OTC drugs or herbal supplements without medical supervision.

Tell the prescribing physician about all other medicines you are taking, including eyedrops.

ALCOHOL

Alcohol (ethyl alcohol, ethanol) can be classified as a psychotropic drug and a CNS depressant. It is the number one drug problem in the United States, accounting for nearly 100,000 deaths per year and is directly responsible for more than half of traffic accidents (one-third of all U.S. traffic fatalities).

Alcohol is a fast-acting depressant, pharmacologically similar to ether. The body reacts to alcohol with excitement, sedation, and finally anesthesia. Large amounts of alcohol can result in alcoholic stupor, cerebral edema, and depressed respiration.

Alcohol is rapidly absorbed from the GI tract into the bloodstream. Alcohol depresses primitive areas of the cortex first and then decreases control over judgment, memory, and other intellectual and emotional functioning. Within a few hours, motor areas are affected, producing unsteady gait, slurred speech, and incoordination. Prolonged use can cause permanent CNS damage and result in peripheral neuritis, convulsive disorders, Wernicke's syndrome, and Korsakoff's psychosis with mental deterioration, memory loss, and ataxia.

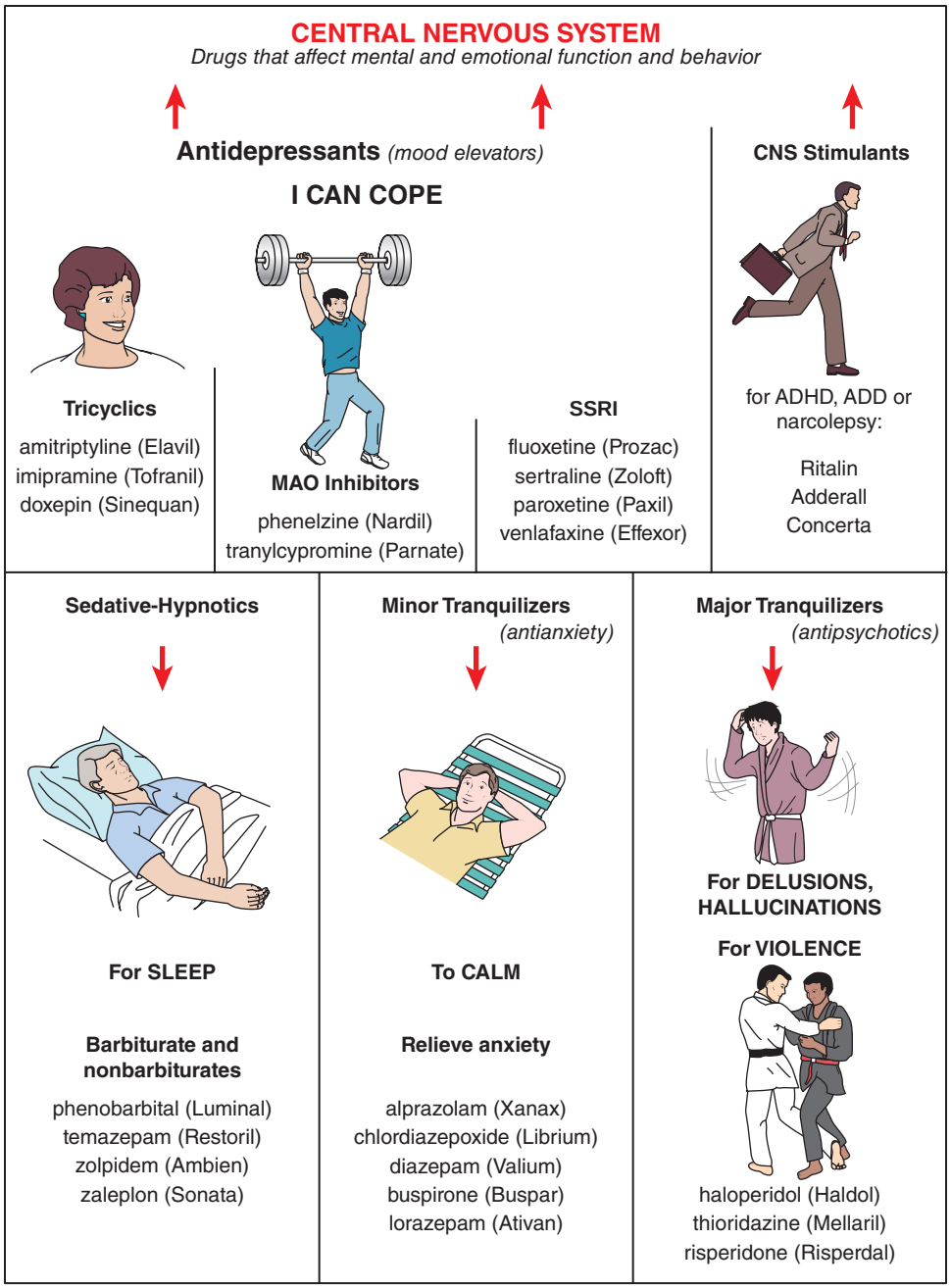


FIGURE 20-3 Summary of psychotropic drugs.

Prolonged alcohol use affects almost all organs of the body. Chronic drinking causes liver damage and pancreatitis. Alcohol irritates the mucosa of the digestive system, leading to gastritis, ulceration, and hemorrhage. Alcohol can also lead to malabsorption of nutrients and malnutrition.

Cardiovascular effects include peripheral vasodilation (producing the flushing and sweating seen with intoxication) and vasoconstriction of the coronary arteries. Alcohol increases the heart rate and, with chronic use, can cause cardiac myopathy, either directly or through metabolic and electrolyte imbalances. Potassium deficiency can cause cardiac arrhythmias.

Studies have shown an inverse association between consumption of wine and coronary heart disease. In another study, it was determined that consumption of one or two drinks per day (five to six days each week) resulted in a reduced risk of MI compared with nondrinkers. All this must be tempered with the deleterious effects of alcohol and the potential for abuse.

Alcohol Poisoning

Symptoms of acute alcoholic poisoning include cold, clammy skin; stupor; slow, noisy respirations; and alcoholic breath.

Mortality associated with acute alcohol poisoning alone is uncommon, but can be an important factor when mixed with recreational drugs.

Treatment includes close observation for:

Respiratory problems. Establish and maintain airway.

Vomiting. Prevent aspirations.

Seizures.

Cerebral edema. Diuretics sometimes required (e.g., mannitol).

Electrolyte imbalance. IV fluids with thiamine, folic, and vitamins added.

Delirium tremens. Treated with IV benzodiazepines.

Fetal alcohol syndrome (FAS) is a teratogenic effect of ethanol. As few as two drinks early in pregnancy has been associated with FAS, although more commonly seen in infants whose mothers consumed four or five drinks per day.

Chronic Alcoholism

Symptoms of chronic alcoholism include:

Frequent falls and accidents

Blackouts and memory loss

Dulling of mental faculties

Neuritis and muscular weakness

Irritability

Tremors

Conjunctivitis

Gastroenteritis

Neglect of personal appearance and responsibilities

Treatment of chronic alcoholism can include an intensive in-house rehabilitation program in treatment facilities. Treatment frequently includes:

Vitamin B (thiamine) IM or PO, multiple vitamins, and folic acid

Low-carbohydrate and high-protein diet to combat hypoglycemia

Elimination of caffeine (in coffee, tea, chocolate, and soft drinks)

Reeducation of the patient, with intensive individual, group, and family counseling, including Alcoholics Anonymous techniques

Sometimes disulfiram (Antabuse) is used, with patient cooperation, as part of *behavior modification*. Patients receive daily doses of disulfiram and are taught to expect a very unpleasant reaction if even a small amount of alcohol is ingested. There is some evidence that drinking frequency is reduced, but minimal evidence that it facilitates abstinence. This treatment is used less frequently because of severe reaction potential and poor compliance.

Disulfiram-alcohol reactions can include:

Flushing and throbbing headache

Nausea and vomiting

Sweating and dyspnea

Palpitation, tachycardia, and hypotension

Vertigo and blurred vision

Anxiety and confusion

PATIENT EDUCATION

Patients taking disulfiram should be instructed regarding:

- Not to take disulfiram within 12 hours of alcohol-containing preparations
- Avoidance of cough syrups, sauces, vinegars, elixirs, and other preparations containing alcohol
- Caution with external applications of liniments, lotions, aftershave, or perfume
- Signs of disulfiram-alcohol reaction
- Reporting to emergency facility if effects do not subside or with severe reaction
- Carrying identification card noting therapy
- Avoiding other medications that may interact with disulfiram (e.g., anticoagulants and phenytoin)

Another treatment for alcoholism includes the use of daily maintenance doses of naltrexone (ReVia), as part of counseling programs, to keep alcoholics sober after detoxification. Naltrexone acts by blocking the pleasurable sensations associated with alcohol, and therefore lessens the desire or craving to drink. Naltrexone reduces the frequency and risk of heavy drinking, but does not necessarily enhance abstinence.

Naltrexone is also used in treatment programs for opiate addicts (e.g., heroin and morphine). After withdrawal from the drugs (opioid free for 7–10 days), it helps to prevent relapses. It acts by robbing the drugs of their pleasurable effects.

CAUTION If naltrexone is given to someone currently dependent on opiates, it can send the addict instantly into severe, life-threatening withdrawal.

Side effects of naltrexone are usually minor and include:

Nausea and joint pains

Liver damage can occur with doses larger than recommended dose of 50 mg daily

Contraindications for use of naltrexone include:

Patients with acute or severe liver or kidney problems.

More recent research has identified a drug that has proven more effective than other drugs for reducing or eliminating problematic alcohol consumption. Topiramate (Topamax) is an anticonvulsant typically used to treat partial seizures. Topamax can be taken while still drinking alcohol, acts by eliminating excess dopamine released by drinking alcohol, and seems to decrease alcohol cravings, especially in patients with severe, chronic alcohol dependence. (See Chapter 22, Anticonvulsants for dosage.)

DRUG ABUSE

Drug abuse can be defined as the use of a drug for other than therapeutic purposes. Drug **addiction** is a common problem (9.4% of the U.S. population) and consists of the combination of all four of the following side effects: tolerance, psychological dependence, physical dependence, and withdrawal reaction with physiological effects. Habituation consists of psychological dependence only. **Chemical dependency** is the term in common usage today to describe a condition in which alcohol or drugs have taken control of an individual's life and affect normal functioning.

Health care practitioners have ready access to many prescription drugs and, therefore, sometimes become involved in illegal misuse of controlled substances. Prescription drugs most often abused by medical personnel are hydrocodone, oxycodone, and the benzodiazepines. Counteractive measures include accurate record keeping of all controlled substances and recognition of the side effects and symptoms associated with drug abuse. (See Chapter 19 for discussion of narcotic analgesics and discussion earlier in this chapter of the anxiolytics.) Report suspected abuse to the person in authority.

This section describes four types of drugs that can be produced illegally: marijuana, cocaine, the hallucinogens (LSD and PCP), and the amphetamines.

Amphetamines

While amphetamines can be produced and prescribed legally, they are also produced in illegal labs. Two examples are methamphetamine ("crystal," "crank," "ice," "meth," "speed") and methylenedioxymethamphetamine (MDMA, "Ecstasy"). At normal dosage levels, administration of an amphetamine may produce tolerance within a few weeks. However, in hypersensitive individuals, psychotic syndrome may occur within 36–48 h of a single large dose of amphetamine. Some emotionally unstable individuals come to depend on the pleasant mental stimulation the drugs offer.

Symptoms of chronic abuse of amphetamines include:

- Emotional lability, irritability
- Anorexia
- Mental impairment, confusion, amnesia, neurotoxicity
- Occupational deterioration, social withdrawal
- Continuous chewing or teeth grinding resulting in trauma or ulcers of the tongue and lip
- Photophobia—frequently wearing sunglasses indoors
- Paranoid syndrome with hallucinations with prolonged use of high doses
- Tooth decay ("meth mouth")

Symptoms of acute toxicity from amphetamines can include:

- Strokes, cardiovascular symptoms including flushing or pallor, palpitation, tachypnea, tremor, extreme fluctuations of pulse and blood pressure, cardiac arrhythmias, chest pain, circulatory collapse
- Dilated pupils, diaphoresis, and hyperpyrexia
- Mental disturbances such as confusion, delirium, belligerence, combativeness, restlessness, paranoia, and suicidal or homicidal tendencies
- Fatigue and depression usually follow CNS stimulation

Treatment: There is no specific antidote for amphetamine overdosage. Treatment of an overdose is symptomatic and includes attention to airway, breathing, circulation, and administration of sedative drugs such as benzodiazepines. General physiological supportive measures include treatment for shock or cardiac irregularities as appropriate. Administration of activated charcoal may help if it can be administered within one to two hours and the substance was ingested. External cooling devices may be used to treat hyperthermia since antipyretics are not effective in this situation.

Abrupt withdrawal of amphetamines may unmask mental problems. Therefore, patients require careful supervision during withdrawal and long-term follow-up may be required since some manifestations (e.g., depression) may persist for prolonged periods.

In an attempt to temper the meth epidemic, the Combat Methamphetamine Epidemic Act of 2005 (which took effect in 2006) banned over-the-counter (OTC) sales of ingredients commonly used to make methamphetamine. Pseudoephedrine (PSE), a popular and effective oral nasal decongestant, was the primary target of the Act. PSE can now only be stored and sold under special conditions ("behind the counter") by pharmacies.

Marijuana

Tetrahydrocannabinol (THC) is the active ingredient in marijuana. Although classified technically as a CNS depressant, it also possesses properties of a euphoriant, sedative, and hallucinogen. Marijuana is currently under investigation as a possible treatment for glaucoma. Marinol (dronabinol—a

synthetic form of THC) is approved for prevention of chemotherapy-induced nausea and vomiting, and is also used as an appetite stimulant in cachexia associated with AIDS or cancer.

The *Cannabis* plant grows over the entire world, especially in tropical areas. Potency varies considerably from place to place and time to time.

THC, the active ingredient released when marijuana is smoked, is fat-soluble and is stored in many fat cells, especially in the brain and reproductive organs. THC metabolizes slowly. A week after a person smokes one marijuana cigarette, 30%–50% of the THC remains in the body, and four to six weeks are required to eliminate all of the THC.

Side effects of marijuana include:

- Short-term memory loss, impaired learning, and slowed intellectual performance
- Perceptual inaccuracies, impaired reflex reaction (dangerous with driving)
- Apathy, lethargy, and decreased motivation
- Increased heart rate, anxiety, and panic attacks
- Lung irritation, chronic cough, frequent respiratory infections
- Reduced testosterone level and sperm count
- Reduced estrogen level, crossing of placental barrier, and transmission through mother's milk; miscarriage and stillbirth possible
- Delayed development of coping mechanisms in children and adolescents

Cocaine

Cocaine is a CNS stimulant and produces euphoria and increased expenditure of energy. The only approved medical use is as a local anesthetic, *applied topically only*, to mucous membranes of the laryngeal, nasal, and oral cavities.

Cocaine is highly addictive, causing dependence after even short-time use. It is abused by intranasal application (sniffing or snorting), intravenous injection, or by inhalation (smoking "crack"). Nasal application can damage mucous membranes and/or the nasal septum. The effects of intravenous use are extremely rapid and dangerous and can be fatal. Smoking causes the most rapid addiction, sometimes after only one use. Cocaine crosses the placental barrier and has resulted in babies who are irritable, jittery, anorexic, and seizure prone. Cocaine use has caused numerous crimes and deaths. Severe depression can be associated with withdrawal, which is a lengthy and difficult process.

Side effects of cocaine, which are serious, include:

- Euphoria, agitation, and excitation
- Hypertension, chest pain, tachycardia, cardiac arrhythmias, or cardiac failure
- Anorexia, nausea, and vomiting

- Tremor and seizures
- Hallucinations, possible psychosis, and possible violent behavior
- Respiratory failure, strokes, and possible death from circulatory collapse

Perforated nasal septum from prolonged nasal use

Hallucinogens

Lysergic acid (LSD) and phencyclidine (PCP), an animal tranquilizer, are hallucinogens. They produce bizarre mental reactions and distortion of physical senses. Hallucinations and delusions are common with confused perceptions of time and space (e.g., the user can walk out of windows because of the impression that he or she can fly). PCP is also an amnesic.

Side effects of hallucinogens include:

- Increased pulse and heart rate and rise in blood pressure and temperature
- Possible "flashbacks" months later
- Panic or paranoia (lack of control)
- Possible psychotic episodes; chronic mental disorders

Possible physical injury to self or others

Dextromethorphan (DXM)

Dextromethorphan (DXM), a semisynthetic morphine derivative, is a safe, effective, nonaddictive, OTC cough suppressant when used appropriately. Unfortunately, DXM (primarily the one found in Robitussin and Coricidin HBP products) is often abused by teens because of its phencyclidine-like euphoric effect, and the abuse of this agent may also be associated with psychosis and mania. The abuse of DXM can cause serious adverse events, such as brain damage, seizure, loss of consciousness, irregular heartbeat, and even death.

Flunitrazepam (Rohypnol)

Flunitrazepam (Rohypnol), an illegal drug of a different type, is a potent benzodiazepine that is approved for use in Central and South America for ethanol withdrawal. Not approved in the United States, it is being used here as a recreational drug (sometimes snorted to offset cocaine withdrawal) and is known on the street as "roofies." It has also acquired the title "date-rape drug" due to its ability to induce amnesia, preventing the victim from recalling specific events while under the influence of the drug.

The Role of the Medical Personnel

The role of the medical personnel in combating drug abuse includes:

Thorough knowledge of psychotropic drugs, action, and side effects

Willingness to participate in education of the patient, the patient's family, and others in the community

Giving competent care to those under the influence of drugs in a nonjudgmental way

Recognizing drug abuse and making appropriate referrals *without exception*

Complete and accurate record keeping of controlled stocks of drugs that could be considered potential drugs of abuse

It is the responsibility of all medical personnel not only to recognize drug abuse, but also to report any observed drug abuse to the proper person in authority. To look the other way not only enables the individual to continue to harm himself or herself but also endangers those in his or her care.

There are many services available to help medical personnel deal with drug abuse problems. Check with your state licensing agency or certification board for information about programs in your area, such as the Impaired Nurse program. Local mental health clinics or psychiatric facilities can also provide assistance and information. Other agencies that can provide information include:

National Institute on Drug Abuse
www.nida.nih.gov

National Institute on Alcohol Abuse and Alcoholism of the National Institutes of Health
ww.niaaa.nih.gov

CASE STUDY – A

Psychotropic Medications

Shauna Lee, a 25-year-old secretary, presents in the physician's office with a history of depression for one month. She complains of crying frequently, loss of appetite, and insomnia. The physician prescribes Tofranil. The patient should be given the following information:

1. She should expect to feel better
- a. In a few days
- b. In a few weeks
- c. One hour after taking medicine
- d. One day after taking medicine

2. The medicine should be taken
- a. Before meals
- b. With meals
- c. In the morning
- d. At bedtime

3. She can expect all of the following side effects EXCEPT
- a. Increased appetite
- b. Improved sleep
- c. Weight loss
- d. Dry mouth

4. She should be told to report any of the following side effects EXCEPT
- a. Dizziness
- b. Palpitations
- c. Blurred vision
- d. Increased thirst

CASE STUDY – B

Psychotropic Medication

Mr. Elzware, a 90-year-old nursing home resident with Alzheimer's, Parkinson's, and enlarged prostate, has been pacing the hall talking loudly in a confused way. He is wringing his hands. The nurse calls the physician's office and requests Haldol "to calm him down." Both the nurse in the nursing home and the medical assistant in the physician's office should be aware of the following facts about Haldol:

1. Haldol is only an appropriate medication for which condition listed below?
   a. Nervousness
   b. Confusion
   c. Uncooperativeness
   d. Combativeness

2. Haldol is appropriate in which of the following conditions?
   a. Seizure disorder
   b. Parkinson's disease
   c. Prostatic hypertrophy
   d. Paranoid psychosis
   e. Depression

3. Agitation can be caused by all of the following EXCEPT
   a. Pain
   b. Constipation
   c. Senility
   d. Urinary retention

4. Geriatric patients receiving antipsychotic medication are at increased risk of having extrapyramidal reactions including all of the following EXCEPT
   a. Dystonia
   b. Diaphoresis
   c. Tardive dyskinesia
   d. Parkinsonian syndrome

5. The following statements are true of tardive dykinesia EXCEPT
   a. Can be permanent
   b. Cured with medicine
   c. Assessed with AIMS test
   d. Manifested by tics

6. Side effects of antipsychotics, like Haldol, can include all of the following EXCEPT
   a. Depression
   b. Weakness
   c. Blurred vision
   d. Increased appetite

CHAPTER REVIEW QUIZ

Match the medication in the first column with the classification in the second column. Classifications may be used more than once.

Medication	Classification
1. _____ Xanax	**a.** Antipsychotic
2. _____ Lithium	**b.** Anxiolytic
3. _____ Risperdal	**c.** Antidepressant
4. _____ Amitriptyline	**d.** CNS stimulant
5. _____ Prozac	**e.** Antimanic
6. _____ Adderall	
7. _____ Buspar	
8. _____ Zyprexa	
9. _____ Ativan	
10. _____ Wellbutrin	

Choose the correct answer.

11. Ritalin and Adderall, prescribed for ADHD, can cause all of the following EXCEPT:
a. Motor tics **c.** Headache
b. Growth spurt **d.** Anorexia

12. Modafinil (Provigil) is approved for the following conditions EXCEPT:
a. Sleep disorders **c.** Obesity
b. Narcolepsy **d.** Sleep apnea

13. SSRIs, for example Zoloft and Effexor, can have the following side effects EXCEPT:
a. Sexual dysfunction **c.** Diarrhea
b. Weight gain **d.** Dizziness

14. Remeron would be used to treat patients with the following conditions EXCEPT:
a. Depression **c.** Anxiety
b. Bipolar disorder **d.** Agitation

15. Signs of lithium toxicity could include all of the following EXCEPT:
a. Hypertension **c.** Tremors
b. Blurred vision **d.** Confusion

16. Benzodiazepines, for example Xanax, used long term, can cause the following side effects EXCEPT:
a. Photosensitivity **c.** Depression
b. Tachycardia **d.** Confusion

17. Which of the following statements is NOT true of tardive dyskinesia caused by antipsychotics?
a. Can be permanent **c.** More in females
b. AIMS test detects **d.** Artane treats

18. Chronic alcoholism can result in all of the following EXCEPT:

a. Memory loss
b. Esophageal varices
c. Bradycardia
d. Neuritis

19. Chronic amphetamine abuse can cause all of the following EXCEPT:

a. Cardiac irregularities
b. Increased appetite
c. Photophobia
d. Psychosis

20. Side effects of frequent marijuana use can include all of the following EXCEPT:

a. Reduced testosterone
b. Slowed reflexes
c. Memory loss
d. Irritability

Go to your StudyWARE™ CD-ROM and have fun learning as you play games and answer case study-related questions to help reinforce key concepts you learned in this chapter.

Go to your Study Guide and complete the review questions for this chapter.

Chapter 21

Musculoskeletal and Anti-inflammatory Drugs

Objectives

Upon completion of this chapter, the learner should be able to

1. Identify commonly used skeletal muscle relaxants
2. Describe the side effects to be expected with muscle relaxants
3. List the drugs that can interact with the muscle relaxants and cause serious potentiation of effect
4. Differentiate among the anti-inflammatory drugs, antirheumatic drugs, and drugs used to treat acute episodes of gout
5. Explain the serious side effects of NSAIDs
6. List drug interactions with NSAIDs
7. Explain appropriate patient education for those taking skeletal muscle relaxants and NSAIDs
8. Describe medications for osteoporosis prevention and treatment
9. Compare and contrast a **COX-2 inhibitor** and other NSAIDs
10. Define the Key Terms and Concepts

Key Terms and Concepts

Anti-inflammatory

COX-2 inhibitor

Gout

Hormone replacement therapy

NSAIDs

Osteoporosis therapy

Skeletal muscle relaxants

Disorders of the musculoskeletal system are rather common. Drugs used to treat such conditions may be classified in two broad categories: skeletal muscle relaxants and nonsteroidal anti-inflammatory drugs (NSAIDs). Corticosteroid therapy for inflammatory conditions is discussed in Chapter 23.

SKELETAL MUSCLE RELAXANTS

Some disorders of the musculoskeletal system can be attributed to structural defects (e.g., ruptured disks) that may require surgical intervention rather than medication. However, many disorders associated with pain, spasm, abnormal

contraction, or impaired mobility do respond to medications classified as **skeletal muscle relaxants**. Acute, painful musculoskeletal conditions, such as backache or neck strain, are treated with a combination of muscle relaxants, rest, physical therapy (e.g., hot or cold packs), and mild analgesics (e.g., NSAIDs). Muscle relaxants are given only on a short-term basis, and, after the acute pain subsides, exercises are usually prescribed by the physician to strengthen the weak muscles.

Most muscle relaxant drugs affect the spinal cord and brain, with no direct effect on skeletal muscle. The resulting action reduces muscle spasm, causes alterations in the perception of pain, and produces a sedative effect, promoting rest and relaxation of the affected part. Drugs used to treat acute, painful musculoskeletal conditions include diazepam (Valium) and methocarbamol (Robaxin).

A different type of muscle relaxant, dantrolene, causes a direct effect on skeletal muscles and is used in the management of spasticity resulting from upper motor neuron disorders such as multiple sclerosis or cerebral palsy. This medication is ineffective for amyotrophic lateral sclerosis (ALS) and is not indicated for the treatment of muscle spasms resulting from rheumatic disorders or musculoskeletal trauma.

Another type of muscle relaxant includes *neuromuscular blocking agents (NMBAs)* such as succinylcholine or rocuronium (Zemuron), used during surgical, endoscopic, or orthopedic procedures. These drugs are potentially very dangerous and can result in respiratory arrest because of the potential to paralyze the major muscle of ventilation, the diaphragm. Neuromuscular blocking agents are administered only by anesthesiologists or specially trained personnel skilled in intubation and cardiopulmonary resuscitation.

NMBAs must be used with caution because of possible serious central nervous system (CNS) problems, such as respiratory arrest and allergic reactions. Antidotes such as neostigmine (Prostigmin) may be indicated. Prostigmin may also be used in the diagnosis and treatment of myasthenia gravis. See Chapter 13 for discussion of cholinergic drugs.

Side effects of skeletal muscle relaxants can include:

- Drowsiness, dizziness, or dry mouth
- Weakness, tremor, ataxia
- Headache
- Confusion and nervousness
- Slurred speech
- Blurred vision
- Hypotension
- Gastrointestinal (GI) symptoms, including nausea, vomiting, diarrhea, or constipation
- Urinary problems, including enuresis, frequency, or retention
- Hypersensitivity reactions including liver toxicity with dantrolene and tizanidine
- Respiratory depression

Contraindications with skeletal muscle relaxants and:

- Hypersensitivity to the muscle relaxant
- Pregnancy or lactation

Caution with skeletal muscle relaxants and:

- History of drug abuse
- Impaired kidney function
- Liver disorders
- Blood dyscrasias
- Chronic obstructive pulmonary disease (COPD)
- Cardiac disorders
- Older adults
- Abrupt discontinuation
- Closed-angle glaucoma

Interactions with potentiation of effect with skeletal muscle relaxants and:

- Alcohol
- Analgesics
- Psychotropic medications
- Antihistamines

The MedlinePlus website www.nlm.nih.gov/medlineplus/backpain.html is a good resource for patient education and written materials on back pain.

See Table 21-1 for a summary of the skeletal muscle relaxants.

Skeletal Muscle Relaxants

Patients taking skeletal muscle relaxants should be instructed regarding:

- Potential side effects (e.g., drowsiness, dizziness, weakness, tremor, blurred vision, hypotension, respiratory distress, or GI disorders); care with driving
- Avoidance of other CNS depressants at the same time (e.g., tranquilizers, antihistamines, or alcohol), which can cause serious CNS depression, and care with analgesics, only as prescribed by a physician
- Importance of following the physician's orders regarding rest and physical therapy (e.g., heat and firm mattress or bed board with back problems) and exercises as prescribed (after the acute pain subsides) to strengthen the weak muscles
- The acronym RICE (rest, ice, compression [elastic bandage], elevation) represents appropriate care initially for musculoskeletal injuries to extremities. A recent addition has been the focus on Prevention of the injury; some modify the acronym to PRICE.
- Taking the medication only as long as absolutely necessary and observing caution regarding prolonged use, which could lead to physical or psychological dependence and withdrawal symptoms (e.g., seizures from abrupt Valium withdrawal after prolonged use)

Table 21-1 Skeletal Muscle Relaxants

GENERIC NAME	TRADE NAME	DOSAGE	COMMENTS
baclofen	Lioresal	PO 10–20 mg 3–4 × per day; intrathecal 300–800 mcg	For spasticity associated with spinal cord injury or spinal cord diseases
carisoprodol	Soma	PO 250–350 mg 3–4 × per day	Caution with asthma; watch for abuse potential
cyclobenzaprine	Flexeril	PO 5 –10 mg 3 × per day	Strongly anticholinergic side effects
dantrolene	Dantrium	PO 25–100 mg 2–4 × per day (titrate to lowest effective dose)	For multiple sclerosis and cerebral palsy, not for trauma or rheumatic disorders
methocarbamol	Robaxin	4–8 g PO daily div. doses also IM, IV	For acute painful musculoskeletal conditions
tizanidine	Zanaflex	PO 2–8 mg 1–3 × per day (6–8 h intervals)	For increased muscle tone associated w/spasticity, e.g., multiple sclerosis or spinal cord trauma

Note: Representative sample; other products are available.

ANTI-INFLAMMATORY DRUGS

Anti-inflammatory drugs are used to treat disorders in which the musculoskeletal system is not functioning properly due to inflammation. Such conditions as arthritis, bursitis, spondylitis, gout, and muscle strains and sprains can cause swelling, redness, heat, pain, and limited mobility. Analgesics and corticosteroids are used at times for acute stages of these disorders and are discussed in Chapters 19 and 23. The corticosteroids are not used for extended periods of time because of serious side effects. However, nonsteroidal anti-inflammatory drugs (NSAIDs) are frequently given for lengthy time periods in maintenance doses as low as possible for effectiveness.

Nonsteroidal Anti-inflammatory Drugs

NSAIDs inhibit synthesis of prostaglandins, substances responsible for producing much of the inflammation and pain of rheumatic conditions, sprains, and menstrual cramps. No cure has been found for rheumatic disorders, but many medications are used to alleviate the pain and crippling effects. Because of lower metabolic rates and other complications, older adults are particularly susceptible to side effects from NSAIDs (e.g., "silent bleeding") and should be cautioned to report any untoward signs or symptoms to their doctor without delay.

The salicylates (e.g., aspirin) are the oldest drug in this category with analgesic, anti-inflammatory, and antipyretic effects (see Chapter 19). Many nonsalicylate NSAIDs are on the market, and some are tolerated better than aspirin by some patients, especially as short-term analgesics. However, with large doses and/or long term, they all share many of the same side effects and interactions to a greater or lesser degree. Patients on

prolonged therapy with any of the NSAIDs should be monitored carefully. Older adults or debilitated patients do not tolerate ulceration or bleeding (which can be "silent") as well as other individuals, and most reports of fatal GI events are in these populations. If chronic anti-inflammatory therapy must be continued despite GI ulceration, several options for the patient are available. Ideally after the ulcer heals, the patient could resume the NSAID with either misoprostol or a proton pump inhibitor with close clinical monitoring for ulcer recurrence. Combination products are available, for example Arthrotec, which combines diclofenac (Voltaren) with misoprostol (Cytotec) to protect the gastric mucosa. (See Chapter 16, Treatment of Ulcers.)

The FDA has issued a warning regarding over-the-counter (OTC) nonselective NSAIDs: They should be used in strict accordance with label directions. Self-treatment with an OTC NSAID should not exceed ten days, unless directed by a physician.

COX-2 Inhibitor

Celecoxib (Celebrex) is an NSAID that exhibits anti-inflammatory, analgesic, and antipyretic activities by *selectively* inhibiting cyclooxygenase-2 (COX-2) prostaglandin synthesis. However, it does not inhibit COX-1 and, therefore, does not inhibit platelet aggregation (clotting) or inhibit the production of mucosal-protective prostaglandins. Consequently, it does not pose the bleeding risks of the other *nonselective* NSAIDs described previously. Due to the specific action inhibiting COX-2 prostaglandin synthesis, Celebrex has the *potential* to cause fewer gastric problems and pose less risk of GI bleeding unless used concurrently with aspirin.

Earlier studies have suggested that there is a "good" and a "bad" prostaglandin as far as the heart is concerned. Suppressing both types in the way nonselective NSAIDs do would theoretically help the heart. The selective COX-2s shut down only the "good" prostaglandin, raising the risk of high blood pressure, atherosclerosis, and clotting. However, both traditional NSAIDs and the COX-2s can increase the risk of adverse events in patients who have a history of or who are at high risk for cardiovascular disease. Evidence is more compelling for the COX-2s, but data does indicate a possible risk with traditional NSAIDS. Until studies defining the cardiovascular safety of these agents are complete, the benefits and risks in terms of pain relief and cardiovascular and GI safety must be weighed carefully for each individual.

The FDA has posted extensive NSAID (and acetaminophen) medication information at http://www.fda.gov/cder/drug/analgesics/default.htm. The health care practitioner has the responsibility to stay informed of the latest developments in this area.

Side effects of NSAIDs frequently include:

- GI ulceration and bleeding—may not be preceded by warning signs or symptoms
- Epigastric pain, nausea, heartburn, and gastroesophageal reflux disease (GERD)

Myocardial infarction, thromboembolism, stroke, hypertension, heart failure

Fluid retention, peripheral edema

Constipation

Tinnitus and hearing loss

Headache or dizziness

Visual disturbances

Hematuria and albuminuria (albumin in urine)

! Rash, hypersensitivity reactions, bronchospasm (especially with aspirin)

! Blood dyscrasias, especially prolonged bleeding time; anemia

Liver toxicity

Contraindications or extreme caution with NSAIDs applies to:

Asthma—may manifest aspirin sensitivity as bronchospasm

Cardiovascular disorders (e.g., hypertension, heart failure (HF))

Kidney disease

Liver dysfunction

History of GI ulcer or inflammatory bowel disease

Blood dyscrasias, especially clotting disorders or anemia

Children with viral infections (danger of Reye's syndrome with salicylates)

GERD

Older adults, pregnancy, lactation

Those with aspirin and NSAID hypersensitivity

Those with sulfonamide hypersensitivity should not take Celebrex

These medications should be given with meals or milk to reduce GI side effects. Enteric-coated, timed-release capsules or buffered aspirin are sometimes also recommended to reduce gastric irritation.

Interactions of NSAIDs (especially salicylates) are many, but the most important clinically occur with:

Alcohol, which potentiates possibility of GI bleeding

Anticoagulants, which potentiate possibility of bleeding (also true of vitamin E)

Corticosteroids, which increase chance of GI effects with prolonged administration of NSAIDs

Aspirin + NSAIDs—increased adverse GI effects (diminish GI risk-reducing effects of COX-2s; decrease antiplatelet effects of aspirin)

Antihypertensives (attenuated response)

Lithium (decreased clearance)

Methotrexate, with potentiation and increased risk of methotrexate toxicity

Uricosurics (probenecid or sulfinpyrazone), whose action is antagonized by salicylates

Gout Medications

Gout is a metabolic disorder characterized by accumulation of uric acid crystals in various joints, especially the big toe, ankle, knee, and elbow, with resultant pain and swelling. Colchicine is a specific drug that is used to *relieve inflammation in acute gouty arthritis.* It is also used in the chronic management of gout.

Side effects of gout medications can include:

Rash

GI upset, diarrhea

Blood disorders

Always encourage large fluid intake to facilitate excretion of uric acid crystals. Advise patients to avoid alcohol (increases risk of adverse GI effects and increases serum urate concentrations).

Other medications for chronic gout are discussed in Chapter 15. They act in a different way and are not effective against inflammation in acute cases of gout or gouty arthritis.

See Table 21-2 for a summary of the NSAIDs and gout medication.

PATIENT EDUCATION

Patients taking NSAIDs should be instructed regarding:

- Administration with food to reduce gastric irritation
- Caution with dosage (follow physician's directions carefully regarding amount of drug to reduce chance of overdose)
- Discontinuing drug and reporting to physician any sign of abnormal bleeding (gums, stool, urine, and bruising), epigastric pain or nausea, ringing in the ears or hearing loss, visual disturbances, weight gain or edema, and skin rash
- Avoiding taking any other drugs, either prescribed or OTC, without checking first with a physician or pharmacist regarding possible interactions and duplication of medication
- When taking gout medications (e.g., colchicine), always taking large amounts of fluids; avoiding alcohol
- Avoiding taking large amounts of aspirin or other NSAIDs with kidney, liver, or heart disease or with history of GI ulcer (with these conditions, take only under medical supervision). Patients with asthma may manifest sensitivity to aspirin and other NSAIDs.
- The danger that GI ulceration and bleeding can occur without previous warning signs or symptoms
- Discontinuing NSAIDs 7–14 days (or as directed) before elective surgery or dental procedures to reduce the risk of serious bleeding
- Not taking Celebrex if allergic to sulfa

Table 21-2 Nonsteroidal Anti-inflammatory Drugs and Gout Medication

GENERIC NAME	TRADE NAME	DOSAGE
Nonselective (Traditional) NSAIDs		
diclofenac	Voltaren DR	PO 150–225 mg daily in div. doses
	Voltaren XR	PO 100 mg 1–2 × per day
ibuprofen	Motrin, Advil (OTC)	200–800 mg 4 × per day
indomethacin	Indocin	PO, R up to 200 mg daily in div. doses
	Indocin SR	PO 75 mg 1–2 × per day
ketorolac	(Toradol)*	PO 20 mg × 1, then 10 mg q4–6 h (5 days max) IM/IV 15–30 mg q6 h (5 days max)
naproxen	Naprosyn, Anaprox, Aleve (OTC)	220–550 mg BID (q12 h)
oxaprozin	Daypro	PO 600–1,200 mg once daily
Partially Selective NSAIDs		
etodolac	(Lodine)*	PO 600–1,200 mg daily in div. doses
meloxicam	Mobic	PO 7.5–15 mg daily
nabumetone	(Relafen)*	PO 1,000–2,000 mg daily
Selective COX-2 Inhibitor		
celecoxib	Celebrex	PO 100–200 mg BID
Combinations		
diclofenac/misoprostol	Arthrotec 50, 75	PO 50 mg 3–4 × per day; 75 mg BID
Gout Medication		
colchicine		PO 0.6–1.8 mg daily in div. doses

Note: Other NSAIDs are available. This is a representative list.

*Brand name no longer marketed, but name is still commonly used.

OSTEOPOROSIS THERAPY

Osteoporosis (porous bone) is a disease characterized by low bone mass and deterioration of bone tissue, leading to bone fragility and increased susceptibility to fracture, especially of the hip, spine, and wrist. It most commonly affects older populations, primarily postmenopausal women. **Osteoporosis therapy** includes calcium and vitamin D supplementation and several prescription medications currently approved for the prevention and/or treatment of osteoporosis.

Hormones

Estrogens

As discussed in Chapter 24, **hormone replacement therapy** (HRT)—estrogen with or without progestin—is recommended for postmenopausal osteoporosis prevention (secondary to estrogen deficiency) *only* when unable to take other agents, and benefits outweigh risks. The FDA recommends prescribing the lowest possible dose for the shortest period of time. If started soon after menopause, estrogen prevents the accelerated phase of bone loss that occurs in the first five years after the onset of menopause.

Selective Estrogen-Receptor Modifiers (SERMs)

Raloxifene (Evista) is a selective estrogen receptor *modifier* with estrogen agonist activity on bone and lipids and estrogen antagonist activity on breast and uterine tissue. These properties result in increased bone mineral density and reduced fracture risk without promoting breast or endometrial cancer.

The incidence of vaginal bleeding and breast tenderness is lower with raloxifene than with HRT. However, in contrast to HRT, raloxifene can cause hot flashes and muscle cramps in the legs. Raloxifene is contraindicated in pregnancy and women with a history of thromboembolic disorders.

Calcitonin-Salmon

A synthetic form of the hormone calcitonin is available as a nasal spray (Miacalcin) or as a subcutaneous injection for the treatment of postmenopausal osteoporosis in women who are more than five years past menopause. It increases spinal bone density and provides an analgesic effect in acute vertebral fractures. Calcitonin is reserved for women who refuse or cannot tolerate HRT or in whom HRT is contraindicated. Local nasal effects (e.g., irritation, redness, rhinitis, and epistaxis [nose bleed]) are the most common adverse effects from the nasal spray.

Store the unopened bottle of calcitonin in the refrigerator. Once the pump has been activated, store at room temperature in an upright position. Discard all unrefrigerated bottles after 30 days.

Parathyroid Hormone

Teriparatide (Forteo) is an injectable form of parathyroid hormone approved for postmenopausal women and men with osteoporosis who are at a high risk for having a fracture. It increases GI calcium absorption and renal tubular reabsorption of calcium, increasing bone mineral density, bone mass, and strength. Common adverse effects include nausea, hypotension, dizziness, and leg cramps.

Bisphosphonates

Bisphosphonates are nonhormonal agents that act directly to inhibit bone reabsorption, thereby increasing bone mineral density at the spine and hip, as well as decreasing the incidence of first and future fractures. Alendronate (Fosamax), ibandronate (Boniva), and risedronate (Actonel) have been approved for both the prevention and treatment of osteoporosis and are considered first-line therapy. The bisphosphonates are also indicated for management of Paget's disease of the bone, a chronic disorder characterized by fractures, skeletal abnormalities, and significant bone pain.

Side effects of bisphosphonates, rare and mild, can include:

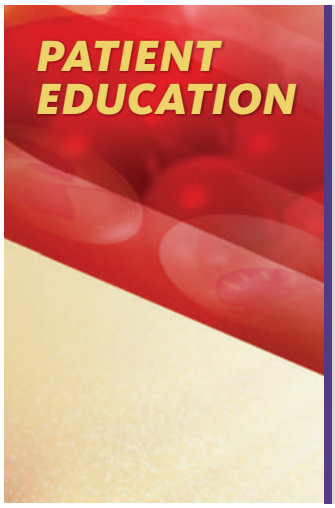
- GI distress (nausea, dyspepsia, esophagitis)
- Abdominal and chest pain

Caution with bisphosphonates and active upper GI problems, for example, dysphagia, GERD, gastritis, or ulcers

Contraindications and cautions for bisphosphonates with:

- Hypocalcemia
- Renal failure
- Inability to sit upright for 30-60 min after taking drug

See Table 21-3 for a summary of osteoporosis therapy.



Patients taking bisphosphonates should be instructed regarding:

- The importance of taking the medicine with a full glass of water (6–8 oz) at least 30 min before the first food, beverage, or medication of the day
- Not lying down for at least 30–60 min to prevent reflux and avoid esophageal irritation
- Taking supplemental calcium and vitamin D if dietary intake is inadequate
- Weight-bearing exercises
- Modification of cigarette smoking and alcohol and caffeine consumption, if these factors exist

Table 21-3 **Agents for Osteoporosis Prevention and Therapy**

GENERIC NAME	TRADE NAME	PREVENTION DOSE	TREATMENT DOSE	COMMENTS
Hormones				
Selective Estrogen Receptor Modifier				
raloxifene	Evista	PO 60 mg daily	PO 60 mg daily	Can be given without regard to meals
Calcitonin-Salmon				
calcitonin-salmon	Miacalcin	Not indicated	Intranasally 200 units (one activation) daily	Alternate nares
Parathyroid Hormone				
teriparatide	Forteo	Not indicated	Subcu 20 mcg daily	For up to 2 years
Bisphosphonates				
alendronate	Fosamax	PO 5 mg daily ac	PO 10 mg daily ac	See Patient Education
		PO 35 mg qwk ac	PO 70 mg q wk ac	
			PO 40 mg daily ac × 6 mo	For Paget's disease
ibandronate	Boniva	PO 2.5 mg daily ac	PO 2.5 mg daily ac	See Patient Education
		PO 150 mg qmo	PO 150 mg qmo	
risedronate	Actonel	PO 5 mg daily ac	PO 5 mg daily ac	See Patient Education
		PO 35 mg qwk ac	PO 35 mg q wk ac	
		PO 150 mg qmo	PO 150 mg q mo	
			PO 30 mg daily ac × 2 mo	For Paget's disease

Note: Other dosing regimens are available.

CASE STUDY – A

Musculo-skeletal Drugs

David Sanchez, a 35-year-old construction practitioner, is diagnosed with muscle strain of the lumbar spine. Valium 5 mg q4h PRN is prescribed. His discharge instructions should contain the following information.

1. Muscle relaxants are only appropriate for which condition?
- a. Chronic pain
- b. Muscle weakness
- c. As prophylactic
- d. Acute muscle spasm

2. Muscle relaxants are contraindicated in some cases. Which one below would be appropriate for use?
- a. Muscular dystrophy
- b. Myasthenia gravis
- c. Acute back pain
- d. For children

3. Caution must be used with all of the conditions below EXCEPT
- a. COPD
- b. Diabetes
- c. Nephritis
- d. Cirrhosis

4. All of the following side effects are possible EXCEPT
- a. Dizziness
- b. Insomnia
- c. Urinary retention
- d. Blurred vision

5. Interactions with possible potentiation of effect can occur with all of the following EXCEPT
- a. Alcohol
- b. Analgesics
- c. Antihistamines
- d. Antacids

CASE STUDY – B

Anti-inflammatory Drugs

Rita Robbins, age 65, comes into the physician's office with complaints of knee pain. The physician prescribes naproxen 500 mg q12h for arthritis. She should be given the following information.

1. How should the drug be administered?
- a. Before meals
- b. With fruit juice
- c. With meals
- d. With alcohol

2. Which of the following statements is true of NSAIDs?
- a. Rapidly effective
- b. Cure arthritis
- c. Contraindicated with older adults
- d. May be used long term

3. Side effects of NSAIDs can include all of the following EXCEPT
- a. Gastric bleeding
- b. Blurred vision
- c. Anxiety
- d. Heartburn

4. NSAIDs are contraindicated in all of the following conditions EXCEPT
- a. COPD
- b. NSAID ulcer
- c. Hypersensitivity to NSAID
- d. Perioperative pain in the setting of CABG surgery

5. There are possible serious side effects from interactions of NSAIDs with all of the following EXCEPT
- a. Alcohol
- b. Antacids
- c. Anticoagulants
- d. Clopidogrel (Plavix)

CHAPTER REVIEW QUIZ

Match the medication in the first column with the appropriate classification in the second column. Classifications may be used more than once.

Medication	Classifications
1. _____ Dantrolene	**a.** Combination NSAID
2. _____ Arthrotec	**b.** Osteoporosis therapy
3. _____ Mobic	**c.** Muscle relaxant for multiple sclerosis
4. _____ Colchicine	**d.** Muscle relaxant for acute muscle strain
5. _____ Actonel	**e.** Partially selective NSAID
6. _____ Voltaren	**f.** Nonselective NSAID
7. _____ Flexeril	**g.** Gout medication
8. _____ Nabumetone	**h.** COX-2 inhibitor
9. _____ Evista	
10. _____ Celebrex	

Choose the correct answer.

11. Which muscle relaxant would NOT be used to treat acute muscle strain?
    a. Valium
    b. Succinylcholine
    c. Soma
    d. Robaxin
12. The following statements are true for skeletal muscle relaxants EXCEPT:
    a. Affect the brain
    b. Alter pain perception
    c. Reduce spasm
    d. Used long term
13. Which is not a side effect of skeletal muscle relaxants?
    a. Dry mouth
    b. Hypertension
    c. Confusion
    d. Tremor
14. Those at greater risk of adverse effects from NSAIDs include individuals with the following EXCEPT:
    a. Gallbladder disease
    b. Children with flu
    c. Renal dysfunction
    d. Clotting disorders

15. Side effects of nonselective NSAIDs can include all of the following EXCEPT:
- **a.** Liver toxicity
- **b.** Faster clotting
- **c.** Tinnitus
- **d.** Hematuria

16. Which is NOT true of colchicine therapy?
- **a.** Gout prophylaxis
- **b.** Fluids encouraged
- **c.** Take ac
- **d.** For gouty arthritis

17. Which is NOT true of Evista?
- **a.** Can cause hot flashes
- **b.** Can cause breast cancer
- **c.** Increases bone density
- **d.** Estrogen antagonist

18. Which is NOT true of Miacalcin?
- **a.** Increases bone density
- **b.** Can cause epistaxis
- **c.** Estrogen modifier
- **d.** Nasal spray

19. Which is NOT true of Fosamax?
- **a.** Osteoporosis treatment
- **b.** Take with juice
- **c.** Take ac
- **d.** Remain upright after taking

20. Celebrex is contraindicated for those individuals allergic to which of the following?
- **a.** Penicillin
- **b.** Aspirin
- **c.** Sulfa
- **d.** Quinolones

Go to your StudyWARE™ CD-ROM and have fun learning as you play games and answer case study-related questions to help reinforce key concepts you learned in this chapter.

Go to your Study Guide and complete the review questions for this chapter.

Chapter 22

Anticonvulsants, Antiparkinsonian Drugs, and Agents for Alzheimer's Disease

Objectives

Upon completion of this chapter, the learner should be able to

1. Compare and contrast different types of seizures
2. List the medications used for each type of epilepsy and common side effects
3. List the drugs used for parkinsonism and common side effects
4. Describe the patient education appropriate for those receiving anticonvulsants and antiparkinsonian drugs
5. Describe drug therapy for the treatment of restless legs syndrome
6. Describe the drugs for treatment of Alzheimer's disease
7. Define the Key Terms and Concepts

Key Terms and Concepts

Absence epilepsy
Alzheimer's disease
Anticholinergics
Anticonvulsants
Antiparkinsonian drugs
Epilepsy
Febrile seizures
Mixed seizure
Parkinson's disease
Partial seizures
Psychomotor epilepsy
Restless legs syndrome (RLS)
Status epilepticus
Temporal lobe seizures
Tonic-clonic
Unilateral seizures

ANTICONVULSANTS

Seizures are brief, abnormal neuronal discharges in the brain that occur repeatedly and without warning. **Anticonvulsants** are used to reduce the number and/or severity of seizures in patients with epilepsy. **Epilepsy**, which is the recurrence of unprovoked seizures, is characterized by sudden attacks of altered consciousness, motor activity, or sensory impairment. Treatment is based on type, severity, and cause of seizures. Although less than one half of epileptic seizures have an identifiable cause, seizures may sometimes be associated with cerebrovascular disease, cerebral trauma, intracranial infection or fever, brain tumor, intoxication, or chemical imbalance. Sometimes

the underlying disorder can be corrected, for example, fever, hypoglycemia, or electrolyte imbalance, and anticonvulsive medicine is not indicated.

The International Classification of Epilepsies and Epileptic Syndromes currently classifies seizure disorders into three main categories:

1. *Generalized* seizures—bilaterally symmetrical and without local onset; further classified as convulsive (tonic, clonic, and tonic-clonic) or nonconvulsive (absence, myoclonic, atonic)
2. *Partial* seizures (also known as temporal lobe or psychomotor seizures)—onset limited to one cerebral hemisphere and involve no loss of consciousness (simple) or loss of consciousness (complex symptomatology)
3. *Atypical or Unclassified*—insufficient data to classify

Treatment failure can be the result of inappropriate selection of an anticonvulsant for the specific type of seizure. For example, carbamazepine is used to treat many types of seizures; however it is well known to aggravate myoclonic and absence seizures. Therefore it is important to understand the difference between the various seizure types.

Generalized Seizures

Generalized seizures include tonic-clonic (formerly *grand mal*) and *absence (formerly petit mal)* seizures and occur in about 40% of patients with epilepsy. They are bilaterally symmetrical and without local onset. Tonic pertains to tension or contraction, particularly muscle contraction.

Tonic-clonic seizures are characterized by an abrupt loss of consciousness, falling, with tonic extension of trunk and extremities (tonic phase), followed by synchronous, contractions of the muscles (clonic phase). The attack usually lasts two to five minutes, and urinary and fecal incontinence may occur. During the recovery period, patients are confused and sleepy and may complain of a headache.

Initial treatment consists *only* of preventing injury by removing any objects that could cause trauma, cushioning the head and turning it to the side, and loosening tight clothing, especially collars and belts. Do not try to open the mouth or force anything between the teeth.

If seizures are so frequent that the patient does not regain consciousness (by more than 30 minutes) between seizures, the condition is known as **status epilepticus** and is considered to be a true neurologic emergency. The treatment of choice is IV lorazepam (Ativan) administered slowly. Simultaneous loading with IV phenytoin or fosphenytoin is also recommended.

Absence epilepsy, previously called petit mal, is so called because of the absence of convulsions. It is characterized by a 10–20 second loss of consciousness with no falling and usually occurs initially in children. Absence seizures are not associated with post-recovery drowsiness.

Febrile seizures are the most common childhood seizure disorder, occurring in approximately 3% of children ages 6 months to 6 years. Its presence may signify a serious underlying acute infection such as sepsis or bacterial meningitis. Most febrile seizures are "simple"—single, brief (less than 15 minutes in duration), and generalized.

Partial Seizures

Partial seizures (also known as **psychomotor epilepsy** or **temporal lobe seizures**) account for up to 60% of new cases of epilepsy. They are caused by a lesion in the temporal lobe of the brain and limited to one cerebral hemisphere. Most seizures last from 10 seconds to 5 minutes. Complex symptoms can include confusion, impaired understanding and judgment, staggering, purposeless movements, bizarre behavior, and unintelligible sounds, but no convulsions. A partial seizure may be preceded by a subjective but recognizable sensation (an aura) that a seizure is going to occur.

Unilateral seizures affect only one side of the body. Some patients may have **mixed seizure** patterns combining more than one type. It is important to observe and report type and length of seizures and general responsiveness to medications.

DRUG THERAPY FOR GENERALIZED AND PARTIAL SEIZURES

First Generation Anticonvulsants

Prophylactic treatment of *generalized and partial seizures when indicated* should be started with a single drug such as valproate, lamotrigine, levetiracetam, carbamazepine, oxcarbamazepine, or phenytoin. The dosage should be titrated to achieve seizure control or until the maximally tolerated dose is reached. The aim of therapy is to prevent seizures without oversedation, and the dosage is adjusted according to individual patient response and serum drug levels when available.

Side effects of phenytoin, which frequently decrease with continued treatment, can include:

- Sedation, ataxia, dizziness, and headache
- Blurred vision, nystagmus, and diplopia
- Gingivitis (inflamed gums)
- GI distress, including nausea, vomiting, anorexia, constipation, or diarrhea
- Rash and dermatitis, Stevens-Johnson syndrome (a severe inflammatory disease affecting children and young adults), lupus-like symptoms

Megaloblastic anemia (treated with folic acid)

Osteomalacia (bone softening, treated with vitamin D)

Contraindications or extreme caution with phenytoin applies to:

Kidney or liver disease

Diabetes

Heart failure, bradycardia, heart block, and hypotension

Pregnancy and lactation

Hematological disease

Abrupt discontinuation

Note The FDA has alerted healthcare professionals of an increased risk of suicidal ideation and behavior in patients receiving anticonvulsants to treat epilepsy, psychiatric disorders, or other conditions (e.g., migraine, neuropathic pain). All patients beginning treatment with anticonvulsants or currently receiving such treatment should be closely monitored for emerging or worsening suicidal thoughts/behavior or depression.

There are many drug **interactions** and food/nutrient interactions with phenytoin including:

Cimetidine, isoniazid, salicylates, SSRI's, sulfonamides, topiramate, and trimethoprim may increase levels of phenytoin

Phenytoin may decrease the effectiveness of "azole" antifungals, carbamazepine, estrogens, oral contraceptives, protease inhibitors, quinidine, valproic acid, and theophylline

Another medicine sometimes used for partial, generalized, or mixed seizures is carbamazepine (Tegretol). It has the advantage of minimal sedation and cognitive adverse effects.

Side effects of carbamazepine can include:

Ataxia, syncope (fainting), visual difficulties

! Cardiac, hematological, kidney, liver, and pancreas complications

Rash, Stevens-Johnson syndrome (more likely to occur in Asian patients who test positive for HLA B1502 allele, FDA recommends testing patients of Asian descent prior to starting therapy)

Multiple **interactions** of carbamazepine with:

Phenytoin, phenobarbital, and valproic acid which decrease levels of carbamazepine

Calcium channel blockers, cimetidine, erythromycin, itraconazole, and isoniazid which increase levels of carbamazepine

Grapefruit juice potentiates action and can increase risk of serious adverse effects. Do *not* take grapefruit juice with carbamazepine.

Valproic acid (Depakene, Depakote) is considered a "broad-spectrum" anticonvulsant, useful for the management of many seizure types, including generalized tonic-clonic, absence, and myoclonic seizures.

Side effects of valproic acid include:

! Weight gain, dyspepsia

! Alopecia, rash, tremor

! Hepatotoxicity, pancreatitis, blood dyscrasias

Multiple **interactions** of valproic acid with:

Carbamazepine, phenytoin, phenobarbital, and topiramate which decrease valproic acid levels

Amitriptyline and nortriptyline which increase valproic acid levels

DRUG THERAPY FOR FEBRILE SEIZURES

Routine treatment of febrile seizures involves searching for the cause of the fever and taking measures to control the fever (e.g., with the use of antipyretics). Most children with febrile seizures do not require anticonvulsant drugs. Those that do may be treated with rectal diazepam gel if the seizure lasts longer than 5 minutes. The American Academy of Pediatrics Subcommittee on Febrile Seizures does not currently recommend continuous or intermittent antiepileptic drug (AED) therapy for children with one or more simple febrile seizures. A decision to use prophylactic AEDs for children with complex febrile seizures should be made on an individual basis taking into account underlying risk factors for recurrence.

DRUG THERAPY FOR ABSENCE SEIZURES

The drug of choice for management of absence epilepsy is often ethosuximide (Zarontin), which is effective only for this type of epilepsy and lacks the idiosyncratic hepatotoxicity of valproic acid. Other drugs sometimes used in the treatment of absence seizures, when Zarontin is ineffective, include clonazepam (Klonopin), valproic acid (Depakene), and lamotrigine (Lamictal).

Side effects of the drugs for absence epilepsy can include:

- Sedation, dizziness, headaches, aggression or irritability
- Gastrointestinal (GI) distress including anorexia, nausea, vomiting, diarrhea

Rash, leukopenia

Extreme caution with drugs for absence epilepsy applies to:

Hepatic or renal disease

Pregnancy and lactation

Pancreatitis (with valproate)

Contraindications with drugs for absence epilepsy include:

Medications should never be stopped abruptly

Interactions with ethosuximide include:

Carbamazepine, phenytoin, primidone, phenobarbital, valproic acid, and anti-retroviral protease inhibitors

Alternative formulations of traditional anticonvulsants have been developed, for example, carbamazepine (Tegretol XR—extended release), diazepam (Diastat—rectal), fosphenytoin (Cerebyx—IM/IV), valproate (Depacon—IV; Depakote ER—extended release). The primary advantage of these newer formulations may include improved adherence (fewer doses and/or better tolerability) or the availability of an injectable formulation (e.g., Depacon).

Second-Generation Anticonvulsants

Second-generation anticonvulsants include gabapentin (Neurontin), lamotrigine (Lamictal), levetiracetam (Keppra), and topiramate (Topamax), which are used for adjuvant treatment of partial (psychomotor) and generalized seizures. They are not currently considered superior in efficacy to the first-generation

anticonvulsants in terms of seizure control. However, these agents usually do not require drug level monitoring, have fewer adverse effects (including effects on cognition), fewer drug interactions than first-generation anticonvulsants and may improve adherence with once or twice daily dosing. All agents require a *slow titration period* to avoid central nervous system (CNS) adverse effects. Second-generation anticonvulsants should be used with caution in pregnancy and lactation and should not be abruptly discontinued.

See Table 22-1 for a summary of the anticonvulsants. (Refer to Chapter 19 for a discussion on phenobarbital, and Chapter 20 for a discussion on diazepam.)

Table 22-1 Anticonvulsants

GENERIC NAME	TRADE NAME	DOSAGE	COMMENTS
First Generation			
carbamazepine	Tegretol	PO 400 mg–1.2 g daily in 3–4 div. doses, susp, tabs	For partial, or generalized seizures
	Tegretol XR	PO 200–600 mg BID	Extended release; do not crush/chew
clonazepam	Klonopin	PO, dose varies	For absence and myoclonic seizures
fosphenytoin	Cerebyx	IV, IM, varies	Caution—do not confuse with Celexa (antidepressant) or Celebrex (for arthritis)
phenytoin	Dilantin	PO 200–1,200 mg daily in div. doses, IV varies, no IM	For generalized or partial seizures and status epilepticus
ethosuximide	Zarontin	PO 250 mg–1.5 g daily in div. doses	For absence seizures only
valproic acid	Depakene[a], Depakote DR[b]	PO 15–60 mg per kg daily, 2–3 div. doses	For absence, partial, and generalized seizures
	Depakote ER[c]	8–20% higher than daily dose of Depakote	One dose per day; do not crush/chew
	Depacon	IV 15–60 mg per kg daily, div. doses	
Second Generation			
gabapentin	Neurontin	PO 300–600 mg TID	No drug interactions Decrease dose with renal dysfunction
lamotrigine	Lamictal	PO 100–300 mg BID	Interactions with antiepileptic drugs mostly, monitor liver function Caution—do not confuse with Lamisil (antifungal)
levetiracetam	Keppra	PO 500–3,000 mg daily in div. doses	Broad-spectrum efficacy; no drug interactions
topiramate	Topamax	PO 50–200 mg daily–BID	Interactions with antiepileptic drugs mostly; may affect cognitive function at high doses

[a]Regular release; [b]Delayed release; [c]Extended release.

PATIENT EDUCATION

Patients taking any anticonvulsant medication should be instructed regarding:

- Caution with driving or operating machinery until regulated with the medication, because of drowsiness or dizziness
- Reporting of any side effects, such as rash or eye problems, staggering, slurred speech, and any other symptoms
- Careful oral hygiene until tenderness of the gums subsides as treatment progresses
- Always taking medication on time and *never* omitting dosage (abrupt withdrawal of medication can lead to status epilepticus)
- Wearing Medic-Alert tag or bracelet at all times in case of accident or injury
- Taking medication with food or milk to lessen stomach upset
- Do not significantly alter ingestion of grapefruit juice while on carbamazepine (Tegretol) because of potentiation of effect
- Parents and teachers should be cautioned to observe and report changes in cognitive function, mood, and behavior in children receiving anticonvulsants

ANTIPARKINSONIAN DRUGS

Antiparkinsonian drugs are usually given for **Parkinson's disease (PD)**, a chronic neurological disorder characterized by fine, slowly spreading muscle tremors, rigidity and weakness of muscles, and shuffling gait. As the disease advances, patients develop dementia, confusion, psychosis, sleep disturbances, and declining cognitive function. There is no cure for Parkinson's disease, and the treatment goal is to relieve symptoms and maintain mobility.

The underlying pathology of PD is not completely understood, but normal dopamine activity as it relates to acetylcholine is diminished, and relative overactivity of cholinergic output results. This serves as the foundation of treatments for PD.

Dopamine Replacement

Carbidopa-Levodopa

Levodopa crosses the blood-brain barrier, where it is converted to dopamine. Carbidopa augments the penetration of levodopa into the brain, increasing the therapeutic effect of dopamine in the CNS and reducing its adverse reactions. Sinemet (a combination of levodopa and carbidopa) is most often used for long-term treatment and is recommended as initial drug treatment for those over 70 years of age and those with dementia.

Side effects of Sinemet, which are numerous and frequent, can include:

- Dyskinesias (involuntary movements of many parts of the body)
- Nausea, vomiting, and anorexia (if given with food to prevent nausea, the protein load should be low to avoid competition for transport across the gastrointestinal tract)
- Behavioral changes, anxiety, agitation, confusion, sleep disturbances, depression, hallucinations, psychosis
- Hypotension, dizziness, syncope

Note Side effects may be severe, requiring dosage reduction or withdrawal of the drug.

Contraindications and/or cautions for Sinemet include:

Discontinuing abruptly

Bronchial asthma or emphysema

Cardiac disease or hypotension

Active peptic ulcer

Diabetes, renal or hepatic disease

Glaucoma

Psychoses

Pregnant, postpartum, or nursing women

Interactions of Sinemet may occur with:

Antihypertensives, which may potentiate hypotensive effect

Phenytoin, which antagonizes levodopa

Iron salts that reduce bioavailability

Foods high in protein that reduce absorption

Non-specific (type A) monoamine oxidase inhibitors (MAOIs), which may cause hypertensive crisis

Patients receiving Sinemet for prolonged periods of time may develop a tolerance, resulting in ineffectiveness of the drug, called "wearing off." Sometimes, changing the timing of doses, changing to a controlled release preparation, or adding another agent (such as selegiline, entacapone, or a dopamine agonist), may bring the symptoms back under control.

Dopamine Agonists

The dopamine agonists bromocriptine (Parlodel), pramipexole (Mirapex), and ropinirole (Requip) are commonly used in conjunction with levodopa to delay the onset of levodopa-caused motor complications or used alone in early PD as a "levodopa-sparing" strategy. Dopamine agonists may reduce the required dose of levodopa for patients with advanced Parkinson's.

Bromocriptine (Parlodel), pramipexole (Mirapex), and ropinirole (Requip) are recommended for initial monotherapy in patients less than 70 years old.

These agents have a greater specificity for dopamine receptors and may have a neuroprotective effect, which leads to less dyskinesia, may delay the *wearing off* effect, and can postpone the need for Sinemet by several years.

Side effects of dopamine agonists can include:

- Psychosis, hallucinations, obsessive behavior, confusion, and somnolence
- Hypotension, syncope; edema
- Nausea, and vomiting

Pulmonary, renal, and cardiac valve fibrosis with bromocriptine

Interactions of dopamine agonists may occur with:

Antidopamine agents (i.e., antipsychotics, phenothiazines, metoclopramide) may decrease efficacy

Hypnotic and sedative agents may increase risk of somnolence

MAO B Inhibitors

Selegiline

Selegiline (Eldepryl) and rasagiline (Azilect) are selective MAO type-B inhibitors. They are sometimes prescribed as monotherapy for early PD or after levodopa has been used for several years and begins to "wear off," or become less effective. When Sinemet and selegiline or rasagiline are used *concurrently*, the Sinemet dosage is reduced by 10–30% to lessen the chance of additive side effects.

Side effects of MAO B inhibitors include nausea, dizziness, confusion, abdominal pain, hallucinations, dry mouth, vivid dreams, dyskinesias, and headache. Selegiline is metabolized to amphetamine metabolites and there is controversy as to whether these metabolites contribute to side effects.

Contraindicated with the following drugs, which can interact resulting in *severe* CNS toxicity, hyperpyrexia, hypertensive crisis, and even death. Do *not* use selegiline with:

Meperidine (Demerol)

Tricyclic antidepressants

Selective serotonin reuptake inhibitors (SSRIs); SNRIs

Sympathomimetics (e.g., epinephrine, ephedrine, isoproterenol)

Dextromethorphan; St. John's wort

Abrupt discontinuation

When given at the recommended dosages, there is minimal danger of a hypertensive crisis associated with interactions of other MAOIs and certain foods (the "cheese reaction"). See Chapter 20 for a description of this reaction, which can occur if the recommended dosage is exceeded. No dietary restrictions are recommended for selegiline at the recommended dose.

An orally disintegrating tablet (ODT) formulation of selegilene (Zelapar) is available as an adjunct to levodopa. Selegilene ODT is absorbed through the

buccal membrane, avoiding first-pass hepatic metabolism. This results in a faster onset of action, lower dose, and fewer amphetamine metabolites.

Rasagiline

Rasagiline (Azilect) is currently the only MAO B inhibitor approved as initial monotherapy for PD; it is also approved as an addition to levodopa later in the disease. Rasagiline is given only once daily, has no amphetamine metabolites, and is generally well tolerated. Side effects include headache, nausea, joint pain, hypotension, hallucinations, dyskinesias, depression, and dyspepsia. Contraindications are similar to selegiline.

Anticholinergic Agents

Drugs with anticholinergic and antihistaminic actions were the first to be used for tremors associated with PD and are still useful in early stages of the disease in younger patients and for drug-induced parkinsonism. These agents restore the cholinergic-dopaminergic balance in PD. The **anticholinergics** include synthetic atropine-like drugs, such as benztropine (Cogentin) and trihexyphenidyl, which are used to treat parkinson-like tremors associated with long-term use of antipsychotics or for other forms of parkinsonian syndrome. (See Chapter 13, Cholinergic Blockers.)

Side effects of the anticholinergic agents are:

- Dry mouth
- Dizziness and drowsiness
- Blurred vision
- Constipation or urinary retention
- Confusion
- Depression
- Nausea
- Tachycardia

Contraindications and/or cautions for anticholinergics apply to:

Abrupt discontinuation which leads to rebound symptoms

Use with caution in older patients because of the risk of cognitive impairment. Those with benign prostatic hypertrophy (BPH) are also at risk for urinary retention.

Amantadine

Another drug unrelated to the other antiparkinsonian agents is the antiviral agent amantadine (Symmetrel). It alters dopamine release and has anticholinergic properties. Amantadine is used to treat parkinsonism (extrapyramidal reactions) associated with prolonged use of phenothiazines, carbon monoxide poisoning, or cerebral arteriosclerosis in the older adult. For PD, amantadine is generally used early in the disease as monotherapy and is of little benefit when added to levodopa.

Side effects of Symmetrel, usually dose related and reversible, can include:

- CNS disturbances including depression, confusion, hallucinations, anxiety, depression, irritability, nervousness, and dizziness
- Headache, weakness, and insomnia
- Heart failure, edema, and hypotension
- GI distress, constipation, and urinary retention

Contraindications or extreme caution with Symmetrel applies to:

- Abrupt discontinuation
- Liver and kidney disease
- Cardiac disorders
- Psychosis, neurosis, and mental depression
- Epilepsy
- Patients taking CNS drugs

COMT Inhibitors

Catechol-*O*-methyl-transferase (COMT) inhibitors, such as entacapone (Comtan) and tolcapone (Tasmar), block the enzyme responsible for metabolizing levodopa. COMT inhibitors increase the plasma concentration of levodopa, which enhances the amount of levodopa crossing the blood-brain barrier. This allows the patient's dose of levodopa to be lowered and results in a decrease in the incidence or severity of levodopa dose-related side effects (e.g., dyskinesias, nausea, etc.). COMT inhibitors increase the clinical response time to levodopa (*on* time), while decreasing the *off* time.

Entacapone is also available in combination with carbidopa/levodopa (Stalevo) which provides the convenience of fewer pills, but dosing is less flexible for patients who need varying amounts of levodopa throughout the day.

Side effects of entacapone and tolcapone are similar:

- Orthostatic hypotension
- Hallucinations
- Dyskinesia
- Nausea/vomiting
- Diarrhea (can be severe); abdominal pain
- Orange discoloration of the urine
- Hepatic injury with tolcapone ("Black Box Warning")—the treating physician is to obtain a patient signed consent form acknowledging this risk

Drug interactions: Patients taking entacapone or tolcapone should not receive *nonselective* MAOIs (phenelzine or tranylcypromine), but can take a *selective* MAOI such as selegiline. Concomitant use of CNS depressants should be avoided to prevent additive sedation.

PATIENT EDUCATION

Patients taking antiparkinsonian drugs should be instructed regarding:

- Administration on a regular schedule as prescribed, with food to lessen GI distress; give carbidopa/levodopa with a low-protein meal if food is necessary to offset nausea
- Avoiding abrupt withdrawal of medication, which may greatly increase parkinsonian symptoms
- Several weeks sometimes required before benefit is apparent
- Caution with CNS drugs, alcohol, or antihypertensives (not taking other medicines including vitamins, without physician approval)
- Caution with driving or operation of machinery; drugs may cause drowsiness, dizziness, or lightheadedness
- Reporting adverse side effects to the physician (e.g., involuntary movements, blurred vision, constipation, urinary retention, GI symptoms, palpitations, and mental changes)
- Reporting any signs that the drug is no longer effective after prolonged use (sometimes after months or years the dosage may need to be increased or another drug substituted by the physician); avoiding any dosage changes without medical supervision
- Maintaining physical activity, self-care, and social interaction, an essential part of therapy for Parkinson's disease
- Rising slowly

See Table 22-2 for a summary of the antiparkinsonian drugs.

AGENTS FOR RESTLESS LEGS SYNDROME

Restless legs syndrome (RLS) is a sensorimotor neurologic disorder characterized by a distressing urge to move the legs, often accompanied by a marked sense of discomfort in the legs. RLS is triggered by rest or inactivity and is temporarily relieved by movement. It follows a circadian pattern, with symptoms being most intense in the evening and nighttime. It is usually disruptive to sleep, which is the primary reason patients seek treatment.

RLS etiology is either primary or secondary. Primary RLS involves the CNS and the dopaminergic pathway. The dopamine agonists pramipexole (Mirapex) and ropinirole (Requip), used to treat PD (even though RLS is not related to PD), are FDA approved for RLS treatment as well. The dosages of these agents when used to treat RLS are typically only 10–20% of those used to treat PD and are usually given 1–3 hours before bedtime as a single daily dose. The most worrisome side effects with the dopamine agonists in PD, such as dyskinesias, have not been observed in patients treated for RLS.

Gabapentin (Neurontin), benzodiazepines (such as clonazepam), and opioids (hydrocodone, oxycodone, tramadol) are second-line agents for RLS

Table 22-2 Antiparkinsonian Drugs

GENERIC NAME	TRADE NAME	DOSAGE	COMMENTS
Dopamine Replacement			
carbidopa and levodopa	Sinemet,	PO 10/100–200/2,000 mg in 3–6 div. doses pc	Immediate release tab
	Parcopa		Orally disintegrating tab
	Sinemet CR	PO 25/100–400/2,000 mg in 2–4 div. doses pc	Separate doses by at least 6 h
Dopamine Agonists			
bromocriptine	Parlodel	PO 1.25 mg BID with meals	Used with Sinemet; dosage gradually increased to optimum maintenance dose (up to 40 mg per day)
pramipexole	Mirapex	PO 0.125 mg TID	Increase to a max daily dose of 4.5 mg per day for desired effect balanced against side effects
ropinirole	Requip	PO 0.25 mg TID	Increase to a max daily dose of 24 mg per day for desired effect balanced against side effects
Anticholinergics			
benztropine	Cogentin	PO, IM, or IV 0.5–6 mg daily in one or div. doses	Not for the older adult
			For drug-induced parkinsonism and other forms of parkinsonian syndrome
trihexyphenidyl	(Artane)*	PO 1–15 mg daily in div. doses	For drug-induced parkinsonism and other forms of parkinsonian syndrome
COMT Inhibitor			
entacapone	Comtan	200 mg with each dose of Sinemet max 1600 mg per day	Use only with Sinemet
with carbidopa/ levodopa	Stalevo	PO (various strengths) TID up to 6–8 tabs per day	Do not crush
MAO B Inhibitors			
rasagiline	Azilect	PO 0.5–1 mg daily	Reduce dose with hepatic impairment
selegiline	Eldepryl	PO 5 mg BID (2nd dose no later than 2 PM)	Used when levodopa wears off, levodopa dosage can be decreased
	Zelapar	PO 1.25–2.5 mg daily	Orally disintegrating tablet
Other Agents			
amantadine	Symmetrel	PO 100–400 mg daily div. doses	Also for Tx and prophylaxis of influenza A and drug-induced parkinsonism

*Brand name no longer marketed, but name still commonly used.

cases involving specific symptoms like continuous sleep disturbances or painful sensations in the extremities.

RLS may be secondary to other causes, including iron deficiency (with or without anemia), renal failure, diabetes, rheumatoid arthritis, fibromyalgia, vitamin deficiency (folate, B12), hypothyroidism, and pregnancy. Treatment of secondary RLS focuses on identifying and treating the underlying cause. Medications which have the potential to aggravate RLS symptoms, such as metoclopramide, all neuroleptics, many antidepressants, and antihistamines, should be discontinued if possible.

AGENTS FOR ALZHEIMER'S DISEASE

Alzheimer's disease, or dementia of the Alzheimer's type, is characterized by a devastating, progressive decline in cognitive function, having a gradual onset, usually beginning between 60 and 90 years of age, followed by increasingly severe impairment in social and occupational functioning. Although the precise etiology of Alzheimer's disease is uncertain, cholinergic systems appear to be most clearly compromised and are frequently the target of drug treatment.

Cholinesterase Inhibitors

The first class of agents shown to be efficacious for symptom delay in Alzheimer's disease are the cholinesterase inhibitors. These agents prevent the breakdown of acetylcholine in the synaptic cleft, thereby improving cognitive function, but do not treat the underlying pathology of the disease. They may slow the progression, but do not cure the disease.

Tacrine (Cognex) was the first drug approved in this class, but is associated with significant hepatotoxicity and a frequent dosing schedule and is rarely used today. Donepezil (Aricept), galantamine (Razadyne), and rivastigmine (Exelon) are not associated with hepatotoxicity but do exhibit cholinergic side effects and dizziness. All drugs in this class cause GI upset (nausea, vomiting, diarrhea, anorexia), requiring slow dose titration to improve patient tolerance.

Interactions of cholinesterase inhibitors include:

Anticholinergics may decrease effectiveness—avoid using together

Cholinergics (bethanechol) and succinylcholine—may have a synergistic effect—monitor patient closely

Contraindications/Cautions of cholinesterase inhibitors:

GI bleeding

Jaundice, renal disease

Pregnancy, lactation

NMDA Receptor Antagonist

Memantine (Namenda) is the first *N*-methyl-*D*-aspartate (NMDA) antagonist approved for the treatment of moderate-to-severe dementia of the Alzheimer's type. Memantine is thought to selectively block the excitotoxic effects with

abnormal transmission of the neurotransmitter glutamate while allowing for the physiological transmission associated with normal cell functioning. It can be used as monotherapy or in combination therapy with cholinesterase inhibitors. Memantine may be efficacious in the earlier stages of Alzheimer's disease as well.

Side effects of memantine involve the CNS, are dose-dependent, and include:

- Confusion, cerebrovascular disorder, falls, and agitation
- Dizziness, headache, constipation, cough

Contraindications/cautions include pregnancy, lactation, use in children, and renal disease

Drug interactions with other NMDA antagonists (amantadine, ketamine, and dextromethorphan) and certain antiarrythmics

See Table 22-3 for a summary of Alzheimer's drugs.

Table 22-3 Agents for Alzheimer's Disease

GENERIC NAME	TRADE NAME	DOSAGE	COMMENTS
Cholinesterase Inhibitors			
donepezil	Aricept	PO 5–10 mg at bedtime	May be taken with or without food
	Aricept ODT		Orally disintegrating tablet
rivastigmine	Exelon	PO 1.5 mg BID with food	Increase to 3–6 mg BID (higher doses may be more beneficial)
		Patch 4.6 mg per 24 hrs titrate to 9.5 mg per 24 hrs after 4 weeks	Rotate application sites
tacrine	Cognex	PO 10–40 mg 4 × per day on empty stomach	Monitor serum transaminase levels frequently
galantamine	Razadyne[a]	PO 4–12 mg BID with food	Caution with hepatic/renal disease
	Razadyne ER	PO 8 mg daily with food	Titrate to 16–24 mg once daily; do not crush
NMDA Receptor Antagonist			
memantine	Namenda	PO 5 mg per day initially titrate to 10 mg BID	Can be used as monotherapy or in combo with donepezil CNS side effects, especially agitation

[a]Formerly Reminyl

CASE STUDY – A

Antiepileptics

Sandy Johnson, age 5, has been diagnosed with epilepsy. She has been placed on Dilantin and phenobarbital elixir. Her mother will need all of the following information.

1. Phenytoin (Dilantin) can have all of the following side effects EXCEPT
- a. Sore gums
- b. Headache
- c. Insomnia
- d. Nausea

2. All of the following should be reported to the physician EXCEPT
- a. Dizziness
- b. Increased appetite
- c. Rash
- d. Double vision

3. Sandy's teachers should be alerted to watch for and report all of the following EXCEPT
- a. Behavior changes
- b. Drowsiness
- c. Hyperactivity
- d. Inattention

4. The mother should do all of the following EXCEPT
- a. Give medicine with food
- b. Give medicine on time
- c. Stress oral hygiene
- d. Stop medicine if no seizures

5. Which of the following statements is NOT true?
- a. Doctor may reduce dosage
- b. Children outgrow epilepsy
- c. Side effects often subside
- d. Other drugs sometimes used

CASE STUDY – B

Antiparkinsonian Drugs

Sam Snow, age 80, has Parkinson's disease and has been taking Sinemet for 10 years. He wants to discontinue the drug because he says it's not helping him anymore. He needs the following information.

1. He should be told the following EXCEPT
- a. Tolerance can develop
- b. He can increase the dose
- c. M.D. may change medicine
- d. Withdrawal increases symptoms

2. When Sinemet loses effectiveness, other drugs can be combined with it for better effect. Which is *not* a drug combined with Sinemet?
- a. Requip
- b. Mirapex
- c. Tegretol
- d. Parlodel

3. All of the following can be side effects of Sinemet EXCEPT
- a. Dizziness
- b. Constipation
- c. Involuntary movements
- d. Agitated confusion

4. All of the following may antagonize Sinemet or potentiate side effects EXCEPT
- a. Antihypertensives
- b. Iron
- c. Phenytoin
- d. Aspirin

5. Selegiline (Eldepryl) is sometimes combined with Sinemet. There are serious interactions with selegiline and the following medications EXCEPT
- a. Meperidine
- b. Amantadine
- c. Tricyclics
- d. SSRIs

CHAPTER REVIEW QUIZ

Match the medication in the first column with the condition in the second column that it is used to treat. Conditions may be used more than once.

Medication	Condition
1. _____ Aricept	**a.** Seizures
2. _____ Entacapone	**b.** Absence epilepsy
3. _____ Neurontin	**c.** Parkinson's
4. _____ Lamictal	**d.** Extrapyramidal reactions
5. _____ Zarontin	**e.** Alzheimer's
6. _____ Amantadine	
7. _____ Depakote	
8. _____ Cognex	
9. _____ Topamax	
10. _____ Razadyne	

Choose the correct answer.

11. Side effects of memantine (Namenda), used to treat Alzheimer's, can include all of the following EXCEPT:
    a. Dizziness **c.** Headache
    b. Diarrhea **d.** Confusion

12. All of the following statements are true of Mirapex used to treat Parkinson's EXCEPT:
    a. For patients less than 70 **c.** Less dyskinesia
    b. Slows "wearing off" effect **d.** For monotherapy only

13. Which of the following can interact with carbamazepine (Tegretol), potentiating risk of side effects?
    a. Dairy products **c.** Aspirin
    b. Grapefruit juice **d.** Iron

14. Anticholinergic agents for Parkinsonism, for example benztropine and trihexyphenidyl, are contraindicated or should be used with caution in the following patients EXCEPT:
    a. With bradycardia **c.** Depressed patients
    b. With BPH **d.** Older adults

15. The following statements are true of the drugs for Alzheimer's EXCEPT

a. Delay symptoms
b. Improve cognition
c. Cause dizziness
d. Cure the disease

Go to your StudyWARE™ CD-ROM and have fun learning as you play games and answer case study-related questions to help reinforce key concepts you learned in this chapter.

Go to your Study Guide and complete the review questions for this chapter.

Chapter 23

Endocrine System Drugs

Objectives

Upon completion of this chapter, the learner should be able to

1. Identify the hormones secreted by these four endocrine glands: pituitary, adrenals, thyroid, and islets of Langerhans
2. Describe at least five conditions that can be treated with corticosteroids
3. Explain administration practice important to corticosteroid therapy
4. List at least four serious, potential side effects of long-term steroid therapy
5. Compare and contrast medications given for hypothyroidism and hyperthyroidism
6. Describe side effects of thyroid and antithyroid agents
7. Explain uses and side effects of oral antidiabetics
8. Compare and contrast insulins according to action (rapid, intermediate, and long acting), naming onset, peak, and duration of each category
9. Identify the symptoms of hypoglycemia and hyperglycemia, and appropriate interventions
10. Explain appropriate patient education for those receiving endocrine system drugs
11. Define the Key Terms and Concepts

Key Terms and Concepts

Antidiabetic
Antithyroid
Corticosteroids
Endocrine
Hyperglycemia
Hypoglycemia
Hypothyroidism
Immunosuppressant
Sulfonylurea

Endocrine refers to an internal secretion (*hormone*) produced by a ductless gland that secretes directly into the bloodstream. Endocrine system drugs include natural hormones secreted by the ductless glands or synthetic substitutes. Hormones that affect the reproductive system are discussed in Chapter 24. This chapter covers four categories: pituitary hormones, adrenal corticosteroids, thyroid agents, and antidiabetic agents.

PITUITARY HORMONES

The pituitary gland, located at the base of the brain, is called the master gland because it regulates the function of the other glands. It secretes several hormones such as somatotropin, adrenocorticotropic hormone (ACTH), thyroid-stimulating hormone (TSH), and gonadotropic hormones (FSH, LH, and LTH; see Chapter 24). The two pituitary hormones discussed in this chapter are somatotropin and ACTH.

The anterior pituitary lobe hormone, somatotropin, is called human growth hormone (HGH) because it regulates growth. Insufficient production of HGH will result in growth abnormalities, which should be treated only by an endocrinologist.

Adrenocorticotropic hormone (ACTH) is available only for parenteral use as corticotropin. Cosyntropin (Cortrosyn), a synthetic peptide of ACTH, is used mainly for diagnosis of adrenocortical insufficiency. Treatment of associated disorders is usually reserved for the corticosteroids in which dosage is more easily regulated and which are available in oral form as well.

ADRENAL CORTICOSTEROIDS

The adrenal glands, located adjacent to the kidneys, secrete hormones called **corticosteroids**, which act on the immune system to *suppress the body's response to infection or trauma.* They *relieve inflammation*, *reduce swelling*, and *suppress symptoms* in acute conditions. Corticosteroid use can be subdivided into two broad categories: (1) as replacement therapy when secretions of the pituitary or adrenal glands are deficient and (2) for their anti-inflammatory and **immunosuppressant** properties.

Corticosteroid therapy is *not curative*, but is used as *supportive therapy with other medications.* Some conditions treated with corticosteroids include:

Allergic reactions (e.g., to insect bites, poison plants, chemicals, or other medications) in which there are symptoms of rash, hives, or anaphylaxis

Acute flare-ups of rheumatic or collagen disorders, especially where only a few inflamed joints can be injected with corticosteroids to decrease crippling, or in life-threatening situations, such as rheumatic carditis or lupus

Acute flare-ups of severe skin conditions that do not respond to conservative therapy; topical applications are preferable to systemic therapy, when possible, to minimize side effects

Acute respiratory disorders such as severe asthmaticus (oral inhalations preferable) and sarcoidosis, or to prevent hyaline membrane disease in prematures by administering IM to the mother at least 24 h before delivery

Malignancies (e.g., leukemia, lymphoma, and Hodgkin's disease), in which corticosteroids (e.g., prednisone) are used with other antineoplastic drugs as part of the chemotherapy regimen; treatment of nausea and vomiting associated with chemotherapy (e.g., dexamethasone)

Cerebral edema associated with brain tumor or neurosurgery

Organ transplant, in which corticosteroids are used with other immunosuppressive drugs to prevent rejection of transplanted organs

Life-threatening shock due to adrenocortical insufficiency; treatment of other forms of shock is controversial

Acute flare-ups of ulcerative colitis; short-term only to avoid hemorrhage

Prolonged administration of corticosteroids can cause suppression of the pituitary gland with adrenocortical atrophy, and the body no longer produces its own hormone. To minimize this effect, intermediate-acting corticosteroids (prednisone, methylprednisolone) can be given by alternate-day therapy when they are required for extended time periods. Withdrawal of corticosteroids following long-term therapy should always be gradual with step-down (i.e., tapering) dosage to allow the body's normal hormone production and regulation to return. Abrupt withdrawal can lead to acute adrenal insufficiency, shock, and even death.

Because of potentially serious side effects, corticosteroids are administered for as short a time as possible and *locally if possible* to reduce systemic effects (e.g., in ointment, intra-articular injections, ophthalmic drops, and respiratory aerosol inhalants). Local administration reduces the dosage by avoiding the first pass effect and going directly to the site of need.

For *acute* episodes, some oral corticosteroids are available in *dose packs* (e.g., methylprednisolone, prednisone, DexPak TaperPak) to facilitate dose tapering.

Side effects of the corticosteroids used for longer than very brief periods can be quite serious and possibly include:

Adrenocortical insufficiency, adrenocortical atrophy

Delayed wound healing and *increased susceptibility to infection*

Fluid and electrolyte imbalance, possibly resulting in edema, potassium loss, hypertension, and heart failure

Muscle pain or weakness

Osteoporosis with fractures, especially in older women

Stunting of growth in children (premature closure of bone ends)

Increased intraocular pressure or cataracts

Endocrine disorders, including cushingoid state, amenorrhea, and *hyperglycemia*

Nausea, vomiting, diarrhea, or constipation

Gastric or esophageal irritation, ulceration, or hemorrhage

CNS effects including headache, vertigo, insomnia, euphoria, psychosis, or anxiety

Petechiae, easy bruising, skin thinning and tearing

Contraindications or extreme caution applies to:

Long-term use (regulated carefully); avoid abrupt discontinuation

Viral or bacterial infections (used only in life-threatening situations along with appropriate anti-infectives)

Fungal infections (only if specific therapy concurrent)

Hypothyroidism or cirrhosis (exaggerated response to corticosteroids)

Hypertension or heart failure

Psychotic patients or emotional instability

Diabetes (drugs increase hyperglycemia)

Glaucoma (drugs may increase intraocular pressure)

History of gastric or esophageal irritation (may precipitate ulcers)

Children (drugs may retard growth)

Pregnancy and lactation

History of thromboembolic disorders or seizures

Interactions may occur with:

Barbiturates, phenytoin (Dilantin), and rifampin—require dosage adjustment

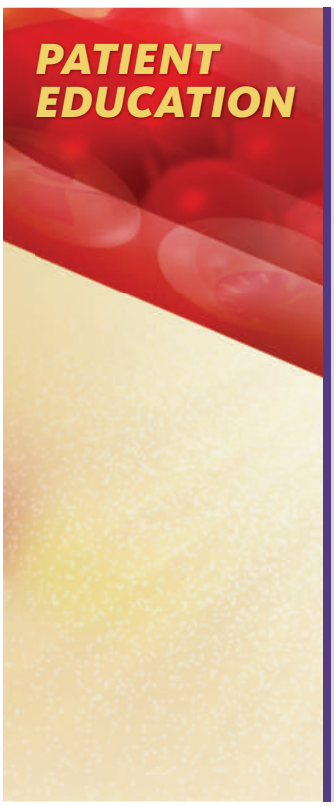
Estrogen and oral contraceptives may potentiate corticosteroids

Nonsteroidal anti-inflammatory agents (e.g., aspirin may increase risk of GI ulceration)

Diuretics, which potentiate potassium depletion, for example thiazides, furosemide

Live-virus vaccines and toxoids (corticosteroids inhibit antibody response)

See Table 23-1 for a summary of the pituitary and adrenal corticosteroids.



Patients taking corticosteroids should be instructed regarding:

- Following exact dosage and administration orders (never taking longer than indicated and *never stopping medicine abruptly*)
- Notifying physician of any signs of infection or trauma *while taking corticosteroids or within 12 months after long-term therapy is discontinued* and similarly notifying surgeon, dentist, or anesthesiologist if required
- Taking oral corticosteroids during or immediately after meals to decrease gastric irritation. Take single daily or alternate-day doses prior to 9 A.M. Take multiple doses at evenly spaced intervals throughout the day, but not near bedtime.
- Avoiding any other drugs at same time (including OTC drugs, e.g., aspirin) without physician's approval. Antacids or other antiulcer drugs are sometimes prescribed
- Side effects to expect with long-term therapy (e.g., fluid retention and edema)
- Dangers of infection, delayed wound healing, osteoporosis, mental disorders
- Reporting any side effects to physician immediately

Table 23-1 Pituitary and Adrenal Corticosteroid Drugs

GENERIC NAME	TRADE NAME	DOSAGE[a]
Pituitary Drugs		
corticotropin (ACTH)	H. P. Acthar Gel	IM, subcu repository gel for injection
cosyntropin	Cortrosyn	IM, IV, for adrenocortical insufficiency diagnosis
Adrenal Corticosteroids[a]		
cortisone		PO for replacement
dexamethasone	Decadron	PO, IV, IM
fludrocortisone	(Florinef)*	PO, for orthostatic hypotension
hydrocortisone	Cortef or Solu-Cortef	PO, IV, deep IM, subcu intra-articular
methylprednisolone	Depo-Medrol or Solu-Medrol	PO, IV, deep IM, intra-articular
prednisone		PO (tab or sol); do not confuse with prednisolone
triamcinolone	Kenalog	IM, intra-articular

Note: Many other products available. Representative list only. Topical products are discussed in Chapter 12 and oral and nasal inhalation products in Chapter 26.
[a]Dosage varies greatly depending on the condition treated; large doses may be given for acute conditions on a short-term basis; long-term therapy can be given on an alternate-day basis with intermediate-acting agents, and dosage is reduced gradually.
*Brand name no longer marketed, but name still commonly used.

THYROID AGENTS

When thyroid levels are low, the pituitary gland releases thyroid-stimulating hormone (TSH). TSH promotes the biosynthesis and secretion of the two bioactive thyroid hormones thyroxine (T4) and triiodothyronine (T3). Thyroxine is the major product of the thyroid gland and much of it is later converted in the body to the T3 form. Thyroid agents can be natural (thyroid) or synthetic (e.g., Synthroid). Thyroid preparations are used in replacement therapy for **hypothyroidism** caused by diminished or absent thyroid function. Synthetic agents, such as levothyroxine (Levoxyl), are generally preferred because T4 is a prohormone and this allows the patient's own physiologic mechanisms to control the production of T3.

Hypothyroid conditions requiring replacement therapy include *cretinism* (congenital; requires immediate treatment to prevent mental retardation) and *myxedema* or adult hypothyroidism due to simple goiter, Hashimoto's thyroiditis or other thyroid disorders, pituitary disorders, medications (amiodarone, lithium), and thyroid destruction from surgery or radiation. Hypothyroidism causes slowed metabolism with symptoms ranging from fatigue, dry skin, thinning hair, weight gain, sensitivity to cold, and irregular menses to mental deterioration (including depression) if untreated.

Hypothyroidism is diagnosed by blood tests (e.g., TSH, free T4 and T3 levels) before medication is given. The use of thyroid agents in weight reduction programs to increase metabolism when thyroid function is normal (euthyroid)

is *contraindicated*, ineffective, and dangerous, leading to decrease in normal thyroid function and possibly life-threatening cardiac arrhythmias.

Transient hypothyroidism is rare, and thyroid replacement therapy for true hypothyroidism must be continued for life, although dosage adjustments may be required. Monitoring for toxic effects and periodic laboratory tests are recommended.

Note
When receiving orders for levothyroxine, caution is advised about decimal point placement (i.e., 0.025 mg vs. 0.25 mg) and dose conversions between mg and mcg, as medication errors have occurred.

Toxic effects are the result of overdosage of thyroid and are manifested in the signs of *hyperthyroidism:*

Palpitations, tachycardia, cardiac arrhythmias, and increased blood pressure

Nervousness, tremor, headache, and insomnia

Weight loss, diarrhea, and abdominal cramps

Intolerance to heat, fever, and excessive sweating

Menstrual irregularities; exophthalmos (bulging eyes)

Contraindications or extreme caution with thyroid applies to:

Cardiovascular disease, including angina pectoris myocardial infarction and hypertension

Older adults (may precipitate dormant cardiac pathology)

Adrenal insufficiency—corticosteroids required first

Diabetes—close monitoring of blood glucose required

Euthyroid persons (normal thyroid function)

Interactions of thyroid may occur with:

Potentiation of oral anticoagulant effects if added after warfarin therapy stabilized

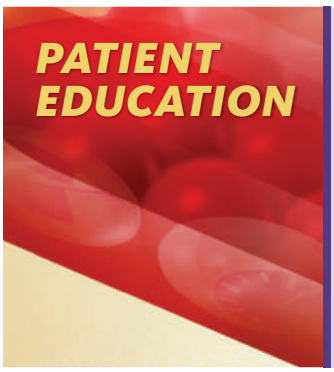
Insulin and oral hypoglycemics (dosage adjustment necessary)

Potentiation of adrenergic effect (e.g., epinephrine)—watch closely!

Estrogens and oral contraceptives (decreased thyroid response)

Aluminum/calcium/iron/magnesium salts, chromium and sucralfate (decreased absorption; space several hours apart if possible)

Soy products (decreased response)



Patients being treated with thyroid medication should be instructed regarding:

- Importance of taking the prescribed dosage of thyroid medication consistently every day. It usually has to be taken for life. Take on empty stomach 30–60 min prior to breakfast
- Importance of reporting any symptoms of overdose (e.g., palpitations, nervousness, excessive sweating, and unexplained weight loss)

Periodic laboratory tests to determine effectiveness and proper dosage

Not changing from one brand to another or to a generic without physician approval

ANTITHYROID AGENTS

Antithyroid agents (e.g., Tapazole and propylthiouracil) are used *to relieve the symptoms of hyperthyroidism* in preparation for surgical or radioactive iodine therapy.

Side effects of antithyroid agents are rare and may include:

Rash, urticaria, and pruritus

Blood dyscrasias (especially agranulocytosis)

Contraindications or caution with antithyroid agents applies to:

Prolonged therapy (seldom used)

Patients older than 40 years old

Pregnancy and lactation

Hepatic disorders

Interactions with other drugs causing agranulocytosis are potentiated.

PATIENT EDUCATION

Patients being treated with antithyroid medication should be instructed to notify the physician immediately of signs of illness (e.g., chills, fever, rash, sore throat, malaise, and jaundice).

See Table 23-2 for a summary of thyroid and antithyroid agents.

Table 23-2 Thyroid and Antithyroid Agents

GENERIC NAME	TRADE NAME	DOSAGE
Thyroid Agents		
levothyroxine (T_4)	Synthroid, Levothroid, Levoxyl	25–200 mcg daily
liothyronine (T_3)	Cytomel	5–25 mcg daily
thyroid	Armour Thyroid	60–180 mg daily
Antithyroid Agents		
methimazole	Tapazole	Tabs, 5–30 mg daily, divided doses
propylthiouracil	PTU	Tabs, 300–400 mg daily, divided doses

ANTIDIABETIC AGENTS

Antidiabetic agents are administered to *lower blood glucose levels* in those with impaired metabolism of carbohydrates, fats, and proteins. Diabetes mellitus is classified as insulin dependent Type 1 (characterized by destruction of pancreatic beta cells) or Type 2 (characterized by insulin resistance and deficiency). Type 1 diabetes was formerly described as juvenile diabetes because it was usually diagnosed in children and young adults. However, adults can also develop Type 1 diabetes and require insulin. Type 2 diabetes is the most common (90–95%) form of diabetes. There is an increase in children and young adults with Type 2 due to an increase in obesity at an earlier age.

The result of long-term, poorly controlled diabetes is vascular injury which is categorized as microvascular or macrovascular. Common microvascular complications include retinopathy, nephropathy, and neuropathy. Common macrovascular complications of diabetes include coronary artery disease (including myocardial infarction), cerebrovascular disease (including stroke), and peripheral vascular disease. Health professionals of all disciplines have a responsibility to care for each patient in such a way that the risk of diabetic complications is minimized.

Insulin

Insulin is required as replacement therapy for Type 1 diabetics with insufficient production of insulin from the islets of Langerhans in the pancreas. Insulin is also required in patients with Type 2 who have failed to maintain satisfactory concentrations of blood glucose with therapy including dietary regulation and oral antidiabetic agents. Insulin is also indicated for stable Type 2 diabetics at the time of surgery, fever, severe trauma, infection, serious renal or hepatic dysfunction, endocrine dysfunction, gangrene, or pregnancy. Insulin (regular) is used in the emergency treatment of diabetic ketoacidosis or coma.

Insulin must be administered parenterally because it is destroyed in the GI tract. All *injected* insulin products currently marketed are one of two types: biosynthetic human, or analog. Biosynthetic insulins are referred to as "human" because their amino acid structure is identical to naturally occurring human insulin. Analog insulin (aspart, detemir, glargine, glulisine, and lispro) differs from human insulin only by substitution or position changes in the human insulin molecule, which mimics normal insulin secretion better than traditional insulins. Biosynthetic and analog insulins are created using recombinant DNA technology.

Most of the insulin used today is U-100, which means that there are 100 units of insulin in each milliliter. The insulin syringe *must be marked U-100* to match the insulin used. Remember that on the 100 unit (1 mL) insulin syringe each line represents 2 units. If a smaller 50 unit (1/2 mL) syringe is used, each line represents 1 unit of insulin (see Chapters 4 and 9 for details). *Always have someone else compare the insulin in the syringe with the dosage ordered to prevent errors*, which could have serious consequences.

Insulin preparations differ mainly in their onset, peak, and duration of action (Table 23-3). Aspart, glulisine, and lispro insulins are ultra-*rapid acting* and have a *very short duration* of action. *Regular* insulin is *rapid acting* and of *short duration*. *Regular* insulin is the *only* type that may be given intravenously

Table 23-3 Insulins

ACTION	PREPARATION	TRADE NAME	ONSET	PEAK	DURATION
Rapid	aspart glulisine lispro	Novolog Apidra Humalog	5–15 min	30–90 min	3–5 hrs
Short	regular	Humulin R Novolin R	30–60 min	2–5 hrs	5–8 hrs
Intermediate	isophane (NPH)	Humulin N, Novolin N	1–3 hrs	6–12 hrs	16–24 hrs
Long	glargine detemir	Lantus Levemir	1–2 hrs	No pronounced peak	up to 24 hrs (dose-dependent)
Mixtures	NPH/reg	Humulin/Novolin 70/30, 50/50	30–60 min	6 –12 hrs	16–24 hrs
	NPH/lispro	Humalog Mix 75/25, 50/50	5–15 min	1–4 hrs	16–24 hrs
	NPH/aspart	Novolog Mix 70/30			

Note: This is a representative list. Other insulin products are also available. Dosage varies. Due to limited use, beef- and pork-derived insulins, and lente and ultralente insulins are no longer available in the United States. Exubera, an orally inhaled form of insulin has been discontinued due to poor product acceptance.
Before giving insulin, always check expiration date on the vial and be sure that regular, aspart, glulisine, and lispro insulins are clear, and isophane insulins are cloudy. Only regular insulins may be administered IV. Isophane insulins are administered only subcutaneously, never IV. Rotate administration sites with each injection. Opened vials may be stored at room temperature without loss of potency for 28 days. Insulin pens and cartridges are never to be shared among patients as this may result in transmission of blood-borne pathogens.

and intramuscularly as well as subcutaneously. All other insulins can *only* be given subcutaneously. Aspart, glulisine, and lispro are clear and rapid acting (onset in approximately 15 min). They peak in about 1 h and last approximately 4 h. They can only be given subcutaneously. *Isophane* (NPH) is intermediate acting; glargine and detemir are long acting.

Regular insulin is sometimes combined with isophane insulin in the same syringe. When two insulins are ordered at the same time, the *regular insulin should be drawn into the syringe first.* Combinations of NPH and regular insulin are also available, for example, Humulin 70/30, or Novolin 70/30. This combination provides rapid onset with a duration of up to 24 h. Insulin *glargine* and insulin mixtures should not be mixed with any of the other available types of insulin.

Regular insulin is sometimes ordered as *corrective action insulin.* This means that the blood is tested for glucose and a specific amount of regular insulin is administered subcutaneously based on the glucose level shown by the test.

For example, the physician might write an order to give regular insulin subcu according to the following blood glucose levels with this corrective action scale:

Blood Glucose	Dosage of Regular Insulin
>350	Call physician for dosage
301–350	12 units
251–300	8 units
200–250	5 units
<200	No insulin

Remember, this is only a *sample* corrective action scale. *Always check the physician's order carefully to determine the exact dosage of insulin, which varies with the individual.* Verification of insulin dosage with another caregiver is very important to prevent one of the most common and most dangerous of medication errors.

There are many different types of insulins available, and many have names or packages that look or sound alike. There has been confusion between "Lente" and "Lantus" and "Humulin" and "Humalog." Confusion is also possible with the premixed products "Humulin 70/30," "Humalog Mix 75/25," "Novolog Mix 70/30," and "Novolin 70/30." *Be extremely careful to give the right insulin and the right dose! If in doubt, consult the pharmacist.*

StudyWARE™ CONNECTION

See It In Action! Go to the StudyWARE™ CD-ROM to view a video on Glucose Testing.

Hyperglycemia

Hyperglycemia, or elevated blood glucose, may result from:

- Undiagnosed diabetes
- Insulin dose insufficient
- Infections
- Surgical or other trauma
- Emotional stress
- Other endocrine disorders
- Medications (e.g., glucocorticoids such as prednisone)
- Pregnancy

Symptoms of hyperglycemia may include:

- Dehydration and excessive thirst
- Anorexia and unexplained weight loss in persons under 40 years old
- Polyuria (frequent urination)
- Fruity breath
- Lethargy, weakness, flu symptoms, and coma if untreated
- Vision problems
- Ketoacidosis—can be determined by testing urine for acetone

Treatment of acute hyperglycemia includes:

- IV fluids to correct electrolyte imbalance
- *Regular* insulin added to IV fluids

Interactions: Insulin action is antagonized by corticosteroids or epinephrine, necessitating increased insulin dosage. Oral contraceptives and estrogen may also increase insulin requirements. Beta-blockers with insulin poses risks of hypoglycemia or hyperglycemia and can mask the signs and symptoms (especially tachycardia) of hypoglycemia. Thiazolidinediones (Actos, Avandia) with insulin results in an increased risk of heart failure and edema.

Interactions of insulin with *potentiation* of *hypoglycemic* effect include:

Alcohol

Monoamine oxidase inhibitors (MAOIs)

Salicylates

Anabolic steroids

Hypoglycemia

Hypoglycemia, or lowered blood glucose, may result from:

Overdose of insulin

Delayed or insufficient food intake (e.g., dieting)

Excessive or unusual exercise

Change in type of insulin, for example, from analog to human insulin

Symptoms of hypoglycemia may develop suddenly, and are manifested usually at peak of insulin action, including:

Increased perspiration, pallor, hunger, nausea, and vomiting

Irritability, confusion, or bizarre behavior

Tremor, weakness, headache, or tingling of the fingers

Blurred or double vision

Tachycardia, shallow breathing

Loss of consciousness and convulsions if untreated

Hypoglycemic reactions in older diabetics may mimic a CVA (cerebrovascular accident)

Treatment of hypoglycemia includes:

If conscious, administration of 4 oz orange juice, candy, honey, or syrup (especially sublingual for faster absorption). After initial treatment, provide a protein snack, for example, peanut butter, cheese, or glass of milk. Then recheck blood glucose.

If comatose, administration of 10–30 mL of 50% dextrose solution IV or administration of 0.5–1 unit of glucagon (1 mg) IM or IV—follow with carbohydrate snack when patient awakens to prevent secondary hypoglycemia.

Avoid giving excessive amounts of sugar or frequent overdoses of insulin, which can result in rebound hyperglycemia (Somogyi effect) from an accelerated release of glucagon. Treatment of rebound hyperglycemia involves reduction of insulin dosage with continuous monitoring of blood glucose.

Oral Antidiabetic Agents

Type 2 diabetes results from insulin resistance combined with relative insulin deficiency. Patients may sometimes be treated with diet alone; that is, low-calorie, low-fat diet, avoiding simple sugars and alcohol, and substituting complex carbohydrates, such as whole grain bread and cereals, brown rice, and vegetables high in fiber. Frequently it is necessary to combine diet and oral antidiabetic agents. Oral antidiabetic agents may be administered as a single daily dose before breakfast, or two divided doses daily, before morning and evening meals. These medications are not a substitute for dietary management. Weight reduction and modified diet are still considered the principal therapy for the management of Type 2 diabetes.

Symptoms of Type 2 diabetes may include:

Excessive weight gain after age 40

Excessive thirst (polydipsia)

Excessive urination (polyuria)

Excessive weakness, poor circulation, and slow healing

Visual problems

Oral antidiabetic agents are available in several pharmacological classes with differing mechanisms of action, offering different avenues for reducing glucose levels. Because they work at different sites, they are often synergistic; some may be used in combination with one another or with insulin.

Sulfonylureas

The oral hypoglycemic drugs known as **sulfonylureas** consist of first-generation agents (e.g., chlorpropamide, tolbutamide) and second-generation agents (e.g., glipizide, glyburide). The second-generation agents have mostly replaced the first-generation agents because of higher potency, shorter duration of action, better tolerance, and fewer drug interactions. The sulfonylureas work by increasing insulin production from the pancreas and by improving peripheral insulin activity.

Side effects of sulfonylureas may include:

- Gastrointestinal (GI) distress (may subside with dosage regulation)
- Dermatological effects, including pruritus, rash, urticaria, or photosensitivity
- Hepatic dysfunction, including jaundice (rare)
- Weakness, fatigue, lethargy, vertigo, and headache
- Blood dyscrasias, including anemia
- Hypoglycemia, especially in older adults
- Possible increased risk of cardiovascular death—controversial
- Weight gain

Contraindications or extreme caution with sulfonylureas applies to:

Debilitated or malnourished patients

Impaired liver and kidney function

Unstable diabetes or Type 1 diabetes

Major surgery, severe infection, and severe trauma

Contraindicated with the older adults—chlorpropamide, which has a longer half-life, greater chance of hypoglycemia, and also a risk of inappropriate antidiuretic hormone secretion (water intoxication)

Interactions of sulfonylureas with *potentiation* of hypoglycemic effect can include:

Beta-blockers, MAOIs, or probenecid

Alcohol with facial flushing (disulfiram-like reaction)

Cimetidine, miconazole, fluconazole, or sulfonamides

Salicylates and other nonsteroidal anti-inflammatory drugs (NSAIDs)

Interactions with antagonistic action (larger dose may be required)

Thyroid hormones

Thiazide and nonthiazide diuretics

Corticosteroids and phenothiazines

Estrogens and oral contraceptives

Calcium channel blockers

Rifampin and isoniazid

When these agents are administered or discontinued in patients receiving sulfonylureas, the patient should be observed closely for loss of diabetic control.

Alpha-Glucosidase Inhibitors

Alpha-glucosidase inhibitors such as acarbose (Precose) delay digestion of complex carbohydrates (e.g., starch) and subsequent absorption of glucose, resulting in a smaller rise in blood glucose concentrations following meals. Acarbose is often used as part of a combination regimen that includes an oral sulfonylurea.

Side effects of alpha-glucosidase inhibitors may include:

High rate of GI effects (flatulence, abdominal distention/pain, loose stools), which tend to diminish with time or a reduction in dose; take at the start (with the first bite) of main meals

Elevated liver enzymes, which are dose-related, generally asymptomatic, and reversible

Contraindications or extreme caution with alpha-glucosidase inhibitors applies to:

Impaired liver and kidney function

Patients with inflammatory bowel disease or intestinal obstruction

Pregnancy, lactation, use in children

Drug interactions with alpha-glucosidase inhibitors include:

Digestive enzymes (effect of acarbose reduced)

Digoxin (reduced serum digoxin concentrations)

Estrogens and oral contraceptives (impaired glucose tolerance)

Biguanides

The biguanides, for example metformin (Glucophage), work by decreasing hepatic glucose output and enhancing insulin sensitivity in muscle. Metformin can be used as initial first-line monotherapy or in combination with sulfonylureas to treat Type 2 diabetics.

Side effects of biguanides may include:

- GI effects (diarrhea, nausea, vomiting, bloating, flatulence, anorexia, weight loss), which are generally mild and resolve during treatment; can take with food to minimize epigastric discomfort

  Lactic acidosis (a rare, but serious metabolic complication) in patients with history of ketoacidosis, severe dehydration, cardiorespiratory insufficiency, renal dysfunction, and chronic alcoholism with liver damage

- Hypoglycemia—rare when used without sulfonylureas or insulin

Contraindications or extreme caution with biguanides applies to:

Impaired liver and kidney function

Patients with heart failure

Administration of radiocontrast dye (could result in acute alteration of renal function); withhold metformin prior to tests with radioactive dye

Pregnancy, lactation, children, and the older adult (especially those who are frail, anorexic, or underweight)

Drug interactions with biguanides include:

Increased metformin effect seen with alcohol, cephalexin, and cimetidine

Radiopaque contrast media (hold metformin the day of and at least 48 h after administration)

Incretin Therapies

Two naturally occurring hormones (incretins) called GIP and GLP-1 have been identified and are released by cells in the GI tract in response to food. GIP activation suppresses the release of glucagon by the pancreas while GLP-1 activation stimulates insulin secretion in order to maintain glucose homeostasis. A problem in Type 2 diabetes is that an enzyme, DPP-4, rapidly inactivates GLP-1, which is already reduced in patients with impaired glucose tolerance. Agents that mimic the actions of incretin hormones may be beneficial therapeutic options.

Exenatide (Byetta), a GLP-1 receptor agonist given *subcutaneously* twice daily, mimics the action of the incretin GLP-1, resulting in enhanced glucose-dependent insulin secretion by pancreatic beta-cells. It also decreases glucagon secretion, delays gastric emptying time, and decreases food intake (increases satiety).

Exenatide is indicated as adjunctive therapy for Type 2 patients who have not achieved glycemic control and are taking metformin, a sulfonylurea, or both. Common **side effects** include nausea/vomiting, diarrhea, dyspepsia, gastroesophageal reflux, and hypoglycemia (when given in combination

with sulfonylureas). It is not recommended for use in patients with severe renal disease.

Sitagliptin (Januvia), given orally once daily, inhibits the enzyme DPP-4, which increases levels of GLP-1 and GIP. This leads to increased insulin secretion, decreased hepatic glucose production, and slowed gastric emptying time. Sitagliptin has generally been weight-neutral and may potentially improve beta-cell function.

Sitagliptin is indicated for use as monotherapy in Type 2 patients or in combination with metformin or a thiazolidinedione when adequate glycemic control has not been achieved. Common **side effects** include abdominal pain, diarrhea, nausea, vomiting, upper respiratory tract infection, and nasopharyngitis. Dosage adjustments are required for renal disease. Monitor patients receiving digoxin when starting sitagliptin.

Meglitinides

Nateglinide (Starlix) and repaglinide (Prandin) stimulate beta cells of the pancreas (via a different receptor than sulfonylureas) to produce insulin. They can be used as monotherapy or in combination with metformin. The combined use of meglitinides with sulfonylureas is not considered justified as both drug classes stimulate insulin secretion.

Side effects of meglitinides may include:

- GI effects (nausea/vomiting, diarrhea, constipation, dyspepsia)
- Hypoglycemia; initial weight gain
- Upper respiratory infection (URI), sinusitis, arthralgia, headache

Contraindications or extreme caution with meglitinides applies to:

Diabetic ketoacidosis

Impaired liver function

Pregnancy, lactation, use in children

Drug interactions with meglitinides include:

Refer to listing under sulfonylureas

Administer repaglinide before meals to maximize absorption

Gemfibrozil (Lopid) may enhance or prolong effects

Thiazolidinediones

Pioglitazone (Actos) and rosiglitazone (Avandia) lower blood glucose by decreasing insulin resistance/improving sensitivity to insulin in muscle, liver, and adipose tissue. They can be used as monotherapy or concomitantly with a sulfonylurea, insulin, or metformin.

Product labeling for both pioglitazone and rosiglitazone includes Black Box warnings regarding the potential for these agents to cause or exacerbate congestive heart failure in some patients, and both are contraindicated with class III or IV heart failure. In addition, a Black Box warning for the potential increase in myocardial ischemia risk has been added to rosiglitazone's label,

although the warning also states that the data concerning increased risk of myocardial ischemia are inconclusive.

Side effects of thiazolidinediones may include:

- Weight gain, fluid retention, edema (Report weight gain over 6.6 lb, sudden onset of edema, or shortness of breath.)
- URI, sinusitis, pharyngitis, headache
- Myalgia
- Anemia
- Hypoglycemia (in combination with insulin or oral hypoglycemics)

Contraindications or extreme caution with thiazolidinediones applies to:

Chronic renal insufficiency

Impaired liver function

Heart failure (causes edema)

May cause resumption of ovulation in premenopausal patients, increasing risk for pregnancy

Pregnancy, lactation, use in children

Note

Conflicting studies have posed the question of possible increased risk of heart attacks in those using rosiglitazone (Avandia). The FDA has ordered further studies in 2010 to reconsider whether this drug should remain on the market. This concern does not apply to pioglitazone (Actos).

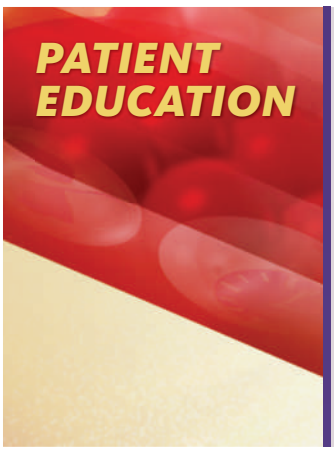
Drug interactions with thiazolidinediones include:

Pioglitazone with oral contraceptives (reduced effectiveness of the contraceptive)

Rosiglitazone with nitrates (increased risk of myocardial ischemia)

"Azole" antifungals (potentiation of hypoglycemic effect)

See Table 23-4 for a summary of the oral hypoglycemics.



Both types of diabetics should be instructed regarding:

- The importance of control with proper drug and diet therapy and *never* skipping meals.
- Early symptoms and treatment of hypoglycemia—carrying ready source of carbohydrate (e.g., lump sugar or candy); orange juice, 4 oz, is also appropriate
- Properly balanced diet (i.e., restricted calories; avoidance of simple sugars, alcohol, and foods high on the Glycemic Index (e.g., white bread, white potatoes, and white rice). Substitute foods low on the Glycemic Index—complex carbohydrates, such as

whole-grain breads and cereal, and brown rice. Reduce fats, increase fiber, and be sure to have an adequate fluid intake.

Regular exercise and maintenance of proper body weight; weight reduction if obese

Importance of reporting to a physician *immediately* if nausea, vomiting, diarrhea, or infections occur (IV fluids may be required to prevent dehydration and acidosis)

Good foot care to reduce chance of infections

Carrying identification card and wearing identification tag

Taking medication (oral or insulin) at approximately the same time each day

Check blood glucose as directed by the physician, especially with hypoglycemia or stress

For Type 1 diabetics (those requiring insulin), the foregoing instructions are important, as well as these additional rules:

Rotate injection sites (Figure 23-1). Insulin is absorbed more rapidly in arm or thigh, especially with exercise. Inject insulin into abdomen if possible for most consistent absorption.

Maintain aseptic technique with injections.

Have someone check the amount of insulin in the syringe before injection, especially with older adults or those with vision impairment (retinal problems are common in diabetics).

Check all insulin for expiration date.

Check regular insulin for clearness; do *not* give if cloudy or discolored.

Rotate isophane insulin vials to mix contents; do *not* give if solution is clear or clumped in appearance after rotation; do not shake the vial; rotate gently between hands (Figure 23-2).

If regular insulin is to be mixed with NPH, draw regular insulin into syringe first.

Unopened vials of insulin should be stored at 2–8°C and should not be subjected to freezing. The vial in use may be stored at room temperature without loss of potency for 28 days.

Avoid exposure of insulin to extremes in temperature or direct sunlight. Do not put vial in glove compartment, trunk, or suitcase.

Regular insulin is sometimes administered as correction for elevated blood glucose readings as ordered by a physician.

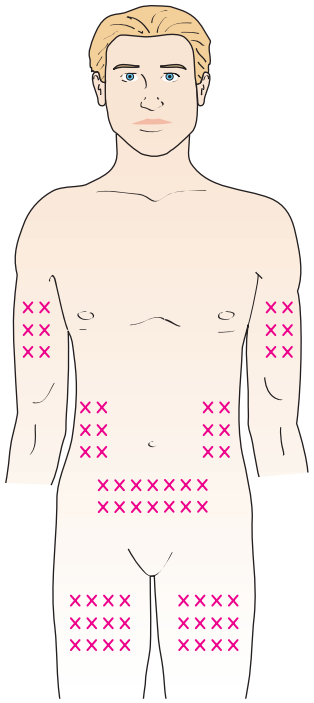
Notify physician of illness, increased stress, or trauma. *More* insulin may be required under these circumstances.

Notify physician if you increase your exercise significantly, or if you are taking less than the usual amount of food. *Less* insulin may be required under these circumstances.

Table 23-4 Oral Antidiabetic Agents

GENERIC NAME	TRADE NAME	USUAL DOSAGE
First-Generation Sulfonylureas		
chlorpropamide		100–500 mg per day w/meal (do not use for older adults)
tolbutamide		250–3,000 mg per day or divided
Second-Generation Sulfonylureas		
glimepride	Amaryl	1–8 mg per day w/meal
glipizide	Glucotrol	2.5–40 mg per day ac or divided
	Glucotrol XL	5–20 mg per day w/meal
glyburide	Diabeta	1.25–20 mg per day or divided w/meal
	Glynase	1.5–12 mg per day w/meal
Alpha-Glucosidase Inhibitors		
acarbose	Precose	25–100 mg TID, w/first bite of meal
miglitol	Glyset	
Biguanides		
metformin	Glucophage	500–2,550 mg per day divided w/meals
	Glucophage XR	500–2,000 mg per day w/pm meal or divided
Incretin Therapies		
exenatide	Byetta	*subcu* 5–10 mcg BID ac (am & pm meal)
sitagliptin	Januvia	PO 50–100 mg daily
Meglitinides		
nateglinide	Starlix	60–120 mg TID ac
repaglinide	Prandin	0.5–4 mg BID 2–4 × per day ac
Thiazolidinediones		
pioglitazone	Actos	15–45 mg per day
rosiglitazone	Avandia	4–8 mg per day or BID divided
Combinations		
glyburide/metformin	Glucovance	1.25/250–20/2,000 mg per day or BID w/meals
rosiglitazone/metformin	Avandamet	2/500–8/2,000 mg per day w/meals or divided
sitagliptin/metformin	Janumet	50/500–50/1,000 mg BID w/meals

Note: In older adults, start with the lowest dose possible and titrate upward to desired glycemic control.



Delmar/Cengage Learning

FIGURE 23-1 Common sites for insulin injection. Sites should be rotated and the site recorded each time on the medication record.

Delmar/Cengage Learning

FIGURE 23-2 Rotate isophane and zinc insulin vials gently to mix contents. Do not shake.

CASE STUDY – A

Endocrine System Drugs

Lois Lane, a 65-year-old patient with glaucoma, asks the physician for prednisone tablets to take long term for osteoarthritis in her knees. She needs the following information.

1. Corticosteroids for severe flare-ups of joint pain are usually administered
- a. By mouth
- b. Topically
- c. Intramuscularly
- d. Intra-articularly

2. The *usual* type of administration of corticosteroids include any of the following EXCEPT
- a. Step-down
- b. Ongoing
- c. Alternate-day
- d. Short-term

3. The following are possible long-term corticosteroid side effects EXCEPT
- a. Osteoporosis
- b. Decreased intraocular pressure
- c. Fluid retention
- d. Gastric bleeding

4. Other side effects can include all of the following EXCEPT
- a. Headache
- b. Anxiety
- c. Sedation
- d. Slow healing

5. Corticosteroids can be used to treat all of the following EXCEPT
- a. Asthma attack
- b. Poison ivy
- c. Organ transplant
- d. Fungal infection

CASE STUDY – B

Antidiabetic Agents

Hope Moore, a 70-year-old Type 2 diabetic, has been taking tolbutamide for 6 years. Her blood glucose is now elevated, and the physician plans to start her on insulin. She will need the following information.

1. The following is true of NPH insulin EXCEPT
- a. Peaks in 6–12 hrs
- b. Can be Humulin N
- c. Used for sliding scale
- d. Acts in 1–3 hours

2. Signs of hypoglycemia can include the following EXCEPT
- a. Tremor
- b. Dehydration
- c. Confusion
- d. Blurred vision

3. Treatment of hypoglycemia could include any of the following EXCEPT
- a. 4 oz orange juice
- b. Candy
- c. Diet cola
- d. Glucagon IM

4. If vomiting and diarrhea occur, the following might be necessary EXCEPT
- a. Decrease insulin
- b. IV fluids
- c. Regular insulin IV
- d. NPH insulin subcu

5. The following is true of regular and NPH insulins EXCEPT
- a. Can be mixed
- b. Rotate injection sites
- c. Keep at room temperature
- d. Both are cloudy

CHAPTER REVIEW QUIZ

Match the medication in the first column with the appropriate classification in the second column. Classifications may be used more than once.

Medication	Classification
1. _____ Glucophage	**a.** Thyroid agent
2. _____ Prednisone	**b.** Antithyroid
3. _____ Humulin R	**c.** Oral Antidiabetic agent
4. _____ Synthroid	**d.** Corticosteroid
5. _____ Avandia	**e.** Insulin–Rapid acting
6. _____ Tapazole	**f.** Insulin–Short acting
7. _____ Isophane	**g.** Insulin–Intermediate acting
8. _____ Prandin	**h.** Insulin–Long acting
9. _____ Lantus	
10. _____ Humalog	

Choose the correct answer.

11. Which is NOT a side effect of long-term corticosteroid use?
    a. Skin thinning **c.** Insomnia
    b. Easy bruising **d.** Hypoglycemia
12. *Corticosteroids should be used with caution* for patients with a history of all of the following conditions EXCEPT:
    a. Congestive heart failure **c.** Asthma
    b. Gastric ulcers **d.** Psychosis
13. Thyroid medication would be prescribed for all of the following EXCEPT:
    a. After thyroidectomy **c.** Cretinism
    b. Weight reduction **d.** Goiter
14. Which is NOT true of treatment with thyroid medication?
    a. Monitored with blood tests **c.** Short-term use
    b. Overdose causes tachycardia **d.** Insulin interactions
15. Which is NOT true of treatment with antithyroid medication?
    a. Before surgery **c.** Short-term use
    b. Used for older adults **d.** Rash possible
16. Which is NOT true of regular insulin?
    a. Combines with NPH **c.** Short action
    b. Given IV **d.** Cloudy

17. Which is NOT true of Aspart and Lispro insulins?
- **a.** Ultra-rapid acting
- **b.** Short duration
- **c.** Long duration
- **d.** Clear

18. Which is NOT true of NPH insulin?
- **a.** Used as correction insulin
- **b.** Combines with Regular
- **c.** Intermediate action
- **d.** Cloudy

19. Which is NOT part of first-line treatment for patients with Type 2 diabetes?
- **a.** Low-calorie diet
- **b.** Oral antidiabetic agents
- **c.** High-fiber diet
- **d.** Insulin

20. Which oral antidiabetic agent is contraindicated for the older adults?
- **a.** Glucophage
- **b.** Chlorpropamide
- **c.** Prandin
- **d.** Avandia

Go to your StudyWARE™ CD-ROM and have fun learning as you play games and answer case study-related questions to help reinforce key concepts you learned in this chapter.

Go to your Study Guide and complete the review questions for this chapter.

Chapter 24

Reproductive System Drugs

Objectives

Upon completion of this chapter, the learner should be able to

1. Identify the uses, side effects, and precautions for the androgens
2. List the uses, side effects, and contraindications for the estrogens and progestins
3. Compare and contrast contraceptives
4. Describe the use of oxytocics and the precautions to be observed
5. Explain the uses of terbutaline, prostaglandins, and magnesium sulfate
6. Describe the uses of GnRH analogs
7. Explain drug therapy for impotence
8. Present appropriate patient education for all drugs in this section
9. Define the Key Terms and Concepts

Key Terms and Concepts

Androgens

Contraceptives

Estrogen

Follicle-stimulating hormone (FSH)

Luteinizing hormone (LH)

Luteotropic hormone (LTH)

Oxytocin

Progesterone

Progestins

Testosterone

Hormones that regulate the functions of the reproductive systems include *endogenous* chemical substances, which originate within different areas of the body. For the purpose of simplification, we will divide the reproductive hormones into four main categories: gonadotropic, androgens, estrogens, and progestins.

The pituitary gland is located at the base of the brain. The anterior lobe secretes four hormones. Those affecting growth, thyroid function, and adrenocorticosteroid production are discussed in Chapter 23. This chapter includes the gonadotropic hormones, which are secreted by the anterior and posterior pituitary lobes.

The gonadotropic hormones include (1) **follicle-stimulating hormone (FSH)**, which stimulates development of ovarian follicles in the female and sperm production in the testes of the male; (2) **luteinizing hormone (LH)**, which works in conjunction with FSH to induce secretion of estrogen,

ovulation, and development of corpus luteum; and (3) **luteotropic hormone (LTH)**, which stimulates the secretion of progesterone by the corpus luteum and secretion of milk by the mammary gland, hence the term *lactogenic hormone*.

ANDROGENS

Androgens, the male hormones, are secreted mainly in the interstitial tissue of the testes in the male and secondarily in the adrenal glands of both sexes. Androgens, which stimulate the development of male characteristics (masculinization), include **testosterone** and androsterone. Inadequate production of androgens in the male may be due to pituitary malfunction or to atrophy, injury to, or removal of the testicles (castration), resulting in eunuchism or eunuchoidism. Eunuchoid characteristics include retarded development of sex organs, absence of beard and body hair, high-pitched voice, and lack of muscular development. Hypogonadism may also result in impotence or deficient sperm production (oligospermia).

Uses of androgens include:

Replacement in cases of diminished testicular hormone with testosterone (e.g., impotence, oligospermia, or andropause [“male menopause”])

Congenital hypogonadism (e.g., cryptorchidism or undescended testicles) or delayed puberty in the male

Acquired hypogonadism (e.g., orchitis, trauma, tumor, radiation, surgery of the testicles, or drug-induced)

Palliative treatment of females with advanced metastatic (skeletal) carcinoma of the breast, for example, methyltestosterone

Endometriosis and fibrocystic breast disease, for example, danazol

Side effects of androgens can include:

- Edema (diuretics may be indicated)
- Acne, increased oiliness of skin and hair, or alopecia

Oligospermia (deficient sperm production resulting in sterility)

Increased or decreased sexual stimulation or libido, impotence

Gynecomastia in males (enlarged breast tissue)

Hirsutism (excessive or unusual growth of hair), deepening of voice, and amenorrhea in females

- Jaundice and hepatitis

Nausea and vomiting

- Premature closure of bone ends in adolescents, with stunting of growth
- Anxiety, depression, headache

Increased low-density lipoprotein (LDL), decreased high-density lipoprotein (HDL), and insulin resistance

Contraindications or caution with androgens applies to:

Cardiac, renal, and liver dysfunction (edema common)

Men suspected of having carcinoma of the prostate or breast cancer (stimulates growth of cancerous tissue)

Geriatric males (may increase risk of prostatic hypertrophy and carcinoma or overstimulation sexually)

Prepubertal males who have not reached their full growth potential (may stunt growth by premature closure of bone ends)

Diabetes, obesity, or dyslipidemia (abnormal lipid profile)

Interactions of androgens may occur with:

Oral anticoagulants (potentiation may cause bleeding)

Decreased blood glucose and decreased insulin requirements in diabetics

Antiandrogens (dutasteride, finasteride)

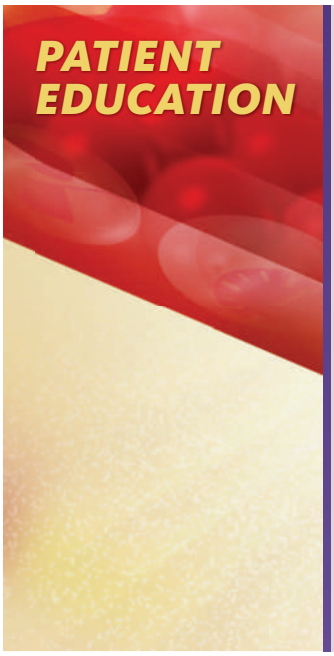
Dangers of illegal use of anabolic steroids: Health care personnel have a responsibility to caution athletes, especially adolescents, regarding the hazards of taking illegal synthetic testosterone products to build muscle power or physique. Besides the *potentially serious adverse side effects* just mentioned, another risk is *the development of psychosis* with delusions, paranoia, depression, mania, and aggression with violence.

All agents in this class are classified as a controlled substance (C-III) by the DEA due to abuse potential.

See Table 24-1 for a summary of the androgen agents.

Table 24-1 Androgen Agents

GENERIC NAME	TRADE NAME	DOSAGE	USES
danazol	Danocrine	100–400 mg BID	Endometriosis, fibrocystic breast disease
methyltestosterone	Android, Testred	PO, buccal dose varies	Advanced breast cancer; replacement therapy
with estrogen	Estratest	PO, dose varies	Menopausal symptoms if estrogen alone insufficient
oxandrolone	Oxandrin	PO 2.5–20 mg per day div doses	Treatment of cachexia
testosterone	Depo-Testosterone	Deep IM, pellet implant, buccal; dose varies	Hypogonadism, advanced breast cancer
	Androderm	Patch	
	AndroGel	Transdermal gel	



Patients on androgen therapy should be instructed regarding:

- Taking only prescribed drugs according to directions
- Side effects to report, especially edema, jaundice, nausea, or vomiting
- Sexual effects for males to report, such as decreased ejaculatory volume and excessive sexual stimulation, especially in geriatric patients beyond cardiovascular capacity
- Sexual effects for females to expect (e.g., hirsutism and voice deepening)
- Possibility of stunted growth when administered to adolescent boys before puberty
- To avoid secondary exposure of children, adults who use testosterone gels should wash their hands with soap and warm water after every application and cover the application site with clothing once the gel has dried.

ERECTILE DYSFUNCTION MEDICATIONS

Phosphodiesterase (PDE) inhibitors are a class of drugs given orally for the treatment of male erectile dysfunction (ED), also referred to as impotence. This represents a significant advance as other therapies require direct injection into the penis or insertion of a urethral suppository. Sildenafil (Viagra) was the first PDE inhibitor approved to treat ED, followed by vardenafil (Levitra) and tadalafil (Cialis). These medications require sexual arousal for success.

Side effects of PDE inhibitors can include:

- ! Headache, flushing, vision abnormalities, dizziness
- ! Hearing loss, tinnitus
- Dyspepsia, nasal congestion, rhinitis, diarrhea, rash, back pain
- ! Cardiovascular events (less than 2% of patients) including angina, syncope, tachycardia, palpitation, and hypotension

Contraindications and warnings with PDE inhibitors applies to:

- Concurrent use of nitrates or alpha-blockers (e.g., Flomax, Cardura) with PDE inhibitors potentiates the hypotensive effects
- In the event of an erection persisting > 4 h, advise patient to seek medical assistance immediately (tissue damage and permanent loss of potency may result)
- Older adults and patients with preexisting cardiovascular risk factors
- Hepatic/renal function impairment

Table 24-2 Erectile Dysfunction (ED) Agents

IMPOTENCE AGENTS	TRADE NAME	STARTING DOSE	COMMENTS
sildenafil	Viagra	50 mg PO 1 h before sexual activity (max freq once daily)	Treatment of erectile dysfunction (has no effect in the absence of sexual stimulation)
tadalafil	Cialis	10 mg PO before sexual activity (max freq once q24 h) 2.5 mg PO daily	Onset of action is 30 min; duration is up to 36 h Without regard to timing of sexual activity
vardenafil	Levitra	10 mg PO 1 h before sexual activity (max freq once daily)	

Interactions with PDE inhibitors include:

Nitrates, antiarrhythmics, antiretroviral protease inhibitors, macrolides, quinolones, some antifungals (potentiate/prolong hypotensive effect)

Grapefruit juice—use with caution (may potentiate hypotensive effect)

See Table 24-2 for a summary of the erectile dysfunction (ED) agents.

ESTROGENS

Estrogens, the female sex hormones, are produced mainly by the ovary and secondarily by the adrenal glands. Estrogens are responsible for the development of female secondary sexual characteristics, including breast enlargement, and during the menstrual cycle they act on the female genitalia to produce an environment suitable for fertilization, implantation, and nutrition of the early embryo. Estrogens also affect the secretion of the hormones FSH and LH from the anterior pituitary gland in a complex way. This results in inhibition of lactation and inhibition of ovulation, the latter process utilized in contraceptive therapy.

Estrogen in combination with testosterone is sometimes used in the management of severe menopausal symptoms that do not respond to estrogen alone.

Estrogen therapy (ET), that is, estrogen alone, has been associated with an *increased risk of endometrial carcinoma* in women with an intact uterus. When progestin is combined with estrogen (*combined hormone therapy [HT]*), the risk of endometrial cancer is substantially reduced.

In 2002, the results of the Women's Health Initiative (WHI) study were released. The main thrust of the WHI study was to determine the exact degree to which hormone therapies (HTs) presumably protected the heart and to investigate the degree to which some of the known and potential risks of HTs, such as breast cancer and blood clots, cancelled out any benefits. The WHI also explored whether HTs prevented fractures, colon cancer, and dementia, including Alzheimer's disease.

The WHI study authors announced not only that the risks of *combined HT* outweighed its benefits when used to prevent certain diseases, but it could actually *increase the risk* of certain conditions it was previously believed to prevent, such as heart attack. The American College of Obstetricians and Gynecologists (ACOG) have issued the following recommendations regarding HT:

1. *Combined HT should not be used* for prevention of diseases such as cardiovascular disease, due to the small but significant *increased risk of conditions such as breast cancer, heart attack, stroke, and blood clots;*
2. *Estrogen-alone therapy* used for women who have had a hysterectomy *should not be used for the prevention of diseases, due to the increased risks of blood clots and stroke. Although ET carries fewer risks than combined HT, women with a uterus should not use estrogen alone due to their increased risk of uterine cancer;*
3. HTs are still the most effective therapies and are appropriate for the relief of moderate to severe vasomotor symptoms, so long as a woman has weighed the risks and benefits with her doctor; and
4. Women on combined HT or ET should take the *smallest effective dose for the shortest possible time (preferably ⩽ 5 years) and annually review the decisions to take hormones.*

The WHI studies, designed to examine the risk-benefit profile associated with hormone therapy, have generated considerable confusion as well as controversy, and their results may not apply to younger, symptomatic menopausal women and those who use alternative regimens (low dose, transdermal delivery). Although further study is needed, emerging evidence suggests that risks for blood clots *may* be lower in women at risk for such problems using lower doses and transdermal delivery of hormones rather than the standard-dose oral conventional regimen used in the WHI studies. One reason may be that pills are broken down in the liver, where proteins involved in the formation of blood clots are activated. The estrogens in skin patches are released directly into the blood stream, bypassing the liver completely. Research is ongoing, and the American College of Obstetricians and Gynecologists (ACOG) recommendations may change. Please refer to their Web site (www.acog.org) for updated information.

Uses of estrogen therapy include:

Contraceptives (combined with progestin)—these combination products are also used to treat menstrual irregularities and dysmenorrhea (painful menstruation)

Menopausal vasomotor symptom relief

Female hypogonadism due to ovarian pathology or oophorectomy (ovary removal)

Postmenopausal prevention of osteoporosis (secondary to estrogen deficiency) *only* if unable to take other agents, and benefits outweigh the risks

Postmenopausal estrogen replacement may reduce cardiovascular heart disease and elevate the HDL levels in younger (50–59 years) women. (Conflicting studies)

Atrophic vaginitis from decreased secretions—low-dose vaginal cream biweekly

Postcoital use after rape or incest (within 24–48 h) of a single large dose to prevent, not terminate, pregnancy.

Palliative treatment for males with advanced, inoperable prostate cancer

Side effects of estrogen therapy, especially with high doses, can include:

- Increased risk of thromboembolic disorders, hypertension, myocardial infarction, and stroke

GI effects, including vomiting, abdominal cramps, bloating, diarrhea or constipation, and weight gain

Skin discolorations (acne may decrease or occasionally increase)

Fluid retention and edema

Increased serum triglyceride levels

Severe hypercalcemia in cancer patients with large doses

Folic acid deficiency (may require folic acid supplements)

Liver function abnormalities, including jaundice, anorexia, and pruritus

Breakthrough or irregular vaginal bleeding

Increased risk of cervical erosion and *Candida* vaginitis

- Headache, especially migraine, and depression

Visual disturbances

Breast tenderness, enlargement, and secretion

- Increased risk of gallbladder disease
- Cancer of the uterus with estrogen alone. Therefore, progesterone is recommended with estrogen. (See Women's Health Initiative study and recommendations at the beginning of this section.)

Contraindications and cautions exist because the use of estrogens, especially in large doses, may be associated with increased risk of several serious conditions. Before estrogen therapy is begun, a complete history and physical examination are essential, and yearly physicals, including Pap test and mammogram, during therapy are important. Estrogens are contraindicated for anyone with a history of the following conditions, and estrogen therapy should be *discontinued with signs of these conditions*:

Hypertension, thromboembolic disorders (DVT, PE), stroke, and myocardial infarction

Liver dysfunction

Breast cancer (except for palliative treatment)

Undiagnosed vaginal bleeding

Visual disturbances, severe headaches, and migraine

Shortness of breath, chest or calf pain

Pregnancy

Other cautions for estrogens include the following:

Prolonged, continued use of high-dose estrogens in postmenopausal women, which has shown an increased risk of endometrial cancer in some studies; therefore, cyclic administration at the *lowest* possible dose, is recommended with progesterone. Regular physical examinations, including a Pap test every year are also recommended.

Pregnancy, in which estrogens can cause serious fetal toxicity, congenital anomalies, and vaginal or cervical cancer for the offspring in later life. Estrogens should *never* be used to treat threatened abortions or if there is any possibility of pregnancy. A pregnancy test should be done before initiating therapy.

Nursing mothers should avoid estrogen.

Caution with diabetes and with heavy smokers

Interactions of estrogen include the following:

Rifampin and isoniazid decrease estrogenic activity, and therefore other forms of contraception should be used with patients receiving rifampin or isoniazid.

Corticosteroid effects are potentiated by estrogen.

Laboratory test interference includes endocrine function tests, decreased glucose tolerance, and thyroid function tests.

Anti-infectives may decrease contraceptive action.

Oral anticoagulant, anticonvulsant, and hypoglycemic actions may be decreased with estrogen.

Sunscreens with estradiol topical emulsion (increases absorption)

PROGESTINS

Progesterone is a hormone secreted by the corpus luteum and adrenal glands. It is responsible for changes in uterine endometrium in the second half of the menstrual cycle in preparation for implantation of the fertilized ovum, development of maternal placenta after implantation, and development of mammary glands. Synthetic drugs that exert progesterone-like activity are called **progestins**.

Uses of synthetic progestins include:

Treatment of amenorrhea and abnormal uterine bleeding caused by hormonal imbalance.

Contraception, either combined with estrogen or used alone.

Postmenopausal—sometimes combined with estrogen in replacement cyclical therapy. (Note the risks.)

Adjunctive and palliative therapy for advanced and metastatic endometrial or breast cancer (Megace). Megace is also used for the anorexia, weight loss, and cachexia associated with acquired immunodeficiency syndrome (AIDS).

Depo-Provera, 100–500 mg IM weekly to monthly has been used in the management of paraphilia (sexual deviancy in males), especially for pedophilia and sexual sadism. The drug has been shown to decrease erotic cravings, but sexual deviance usually returns following discontinuance of the drug.

Side effects of continuous progestin use can include:

- Menstrual irregularity and amenorrhea, breakthrough bleeding, and spotting
- Edema and weight gain
- Nausea
- Breast tenderness, enlargement, and secretion
- Jaundice, rash, and pruritus
- Headache and migraine
- Mental depression
- Thromboembolic disorders
- Vision disorders
- Possible decrease in bone density with prolonged use

Contraindications or cautions with progestin (similar to cautions with estrogen) apply to:

- Any condition that might be aggravated by fluid retention (e.g., asthma, seizures, migraine, and cardiac or renal dysfunction)
- History of mental depression
- History of thromboembolic disorders, especially with tobacco smoking
- History of cerebrovascular accident
- Liver disorders
- Undiagnosed vaginal bleeding
- Pregnancy (progestins are no longer used to treat threatened abortion because of the potential adverse effects to the fetus)
- Breast, cervical, uterine, vaginal cancers (except for palliative treatment)

See Table 24-3 for a summary of the estrogens and progestins. Several different estrogen-progestin combinations are commercially available. Refer to the discussion of each individual agent.

Contraceptive Agents

The use of estrogen-progestin combined hormones as a safe and effective method of birth control has been well established. They act by suppressing release of the pituitary hormones, follicle-stimulating hormone (FSH), and luteinizing hormone (LH), thus resulting in the prevention of ovulation. Additional methods of action have been suggested; that is, changes in the cervical mucus to prevent sperm penetration and changes in the endometrium or lining to the uterus to discourage implantation and cell growth.

Table 24-3 Estrogens and Progestins

GENERIC NAME	TRADE NAME[a]	DOSAGE	USES/COMMENTS
Estrogens			
estradiol	Estrace	PO, intravaginal	Menopause, prostate cancer, breast cancer, dysfunctional uterine bleeding
	Vagifem	vaginal tabs	atrophic vaginitis
	Estrasorb, EstroGel	Topical emulsion, Transdermal gel	Only for menopausal symptoms
	Estraderm, Vivelle,	Transdermal, dose varies	
	Depo-Estradiol	IM, dose varies	Female hypogonadism, prostate cancer, menopausal symptoms
conjugated estrogens	Premarin	PO, vaginal cream parenteral; dose varies with condition symptoms	Female hypogonadism, breast & prostate cancer, menopausal symptoms
esterified estrogens	Menest	PO, dose varies with condition	Female hypogonadism, breast & prostate cancer, menopausal symptoms
Progestins			
medroxyprogesterone	Provera Depo-Provera	PO tabs IM, dose varies	Abnormal uterine bleeding, menopausal symptoms, endometrial cancer, contraception
megestrol acetate	Megace, Megace ES (625 mg/5 mL daily)	PO 160–800 mg daily, div. doses	Endometrial and breast cancer, anorexia, and cachexia of AIDS
Estrogen-Progestin Combinations			
conjugated estrogens/ medroxyprogesterone	Premphase, Prempro	PO, dose varies	For menopausal symptoms
estradiol/norethindrone	CombiPatch	Transdermal, 1 patch 2× per wk (q3–4 days)	For female hypogonadism, menopausal symptoms

Note: Because of adverse side effects, estrogen and progestin products should be administered at the lowest possible dose for effectiveness.
[a]List of trade names is not all-inclusive as the number of products are too numerous to mention.

The *progestin-only* **contraceptives** prevent pregnancy by inhibiting ovulation, changing the amount or thickness of cervical mucus, thus inhibiting sperm transport, and creating a thin, atrophic endometrium not conducive to sustaining the fertilized ovum. The progestin-only preparations may be indicated for women who cannot tolerate estrogenic side effects or for whom estrogen is contraindicated. Examples would be estrogen-related headaches, or hypertension. Other indications include breast-feeding women, since *progestin has no effect on lactation or nursing infants*. Young women who have a

history of noncompliance on oral contraceptives might benefit from injections or intrauterine devices (IUDs). The failure rate for progestin-only preparations ranges from 0.1%–0.3% for injections and implants, and 2%–3% for IUDs.

Uses of *combined* or *progestin-only* contraceptives include:

Prevention of pregnancy.

Treatment and/or improvement of other medical conditions, such as endometriosis; painful, heavy periods; irregular cycles; and acne.

Other medical benefits of oral contraceptives include decreased incidence of ovarian cysts, ovarian or endometrial cancer, benign breast disease, and ectopic pregnancy. There is also a protective effect against pelvic inflammatory disease.

Minor side effects of contraceptives include:

Nausea

Increased breast size, tenderness

- Fluid retention
- Weight gain or loss
- Bleeding between periods, breakthrough bleeding

Scanty menstrual flow (considered a benefit)

Changes in libido

Mood changes

Facial discoloration

Serious side effects of estrogen can include:

- Migraine headaches or headaches increasing in frequency and severity
- Severe depression

Blurred vision or loss of vision

Absolute contraindications for estrogen products include:

Thrombophlebitis or thromboembolic disorder or history thereof

History of cerebrovascular accident

History of chest pain or MI

Known or suspected history of breast cancer or other estrogen-dependent malignancy, or preexisting cervical cancer

Pregnancy

History of liver disease or impaired liver function

In addition to the preceding contraindications, estrogen-progestin contraceptives should be used with caution in the following conditions:

Women over 35 and currently smoking 15 or more cigarettes a day

Migraine headaches that start after initiating oral contraceptives

Seizure disorder

Hypertension with resting diastolic above 90 or systolic above 140

High cholesterol

Diabetes mellitus

Undiagnosed vaginal bleeding

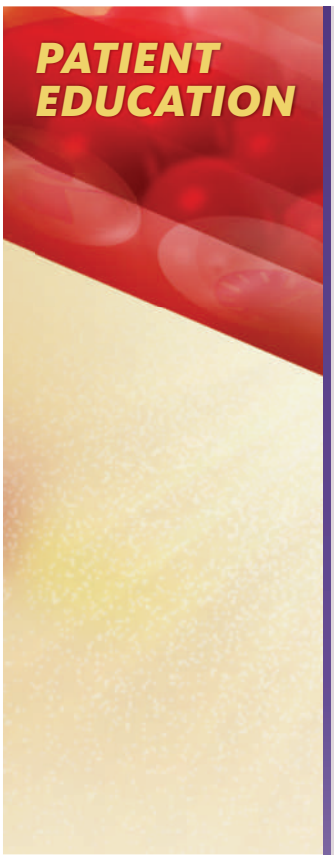
Confirmed sickle cell disease

Lactation

Oral contraceptives may accelerate development of gallbladder disease in women already susceptible

Interactions of estrogen products may occur with:

Many drugs may interact with oral contraceptives and alter the effectiveness, including pain relievers, alcohol, anticoagulants, antidepressants, tranquilizers or barbiturates, corticosteroids, antibiotics, antiretrovirals, asthma drugs, beta-blockers, anticonvulsants, oral hypoglycemic drugs, St. John's wort, and vitamin C.



PATIENT EDUCATION

Women taking oral contraceptives should be instructed regarding the use of backup contraception for the first month on oral contraceptives, and for the first 2 weeks with Depo-Provera.

- Taking the contraceptive at the same time every day. Every product comes with specific directions to follow if an oral contraceptive dose is missed. The general instruction is that the pill should be doubled up until the patient has caught up, using a backup method until period begins. If three pills or more are missed, the patient is instructed to throw away the pack until she starts her period, and then begin a new pack of pills. Stop oral contraceptives if pregnancy is suspected and stop smoking.
- Use backup contraception when taking other medicines that may alter effectiveness (see Interactions).
- Reporting the following symptoms to your health care provider should they occur while on oral contraceptives: chest pain, shortness of breath, severe headache, dizziness, weakness, numbness, eye problems, breast lumps, or severe leg pains in the calf or thigh.
- Oral contraceptives do not protect against HIV, AIDS or other sexually transmitted diseases.

CHOICE OF CONTRACEPTIVES

Estrogen-progestin oral contraceptives are available in several formulations and varieties of chemical preparations. They are usually classified according to their estrogen content and formulation as follows:

1. Monophasic preparations contain the same proportion of estrogen and progestin in each tablet.
2. Biphasic preparations contain two sequences of progestin doses and less than 50 mcg estrogen.
3. Triphasic preparations contain three sequences of progestin doses and less than 50 mcg estrogen.

Extended cycle oral contraceptives differ from traditional 21/7 products by decreasing or eliminating the hormone-free interval (HFI). Consecutive days of hormone therapy may extend to 84 or 365 days, with the HFI shortened to zero, two, or four days instead of the typical seven-day interval. Reasons for considering an extended-cycle product include decreasing the typical menstrual symptoms experienced during the HFI; improving efficacy in women who forget to restart the pill; and patient preference to decrease the frequency of menstrual-like bleeding.

Choice of a particular contraceptive will be made after considering the patient's history, hormone-related side effects, prior use, and desired effect. In general, whenever possible the smallest dose of estrogen and progestin should be used that is compatible with a low failure rate and meets the individual needs of the woman. Broad categories are listed in Table 24-2. Individual oral contraceptives are too numerous to mention in their entirety; however, a few examples in each category are included.

Progestin-Only Contraceptives

These preparations are recommended for patients who do not tolerate estrogen or in whom it is contraindicated. Choice of method of delivery (i.e., oral tablets, injection, or IUD) should be made to appropriately accommodate the patient's needs and compliance. It should be noted that use of Depo-Provera injections may be considered among the risk factors for development of osteoporosis (partially reversible upon discontinuation).

Progestin-Containing Intrauterine Device (IUD)

Mirena contains a reservoir of levonorgestrel, a synthetic progestin. It releases small amounts of progesterone daily, providing five years of continuous contraception protection. The mechanism of action of the IUD is not fully understood but is generally thought to have an inhibitory effect on sperm migration, change in the ovum transport, and alteration of the endometrium. The progestin in the IUD is thought to offer support to all of these actions.

Cautions and side effects can include:

There are many considerations, contraindications, and side effects that must be addressed when considering the IUD as a method of contraception. These are too numerous to mention in this text. The purpose of including the IUD here is to inform the reader that it is one of several delivery systems in the use of progestin as a contraceptive drug.

Postcoital Contraception

While the use of combined estrogen-progestin contraceptive pills as a means of postcoital contraception is not without risk, it is an available option to women who are exposed to an unintentional risk of pregnancy. This includes such circumstances as a broken condom, rape, defective barrier methods, lost or forgotten oral contraceptives, or any other method that is not available at the time that it is needed. When using postcoital or "morning after" contraception, it is essential that the woman's history is reviewed, that she is informed of the risks and benefits of postcoital contraception, and that she gives informed consent. It must be administered within 72 h of unprotected intercourse. Typical dosages for oral contraceptives in this instance would be Lo\Ovral, Seasonale, or Triphasil, four tablets taken in two doses, 12 h apart, for a total of eight tablets. Side effects, which include nausea and vomiting, headache, and breast tenderness, usually subside within one or two days after treatment. Again, it must be noted that postcoital contraception must be administered within 72 h of unprotected intercourse.

Plan B is the only emergency contraceptive formulation containing 2 tablets of the progestin levonorgestrel. Progestin-only emergency contraception is more effective and causes less nausea and vomiting than the oral contraceptive combinations. The first tablet should be taken as soon as possible but within 72 h after having unprotected intercourse. The second tablet must be taken 12 h after the first. Taken within three days of sexual intercourse, this medication prevents ovulation, or if ovulation has already occurred, *blocks implantation of a fertilized egg*. Plan B is currently approved for over the counter use in women of child-bearing age that are 18 years of age and older. It is a prescription drug for women 17 years of age and younger and sold behind the pharmacy counter so that age can be verified prior to dispensing.

See Table 24-4 for a summary of contraceptive agents.

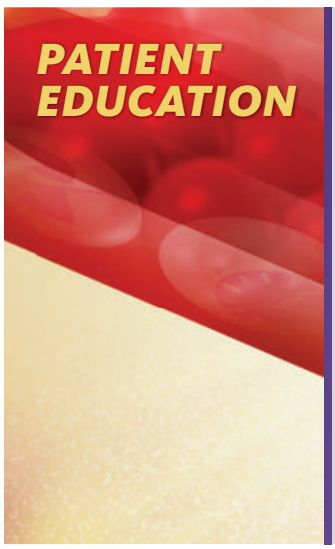
Table 24-4 Contraceptive Agents

GENERIC NAME	TRADE NAME[a]	DOSAGE	USES/COMMENTS
Monophasic Preparations			
50 mcg estrogen	Necon 1/50 Ovcon-50	PO	Contain the same proportion of estrogen and progesterone in each tablet
35 mcg estrogen	Norinyl 1/35 Ortho-Novum 1/35 Brevicon	PO	
30 mcg estrogen	Lo-Ovral Seasonale Yasmin	PO	Extended-cycle regimen
20 mcg estrogen	YAZ	PO	Extended-cycle regimen
	Lybrel		Continuous-cycle regimen
	Ortho Evra	Transdermal	1 patch q7days for 3 wk per cycle

Table 24-4 Contraceptive Agents—*continued*

GENERIC NAME	TRADE NAME[a]	DOSAGE	USES/COMMENTS
Biphasic Preparation—2 sequences progestin/1 part estrogen			
	Seasonique	PO	Extended-cycle regimen
	Mircette		Extended-cycle regimen
Triphasic Preparations—3 sequences progestin/1 part estrogen			
	Trivora	PO, dose varies	
	Ortho-Novum 7/7/7		
	Ortho-Tri-Cyclen		
Progestin-Only Preparations			
	Ortho Micronor	PO	"Mini-pill"
	Depo-Provera	IM, 150 mg q3m	
	Mirena	Intrauterine device (IUD)	
Postcoital Contraception			
	Lo/Ovral, Seasonale	PO, 4 tabs q12h for total of 8 tabs (must be administered within 72 h)	With norgestrel and levonorgestrel containing combination products (dose varies with other products)
levonorgestrel	Plan B	PO, 1 tab q12h for a total of 2 tabs	
	Plan B One-Step	PO, 1 tab single dose	Available OTC for 17+ yrs; Rx only for <=16 years old

Note: Because of adverse side effects, estrogen and progestin products should be administered at the lowest possible dose for effectiveness.
[a]List of trade names is not all-inclusive as the number of available oral contraceptives are too numerous to mention.



Patients taking estrogen, progesterone, or combinations of the two should be instructed regarding:

- Importance of following prescribed schedule with contraceptives
- Taking with or after evening meal or at bedtime, same time every day
- These products do not protect against HIV infection or other STD's
- Minor adverse effects of contraceptives, for example, edema, weight gain, nausea
- Possible serious side effects and the importance of reporting any signs of cardiovascular or kidney disorders, liver or gallbladder dysfunction, rash, jaundice, GI symptoms, visual disturbance,

severe headache, breast lumps, irregular vaginal bleeding, shortness of breath, and chest or calf pain

Increased risk of stroke or myocardial infarction (MI) for smokers

Regular breast self-examination

Complete physical examination including Pap test at least yearly

Avoidance of all estrogen or progestin products if pregnant (however, note that the American Academy of Pediatrics considers both estrogens and progestins to be generally compatible with breast feeding)

DRUGS FOR LABOR AND DELIVERY

In addition to the hormones secreted by the anterior pituitary gland, there is also a hormone secreted by the posterior pituitary lobe: **oxytocin**. This hormone stimulates the uterus to contract, thus inducing childbirth. Oxytocin also acts on the mammary gland to stimulate the release of milk. Synthetic chemicals used to stimulate uterine contractions are called *oxytocics* and include *oxytocin* and prostaglandin E_1 and E_2.

Oxytocin

Uses of oxytocin (IV infusion of dilute solutions slowly and at a carefully monitored rate) include:

Induction of labor with at-term or near-term pregnancies associated with hypertension (e.g., preeclampsia, eclampsia, or cardiovascular-renal disease), maternal diabetes, or uterine fetal death at term

Stimulating uterine contractions during the first or second stages of labor if labor is prolonged or if dysfunctional uterine inertia occurs

Pelvic adequacy and other maternal and fetal conditions must be evaluated carefully prior to induction of labor. Cesarean section may be preferable and safer in some instances.

Side effects of oxytocin can be serious, resulting even in maternal or fetal death. *Extreme caution* with administration and *constant maternal* and *fetal monitoring* are required to prevent dangerous side effects such as:

- Tetanic contractions with risk of uterine rupture

Cervical lacerations

- Abruptio placenta

Impaired uterine blood flow

Amniotic fluid embolism

- Fetal trauma, including intracranial hemorrhage or brain damage

- Fetal cardiac arrhythmias, including bradycardia, tachycardia, and premature ventricular contractions
- Fetal death due to asphyxia

With large amounts of oxytocin, watch for:

- Severe hypotension
- Tachycardia and arrhythmias
- Postpartum hemorrhage

Subarachnoid hemorrhage

Hypertensive episodes

Contraindications/cautions for oxytocin include:

Elective induction of labor merely for physician or patient convenience, which is *not* a valid indication for oxytocin use

Cephalopelvic disproportion, unfavorable fetal position or presentation

Uterine or cervical scarring from major cervical or uterine surgery

Fetal distress when delivery is not imminent

Placenta previa, prolapsed cord, and multiparity

Prolonged use with eclampsia

Prostaglandins

Prostaglandins include dinoprostone or prostaglandin E_2 (Prostin E_2, Cervidil, Prepidil) and the oral synthetic prostaglandin E_1 analog, misoprostol (Cytotec).

Uses of dinoprostone intravaginal gel or vaginal insert include:

Cervical ripening

Uses of dinoprostone vaginal suppositories include:

Therapeutic abortion in the second trimester (beyond the l2th week)

Uterine evacuation in cases of intrauterine fetal death in late pregnancy, benign hydatidiform mole, or fetuses with acephaly, erythroblastosis fetalis, or other congenital abnormalities *incompatible with life*

Side effects of prostaglandins can be minimized by administration of a prior test dose and symptomatic treatment of such effects as:

- GI hypermotility, including nausea, vomiting, diarrhea—decreased by premedication with antiemetics and antidiarrhea agents
- Bradycardia, hypotension, hypertension, and arrhythmias
- Dizziness, syncope, flushing, and fever
- Bronchospasm, including wheezing, dyspnea, chest constriction, and chest pain

Cervical laceration or uterine rupture (less common)

Retained placenta (less common)

Contraindications and precautions for prostaglandins include:

Use only by trained physicians in a hospital where intensive care and surgical facilities are available

Contraindicated with history of pelvic surgery, uterine fibroids, cervical stenosis, and acute pelvic inflammatory disease

Caution with asthma, hypertension, and cardiovascular or renal disease

Previous history of C-section

Mifepristone (RU-486)

Mifepristone (Mifeprex) is an antiprogesterone drug that is used to terminate an unwanted pregnancy (in conjunction with misoprostol). There are detailed requirements (including informed consent) to ensure that women fully understand the process. The drug is sold directly to trained doctors and is not available in pharmacies. Patient education (*Mifepristone Medication Guide*) is very important for the proper administration for this drug treatment.

Mifepristone is only for use very early in pregnancy—within 49 days from the beginning of a woman's last menstrual period. Mifepristone blocks the action of progesterone, a hormone essential for maintaining pregnancy. Without progesterone, the uterine lining thins, so the embryo cannot remain implanted and grow. It requires three visits to a qualified physician to complete the treatment:

1. At the first visit, the physician will determine the gestational status. If the woman qualifies for the procedure, she must sign an informed consent, agreeing to the necessary visits. She will then receive three mifepristone pills to be taken by mouth.
2. The second step requires the woman to swallow a second drug two days later to fully detach the embryo from the uterus and expel it. Misoprostol (Cytotec) causes uterine contractions with miscarriage-like cramping and bleeding.
3. The third step requires a follow-up visit to the physician within two weeks to make sure the abortion is complete. In case of hemorrhage, it might be necessary to consult the physician sooner. Studies have shown that mifepristone is 77%–92% effective in terminating pregnancy. However, in some cases, a curettage of the uterine cavity is required to remove any remaining products of conception.

Side effects of mifepristone can include:

- Diarrhea, nausea
- Uterine hemorrhage in about 5% of patients

Infection—if the embryo is not completely expelled

A malformed child if the second and third steps are not completed

Contraindications of mifepristone include:

Ectopic pregnancy

Any time after 49 days from the beginning of the woman's last menstrual period

Current long-term corticosteroid therapy

Bleeding disorders

Current anticoagulant therapy

Methylergonovine

The semisynthetic ergot alkaloid, methylergonovine (Methergine), is used for prevention and treatment of postpartum and postabortion hemorrhage.

Side effects of Methergine occur most commonly when administered IV undiluted or too rapidly, or in conjunction with regional anesthesia or vasoconstrictors, and can include:

- Nausea and vomiting
- Dizziness, headache, diaphoresis, palpitation, dyspnea, and arrhythmias

Hypertension (more common) or hypotension

Numbness and coldness of extremities with overdose (peripheral vasoconstriction)

Seizures with overdose

Contraindications/cautions of Methergine include:

When administered during third stage of labor, may lead to retained placenta

Contraindicated with cardiovascular disease, especially hypertension, and with hepatic and renal impairment

Patients with preeclampsia or eclampsia

Terbutaline

Terbutaline, although classified as a bronchodilator drug primarily used for pulmonary disorders, is also used with careful monitoring in the management of preterm labor. Its sympathomimetic action inhibits uterine contractions by smooth muscle relaxation. Although the manufacturer does not recommend its use for preterm labor, it is used for this purpose with careful monitoring, both in the hospital setting and with home uterine monitoring. It is available for oral, IV, or subcutaneous administration.

Side effects of terbutaline include:

- Nervousness, tremors, increased heart rate, headache, nausea, vomiting, heart palpitations. Side effects tend to be less severe with a subcutaneous pump, rather than PO.

Caution with terbutaline applies to:

Watching patient closely for signs of pulmonary edema. Should not be used in patients with hypertension, cardiac disease, hyperthyroidism, diabetes, or history of seizures.

Note The manufacturer does not recommend that terbutaline be used for tocolysis (**suppression of uterine contractions**) in preterm labor. The safety of this drug for this purpose has not been adequately established. Tocolytic therapy is recommended only as a method to prevent delivery long enough for a course of corticosteroids to be administered (to enhance fetal lung maturation) and for the patient to be transferred to an appropriate facility with the ability to care for a premature infant.

Magnesium Sulfate

Treatment of severe preeclampsia or eclampsia consists of magnesium sulfate injection for prevention and control of seizures. Magnesium sulfate acts by depressing the CNS and blocking neuromuscular transmission, thus producing anticonvulsant effects. Magnesium sulfate has also been used in the management of uterine tetany associated with the use of oxytocic agents. Magnesium sulfate also acts peripherally, producing vasodilation and lowering the blood pressure. Patients receiving this drug must be monitored closely for vital signs and reflexes.

Side effects of magnesium sulfate, which can be serious and even fatal, can include:

- ! Flaccid paralysis and CNS depression
- ! Circulatory collapse, cardiac depression, and hypotension
- ! Fatal respiratory paralysis

Flushing and sweating

The antidote for overdose of magnesium sulfate (e.g., respiratory depression or heart block) is IV administration of calcium gluconate.

Contraindications or extreme caution when using magnesium sulfate applies to:

Impaired renal function

Heart block or myocardial damage

Use more than 24 h before delivery and within 2 h of delivery because of potential respiratory depression in the neonate

See Table 24-5 for a summary of drugs for labor and delivery.

Table 24-5 Drugs for Labor and Delivery

GENERIC NAME	TRADE NAME	DOSAGE	COMMENTS
Oxytocics[a]			
methylergonovine	Methergine	PO, IM; dosage varies	For postpartum hemorrhage
oxytocin	Pitocin	IV	For induction of labor, postpartum hemorrhage
Prostaglandins			
dinoprostone	Prostin E2	Vaginal supp. 20 mg	For therapeutic abortion
	Cervidil	Vaginal insert	For cervical ripening
	Prepidil	Intravaginal gel	For cervical ripening
misoprostol	Cytotec	Tablets	For pregnancy termination (used with mifepristone)

Table 24-5 Drugs for Labor and Delivery—*continued*

GENERIC NAME	TRADE NAME	DOSAGE	COMMENTS
Adrenergic[b]			
terbutaline		IV, PO, subcu, dose varies	For premature labor
Treatment for Preeclampsia or Eclampsia			
magnesium sulfate		IM, IV; dosage varies	Watch for respiratory complications

[a]Stimulate uterine contractions.
[b]Inhibit uterine contractions in preterm labor.

OTHER GONADOTROPIC DRUGS

Drugs classified as analogs of *gonadotropin-releasing hormones* (GnRH) act in the pituitary to suppress ovarian and testicular hormone production and inhibit estrogen and androgen synthesis. Leuprolide (Lupron) has been used as an antineoplastic agent to inhibit the growth of hormone-dependent tumors. It has been used to reduce the size of the prostate and inhibit prostatic tumor growth. It has also been used following other therapies, for example mastectomy, radiation, and/or other antineoplastic drugs to treat breast cancer. Lupron is sometimes combined with the antiestrogen drug tamoxifen in the treatment of breast cancer (see Chapter 14 for dosage and side effects).

GnRH analogs that inhibit gonadotropin secretion, for example Lupron and Synarel, are used in the management of endometriosis. They inhibit ovulation and stop menstruation, thereby providing pain relief and a reduction in endometriotic lesions. Lupron is administered as a monthly IM injection. Synarel is administered as a nasal spray. Treatment with either is limited to six months. They appear to be better tolerated than the androgen, danazol, in the treatment of endometriosis.

Side effects of the GnRH agonists can include:

- Hot flashes
- Vaginal dryness
- Headache and insomnia
- Emotional or mood swings
- Weight gain or loss
- Nasal congestion
- Acne

Cautions and contraindications apply to:

Not to be considered effective as a contraceptive; patient should use a backup barrier method.

Not safe during pregnancy or lactation.

Prolonged use creates a hypoestrogenic state that may lead to an increased risk of loss of bone density.

Patients must be fully informed of the benefits and risks of the use of GnRH analog drugs and, generally speaking, the therapeutic values should outweigh any potential risks. Patient compliance is enhanced with adequate patient education, counseling, and support.

See Table 24-6 for a summary of other gonadotropin-associated drugs.

Table 24-6 Other Gonadotropin-Associated Drugs

GENERIC NAME	TRADE NAME	DOSAGE	COMMENTS
nafarelin acetate	Synarel	Nasal spray, dose varies	For endometriosis, treatment not to exceed 6 months
Leuprolide acetate	Lupron Depot, Eligard	IM, subcu, dose varies	For endometriosis, some cases of infertility, treatment not to exceed 6 months; also for prostate cancer (see Antineoplastics)

CASE STUDY – A

Reproductive System Drugs

May Griffith, age 38, visits her obstetrician's office for her 6-week postpartum checkup. She smokes. She has a history of thrombophlebitis. She plans to continue nursing her baby. She asks the doctor for a prescription for an oral contraceptive for birth control purposes. She needs all of the following information.

1. Which would be the only appropriate contraceptive type for her?
- a. Estrogen only
- b. Progestin only
- c. Estrogen-progestin combination
- d. Postcoital contraceptive

2. Contraceptives containing estrogen are not advised in which conditions?
- a. History of thrombophlebitis
- b. Coronary artery disease
- c. Lactation
- d. All of the above
- e. Only (a) and (c)

3. Progestin-only contraceptives are available in all of the following forms EXCEPT
- a. Tablets
- b. Suppository
- c. Intramuscular
- d. IUD

4. Side effects of estrogen products can include all of the following EXCEPT
- a. Severe headaches
- b. Depression
- c. Heavy menstrual flow
- d. Fluid retention
- e. Blurred vision

5. Those more at risk for complications with estrogen therapy include all of the following EXCEPT
- a. Diabetics
- b. Smokers
- c. With pernicious anemia
- d. With gallbladder problems

6. Those taking combination birth control pills would be wise to avoid all of the following EXCEPT
- a. Asthma drugs
- b. Antibiotics
- c. Antidepressants
- d. Tobacco
- e. Sex

CASE STUDY – B

Reproductive System Drugs

I. M. Puny, a 16-year-old male weighing 100 pounds, asks the physician to prescribe some "steroids" to improve his physique and increase the size of his muscles. He needs to be given the following information about androgens.

1. Androgens are used in all of the following conditions EXCEPT
- a. Delayed puberty in male
- b. Endometriosis in female
- c. Testicular malfunction
- d. Impaired growth

2. Side effects of androgens can include all of the following EXCEPT
- a. Jaundice
- b. Impotence
- c. Growth spurts
- d. Fluid retention

3. The following statements are true of illegal anabolic steroids EXCEPT
- a. Can cause psychosis
- b. Can stunt growth
- c. Synthetic testosterone
- d. FDA approved

4. Androgens are generally contraindicated in all of the following EXCEPT
- a. Diabetics
- b. Cryptorchidism
- c. Geriatric males
- d. Prepubertal males

Note Always explain medical information in terms the patient can understand.

CHAPTER REVIEW QUIZ

Match the mediation in the first column with the conditions they are used to treat. Conditions may be used more than once.

	Medication	Condition
1. _____	Premarin	**a.** Endometriosis
2. _____	Megace	**b.** Menopausal symptoms
3. _____	Depo-Testosterone	**c.** Prostate cancer
4. _____	Danocrine	**d.** Erectile dysfunction
5. _____	Estratest	**e.** Hypogonadism
6. _____	Terbutaline	**f.** Uterine inertia in labor
7. _____	Cialis	**g.** Infertility
8. _____	Levitra	**h.** Preterm labor
9. _____	Pitocin	**i.** Cachexia of AIDS

Choose the correct answer.

10. Androgens are used for all of the following EXCEPT:
a. Advanced breast cancer **c.** Muscle growth
b. Fibrocystic breast disease **d.** Cryptorchidism

11. Erectile dysfunction medications, for example Viagra, can cause all of the following EXCEPT:
a. Abnormal vision **c.** Headache
b. Hypertension **d.** Flushing

12. Women with a uterus should not use estrogen-alone therapy because it puts them at risk for which of the following:
a. Blood clots **c.** Stroke
b. Uterine cancer **d.** Osteoporosis

13. Combined hormone therapy (estrogen/progestin), for example Prempro, can put posthysterectomy patients at risk for all of the following EXCEPT:
a. Heart attack **c.** Stroke
b. Breast cancer **d.** Uterine cancer

14. Estrogen uses include all of the following EXCEPT:
a. Prostate cancer **c.** Cachexia
b. Atrophic vaginitis **d.** After rape

15. Uses of progestin-only products include all of the following EXCEPT:
a. Cachexia of AIDS **c.** Amenorrhea
b. Threatened abortion **d.** Contraception

16. The following statements are true of (mifepristone) RU486 therapy EXCEPT:
- **a.** For very early pregnancy
- **b.** Available in pharmacies
- **c.** Blocks progesterone
- **d.** Three-step procedure

17. Use of oxytocin for labor induction can have the following serious side effects EXCEPT:
- **a.** Prolapsed cord
- **b.** Cervical laceration
- **c.** Fetal trauma
- **d.** Abruptio placenta

18. Magnesium sulfate, used to treat eclampsia, can have the following serious side effects EXCEPT:
- **a.** CNS depression
- **b.** Hypertensive crisis
- **c.** Respiratory depression
- **d.** Bradycardia

19. Methergine, used for postpartum hemorrhage, can have the following effects EXCEPT:
- **a.** Uterine contractions
- **b.** Dizziness
- **c.** Peripheral vasodilation
- **d.** Diaphoresis

Go to your StudyWARE™ CD-ROM and have fun learning as you play games and answer case study-related questions to help reinforce key concepts you learned in this chapter.

Go to your Study Guide and complete the review questions for this chapter.

Chapter 25

Cardiovascular Drugs

Objectives

Upon completion of this chapter, the learner should be able to

1. Describe the action and effects of digoxin and toxic side effects that require reporting
2. Identify the different types of antiarrhythmics and the side effects of each
3. Identify the most commonly used antihypertensives and the usual side effects, as well as the exceptions to the rule
4. Describe the different types of coronary vasodilators with cautions and side effects
5. Name the six antilipemic agents and describe their action
6. Compare and contrast heparin and coumarin derivatives in terms of administration, action, and antidotes
7. Explain appropriate and important patient education for each of the nine categories of cardiovascular drugs
8. Describe platelet inhibitor therapy and appropriate patient education regarding it
9. Define the Key Terms and Concepts

Key Terms and Concepts

Antiarrhythmic agents
Anticoagulants
Antihypertensives
Antilipemic agents
Bradycardia
Cardiac glycosides
Cardiotonic
Colony stimulating factors
Coronary vasodilators
Digitalization
Hypertension
Hypotension
Ischemia
Platelet inhibitors
Tachycardia
Thrombolytic agents
Vasoconstrictors

Cardiovascular drugs include medications that affect the heart and blood vessels as well as anticoagulant and antiplatelet agents that prevent clotting. The drugs described in this chapter are divided into nine categories: cardiac glycosides, antiarrhythmic agents, antilipemic agents, antihypertensives, vasodilators, vasoconstrictors, anticoagulants, platelet inhibitors, and thrombolytic agents. Some of the drugs described in this chapter fall into more than one category because of multiple actions and uses (e.g., propranolol, which is used to treat cardiac arrhythmias, hypertension, and angina). Diuretics, which also affect the blood vessels and reduce blood pressure, are discussed in Chapter 15. Autonomic Nervous System effects of these drugs are explained in Chapter 13.

CARDIAC GLYCOSIDES

Cardiac glycosides occur widely in nature or can be prepared synthetically. These glycosides act directly on the myocardium to increase the force of myocardial contractions. Cardiac glycosides are used primarily in the treatment of heart failure. They are sometimes also used alone or in conjunction with other medications to *slow* the ventricular response in patients with atrial fibrillation or flutter.

In patients with heart failure, the heart fails to adequately pump nutrients and oxygen to body tissues. Since the heart is failing, the body attempts to compensate by retaining salt and fluid and this may result in both pulmonary and peripheral edema. The heart increases in size to compensate for the increased work load. Symptoms of heart failure include fatigue, weakness, dyspnea, cyanosis, increased heart rate, cough, and pitting edema.

In patients with heart failure, the cardiac glycosides act by *increasing the force of the cardiac contractions* without increasing oxygen consumption, thereby increasing cardiac output. Digoxin also lowers norepinephrine levels which are elevated in heart failure and are toxic to the failing heart. As a result of increased efficiency, the heart beats slowly, the heart size shrinks, and the concurrent diuretic therapy decreases edema.

The most commonly used cardiac glycosides are digitalis products. Of these, digoxin (Lanoxin) is used the most frequently because it can be administered orally and parenterally and has intermediate duration of action.

Digitalization is the process of establishing the correct therapeutic dose of digoxin for maintaining optimal functioning of the heart without toxic effects. There is a very narrow margin between effective therapy and dangerous toxicity. Careful monitoring of cardiac rate and rhythm with EKG (electrocardiogram), cardiac function, side effects, and serum digoxin levels are required to determine the therapeutic maintenance dose. Checking the apical pulse before administering digoxin is an important part of this monitoring process. If the apical pulse rate is less than 60, digoxin may need to be withheld until the physician is consulted. The action taken should be documented.

Modification of dosage is based on individual requirements and response as determined by general condition, renal function, and cardiac function, monitored by EKG. When changing from tablets or IM therapy to elixir or IV therapy, digoxin dosage adjustments may be required.

Toxic side effects of digoxin, which should be reported to the physician immediately, can include:

- Anorexia, nausea, and vomiting (early signs of toxicity)
  Abdominal cramping, distention, and diarrhea
- Headache, fatigue, lethargy, and muscle weakness
- Vertigo, restlessness, irritability, tremors, and seizures
- Visual disturbances including blurring, diplopia (double vision), or halos
- Cardiac arrhythmias of all kinds, especially bradycardia (rate less than 60)
- Electrolyte imbalance, especially potassium—either hyperkalemia or hypokalemia can cause arrhythmias
- Insomnia, confusion, and mental disorders, especially with older adults

Treatment of digoxin toxicity includes:

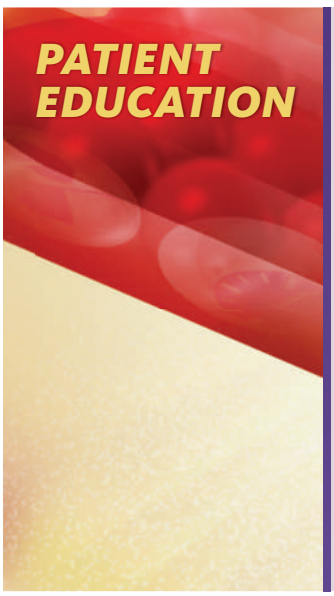
- Discontinuing the drug immediately (usually sufficient)
- Monitoring electrolytes for hyperkalemia, hypokalemia, hypomagnesemia, and hypercalcemia
- Drugs such as atropine for symptomatic bradycardia
- Digoxin-specific Fab fragments (Digibind) as antidote in life-threatening toxicity

Contraindications or extreme caution applies to:

- Severe pulmonary disease
- Hypothyroidism
- Acute myocardial infarction, acute myocarditis, severe heart failure
- Impaired renal function; hypokalemia, hypomagnesemia
- Arrhythmias not caused by heart failure
- Pregnancy and lactation
- High doses in older adults

Interactions of digoxin may occur with:

- Antacids, cholestyramine, neomycin, and rifampin reduce absorption of digoxin (administer far apart).
- Diuretics, calcium, and corticosteroids can increase chance of arrhythmias.
- Macrolides, antiarrhythmics (*especially* quinidine and verapamil), may potentiate digoxin toxicity.
- Adrenergics (epinephrine, ephedrine, and isoproterenol) increase the risk of arrhythmias.



Patients taking digoxin should be instructed regarding:

- Recognition and immediate reporting of side effects
- Holding medication, if any side effects occur, until the physician can be consulted
- Avoiding taking any other medication at the same time without physician approval
- Avoiding all over-the-counter (OTC) medication, especially antacids and cold remedies
- Avoiding abrupt withdrawal after prolonged use; must be reduced gradually under physician supervision
- Checking heart rate (pulse) and blood pressure on a regular basis
- Not changing the brand or dosage form being taken—other brands or dosage forms may act differently

ANTIARRHYTHMIC AGENTS

Antiarrhythmic agents include a variety of drugs that act in different ways to suppress various types of cardiac arrhythmias, including atrial or ventricular tachycardias, atrial fibrillation or flutter, and arrhythmias that occur with digoxin toxicity or during surgery and anesthesia. The choice of a particular antiarrhythmic agent is based on careful assessment of many factors, including the type of arrhythmia; frequency; cardiac, renal, or other pathological condition; and current signs and symptoms.

The role of the health care practitioner is vital in this area in accurate and timely reporting of vital signs, pertinent observations regarding effectiveness of medications and adverse side effects, and modification of precipitating causes. Adequate knowledge of drug action and effects, along with good judgment are essential.

Antiarrhythmic agents are classified according to their effects on the action potential of cardiac cells and their presumed mechanism of action (Class IA, IB, IC, II, III, and IV). Although drugs within the same class are similar, they do not necessarily exert the same actions nor does it imply that another agent within the same class would not be more effective or safer in an individual patient.

Side effects of the individual medications are discussed separately. However, keep in mind that most of the drugs given to counteract arrhythmias have the potential for lowering blood pressure and slowing heartbeat. Therefore, it is especially important to be alert for signs of **hypotension** and **bradycardia**, which could lead to cardiac arrest. Although the antiarrhythmics commonly slow the heart rate, there are exceptions (e.g., procainamide and quinidine, which may cause *tachycardia*). When other cardiac drugs are administered concomitantly, cardiac effects may be additive or antagonistic. Antiarrhythmic agents can worsen existing arrhythmias or cause new arrhythmias and *careful monitoring is essential.*

Arrhythmia detection and monitoring can include EKG rhythm strips and 24 hour Holter monitoring as indicated. Electrolyte surveillance, especially for disorders of potassium and magnesium, is very important for patients on antiarrhythmic agents. Nondrug therapy can include insertion of a pacemaker or an automatic implantable cardioverter-defibrillator (AICD). The AICD has been widely accepted as the most effective treatment for patients with life-threatening ventricular tachycardia or fibrillation and may also be effective in preventing sudden death in certain types of these patients.

Adenosine

Adenosine (Adenocard) is an injectable antiarrhythmic agent with multiple electrophysiologic activities that complicates its placement into a single category. It restores normal sinus rhythm in paroxysmal supraventricular tachycardia (PSVT) by slowing conduction time through the atrioventricular (AV) node. Adenosine also has vasodilatory, antiadrenergic, and negative chronotropic (decrease in rate) properties which act to decrease cardiac oxygen demand.

Adenosine is equal in effectiveness to diltiazem or verapamil in converting PSVT, but is less likely to cause hypotension. Common side effects include

facial flushing, lightheadedness, headache, dyspnea, and chest pressure. Due to its short duration of action, there appears to be no clinically significant adverse reactions of adenosine together with other cardioactive agents (use cautiously with digoxin and verapamil due to additive slowing of cardiac conduction). Adenosine is contraindicated in patients with second- or third-degree heartblock or symptomatic bradycardia (unless a functioning artificial pacemaker is present).

Amiodarone

Amiodarone (Cordarone) is a class III oral and injectable antiarrhythmic agent approved for the treatment of refractory life-threatening ventricular arrhythmias. Despite its problematic organ toxicity profile and "Black Box Warning," amiodarone is widely used for preventing the recurrence of atrial fibrillation. It is considered a "broad spectrum" antiarrythmic with multiple and complex electrophysiologic effects. Amiodarone also inhibits alpha- and beta-receptors, and possesses calcium-channel blocking properties. It relaxes both smooth and cardiac muscle, causing decreases in coronary and peripheral vascular resistance, and systolic blood pressure.

Side effects of amiodarone, some of which are severe and potentially fatal, but may be less of a problem with lower doses (i.e., 200–400 mg/day) include:

Pulmonary fibrosis

Cardiac arrhythmias, induction or worsening of heart failure; hypotension

Nausea/vomiting, constipation, anorexia

Hepatitis (rare)

Hyperthyroidism or hypothyroidism

Neurotoxicity (tremor, peripheral neuropathy, paresthesias)

Visual disturbances; optic neuropathy and/or neuritis (may progress to permanent blindness)

Dermatologic reactions, especially photosensitivity (avoid exposure, wear protective clothing)

Contraindications or extreme caution with amiodarone in:

Patients with second- or third-degree heartblock, marked sinus bradycardia due to severe sinus node dysfunction, and when bradycardia has caused syncope (unless a functioning artificial pacemaker is present); cardiogenic shock

Patients with thyroid disease (due to large amount of iodine contained in amiodarone)

Older Adults (more susceptible to thyrotoxic and neurotoxic adverse effects)

Interactions with amiodarone are numerous and significant, including:

Certain fluoroquinolones, macrolide antibiotics, systemic azole antifungals (QT prolongation)

Warfarin (can result in serious or fatal bleeding if warfarin dose not reduced; effect may persist for months after discontinuation)

Certain antiarryhthmics, digoxin, phenytoin (amiodarone increases serum concentrations of these)

Protease inhibitors and grapefruit juice (increase amiodarone concentrations); beta-blockers, calcium channel blockers, lidocaine (additive adverse cardiac effects)

Cholestyramine, phenytoin, rifampin (serum concentrations of amiodarone decreased, reducing its pharmacologic effect)

Beta-Adrenergic Blockers

Beta-adrenergic blockers, for example, propranolol (Inderal), are class II antiarrhythmics which combat arrhythmias by inhibiting adrenergic (sympathetic) nerve receptors. The action is complex, and the results can include a membrane-stabilizing effect on the heart. Propranolol (Inderal), a nonselective beta-blocker, is effective in the management of some cardiac arrhythmias and less effective with others. It is also used in the treatment of hypertension and some forms of chronic angina. Because it also blocks the $beta_2$ receptors in the lungs, it can lead to bronchospasm. *Low doses* of metoprolol (Lopressor), a selective $beta_1$-antagonist, may be used *with caution* in patients with lung conditions that cause bronchospasm. For additional use of beta-blockers, for example with migraine, see Chapter 13 and Table 13-2.

LEARNING HINT:

$Beta_1$ receptors are found primarily in the heart, and when stimulated cause an increase in rate and force of contraction. $Beta_2$ receptors are found primarily in the lungs (when stimulated cause relaxation or bronchodilation of airways) and blood vessels (when stimulated cause vasodilation). A useful mnemonic is to think how many hearts you have (1) and how many lungs (2): The class of beta-*blockers* therefore would decrease the rate and force of contraction of heart and if nonselective may also cause bronchospasm and mild vasoconstriction of blood vessels.

Side effects of beta-blockers, especially in patients over 60 years old and more commonly with IV administration of the drug, can include:

- Hypotension, with vertigo and syncope
- Bradycardia, with rarely heart block and cardiac arrest
- CNS symptoms (usually with long-term treatment with high doses), including dizziness, irritability, confusion, nightmares, insomnia, visual disturbances, weakness, sleepiness, lassitude, or fatigue

GI symptoms, including nausea, vomiting, and diarrhea or constipation
Rash or hematological effects (rare or transient)

- Bronchospasm, especially with history of asthma
- Hypoglycemia

Impotence reported rarely

Contraindications or extreme caution with the beta-blockers applies to:

Withdrawal after prolonged use (should always be gradual)

Withdrawal before surgery is controversial (weigh risk vs. benefits)

Diabetes—may cause hypoglycemia and mask the tachycardic response to hypoglycemia

Renal and hepatic impairment

Asthma and allergic rhinitis—may cause bronchospasm

Bradycardia, heart block, and congestive heart failure (CHF)

Pediatric use, pregnancy, and lactation

Chronic obstructive pulmonary disease (COPD)

Interactions include *antagonism* of beta-blockers by:

Adrenergics (e.g., epinephrine and isoproterenol)

NSAID's and salicylates

Tricyclic antidepressants

Potentiation of the *hypotensive effect* of propranolol occurs with:

Diuretics and other antihypertensives, for example, calcium channel blockers

MAOI's; phenothiazine and other tranquilizers

Cimetidine (Tagamet), which slows metabolism of drug

Certain antiarrhythmic drugs (e.g., adenosine, digoxin, quinidine), which may potentiate toxic effects

Alcohol, muscle relaxants, and sedatives, which may precipitate hypotension, dizziness, confusion, or sedation

Calcium Channel Blockers

Of the calcium channel blockers available, only verapamil (Calan) and diltiazem (Cardizem) possess significant antiarrhythmic activity. These are Class IV agents indicated for treatment of atrial fibrillation/flutter and PSVT. Verapamil and diltiazem counteract arrhythmias by slowing AV nodal conduction. Calcium channel blockers are also used in the treatment of angina and hypertension.

Side effects of calcium channel blockers can include:

- Hypotension, with vertigo, *headache*
- Bradycardia, with heart block
- Edema
- *Constipation*, nausea, and abdominal discomfort

Note
Do not take grapefruit juice with certain calcium channel blockers since adverse effects may be potentiated.

Contraindications or extreme caution with calcium channel blockers applies to:

Heart block, heart failure, or angina

Hepatic and renal impairment

Pregnancy and lactation

Children

Interactions of calcium channel blockers with other cardiac drugs, for example digoxin, can potentiate both good and adverse effects.

Antagonistic effects with calcium channel blockers include:

Barbiturates, cimetidine, phenytoin, ranitidine, rifampin

Hypotensive effect potentiated with diuretics, ACE (angiotensin-converting enzyme) inhibitors, beta-blockers, and quinidine

Calcium channel blockers **contraindicated** with:

Hypotension and heart block

Certain arrhythmias and severe heart failure

Lidocaine

Local anesthetics (e.g., lidocaine) are administered for their antiarrhythmic effects and membrane-stabilizing action. A Class IB agent, lidocaine has been historically used as a first-line antiarrhythmic agent for acute, life-threatening ventricular arrhythmias, is now considered a second choice behind other alternative agents (e.g., IV amiodarone) for the treatment of ventricular arrhythmias.

Side effects of lidocaine are usually of short duration, are dose related, and can include:

- CNS symptoms, including tremors, seizures, dizziness, confusion, and blurred vision
- Hypotension, bradycardia, and heart block
- Dyspnea, respiratory depression, and arrest

EKG monitoring and availability of resuscitative equipment are necessary during IV administration of lidocaine.

Contraindications or extreme caution with lidocaine applies to:

Patients hypersensitive to local anesthetics of this type (amide type)

Heart block and respiratory depression

Pregnancy, lactation, and children

Interactions of lidocaine with other cardiac drugs may be additive or antagonistic and may potentiate adverse effects. Other interactions may be of minor clinical significance since lidocaine is usually titrated to response.

Procainamide

Procainamide, quinidine, and disopyramide (Norpace) are Class IA antiarrhythmic agents. They act by decreasing myocardial excitability, inhibiting conduction, and may depress myocardial contractility. Class IA agents possess anticholinergic properties. IV procainamide is a potential treatment alternative (to amiodarone) for treatment of ventricular tachycardia during CPR. Orally, Class IA agents are used primarily as prophylactic therapy to maintain normal rhythm after conversion by other methods.

Side effects of Class IA antiarrhythmics are numerous and may necessitate cessation of treatment. They may include:

- Diarrhea, anorexia, nausea and vomiting, and abdominal pain which are common
- *Tachycardia*, QT prolongation, hypotension, and syncope
- Anticholinergic effects, including dry mouth, blurred vision, confusion, constipation, and urinary retention
- Vascular collapse and respiratory arrest with IV administration
- Vision abnormalities or hearing disturbances (with quinidine)
- Blood dyscrasias, including anemia, clotting deficiencies, and leukopenia (relatively rare)
- Hepatic disorders; fever
- Dermatological effects, including rash, pruritis, urticaria

Contraindications or extreme caution with Class IA agents applies to:

- Atrioventricular block and conduction defects
- Electrolyte imbalance
- Digoxin toxicity
- Heart failure and hypotension
- Myasthenia gravis
- Older adults—more susceptible to hypotensive and anticholinergic effects
- Children, pregnancy, and lactation
- Hepatic or renal disorders
- Hypersensitivity to "ester type" local anesthetics with procainamide
- Systemic lupus erythematosis (SLE) with procainamide

Interactions with increased possibility of Class IA agent toxicity may occur with:

- Muscle relaxants, neuromuscular blockers
- Anticholinergics, tricyclic antidepressants, phenothiazines
- Other cardiac drugs, especially digoxin and antihypertensives

Interactions with increased possibility of *quinidine* toxicity may occur with:

- Antiretroviral protease inhibitors
- Antacids or sodium bicarbonate;

Anticonvulsants (e.g., phenytoin and phenobarbital) cause decreased serum levels

Anticoagulants, whose action can be potentiated by quinidine

Propafenone

Propafenone (Rythmol) is an oral Class IC antiarrhythmic agent used to treat symptomatic supraventricular arrhythmias or severe, life-threatening ventricular arrhythmias. It is also useful in converting and maintaining atrial fibrillation to sinus rhythm. Propafenone has local anesthetic effects, direct stabilizing action on myocardial membranes, and beta-adrenergic blocking properties.

Common **side effects** include dizziness, nausea and vomiting, unusual taste, constipation, blurred vision, angina, heart failure, palpitations, arrhythmia, fatigue, headache, dyspnea, rash, and weakness. Use with **caution** in asthma or acute bronchospasm, second or third-degree heart block (in absence of pacemaker), cardiogenic shock, heart failure, bradycardia, marked hypotension, and electrolyte imbalance.

Propafenone serum levels may be elevated when given with quinidine, ritonavir, and certain SSRIs. Propafenone may increase serum levels of beta-blockers, digoxin, and theophylline.

PATIENT EDUCATION

Patients taking antiarrhythmics should be instructed regarding:

- Immediate reporting of adverse side effects, especially palpitations, irregular or slow heartbeat, faintness, dizziness, weakness, respiratory distress, and visual disturbances
- Holding medication, if there are side effects, until the physician is contacted
- Rising slowly from reclining position
- Modification of lifestyle to reduce stress
- Mild exercise on a regular basis as approved by the physician
- Not discontinuing medicine, even if the patient feels well
- Taking proper dosage of medication on time, as prescribed, without skipping any dose
- If medication is forgotten, not doubling the dose
- Taking medication with a full glass of water on an empty stomach, one hour before or two hours after meals, so that it will be absorbed more efficiently (unless stomach upset occurs or the physician prescribes otherwise)
- Avoiding taking any other medication, including OTC medicines, unless approved by the physician
- Discarding expired medicines and renewing the prescription
- Avoiding comparisons with other patients on similar drugs
- Contacting the physician immediately with any concerns regarding medicines

See Table 25-1 for a summary of the antiarrhythmics and digoxin.

Table 25-1 Digoxin and Antiarrhythmics

GENERIC NAME	TRADE NAME	DOSAGE	COMMENTS
Cardiac Glycoside			
digoxin	Lanoxin	PO: tablets, elixir, IM, IV, dosage varies	digoxin serum levels may be monitored (0.5 –0.8 ng per mL for heart failure)
Antiarrhythmics	(grouped by class)		
IA procainamide		IV or IM for emergency	Has anticholinergic properties
IB lidocaine	Xylocaine	IM or IV diluted	Local anesthetic-type **Check IV dilution directions**
IC propafenone	Rythmol	PO, 150–300 mg q8h	
	Rythmol SR	PO, 225–425 mg q12h	
II metoprolol[a]	Lopressor	PO, 25–100 mg BID	Beta-blocker
		IV, 2.5–5 mg IV bolus, repeat q5 min for 3 doses total	
III amiodarone	Cordarone	IV, PO; dose varies	Also a vasodilator; Medication Guide required
IV verapamil[a]	Calan	IV 2.5–10 mg; PO 240–480 mg daily in div. doses	Calcium channel blocker
adenosine	Adenocard	IV bolus 6 mg; then 12 mg prn up to 30 mg	For PSVT; do not confuse with amiodarone

Note: Other antiarrhythmics are available. This is a representative sample by classification.
[a]Has other cardiac uses.

ANTIHYPERTENSIVES

Hypertension is a widespread epidemic that affects as many as one billion people worldwide and approximately 60 million adults in the United States. It is defined as systolic blood pressure (SBP) of 140 or greater or diastolic blood pressure (DBP) of 90 or greater. There is a strong, consistent relationship between blood pressure (BP) and the risk of cardiovascular disease (CVD). High blood pressure increases the risk of angina, myocardial infarction, heart failure, stroke, retinopathy, peripheral arterial disease, and kidney disease and thus requires aggressive treatment.

An additional 59 million adults are considered to have *prehypertension* (SBP range of 120–139 and DBP range of 80–89), a condition that may identify patients who are at higher cardiovascular risk based on BP and higher risk for developing sustained hypertension in later years. The purpose of this classification is to encourage patients to initiate or continue healthy lifestyle practices, rather than to begin antihypertensive drug therapy. Such practices include weight reduction (in overweight and obese patients), use of the *Dietary Approaches to Stop Hypertension* (DASH) eating plan, dietary

sodium reduction, increased physical activity, modified alcohol use, and smoking cessation.

Antihypertensives (hypotensives) do not cure hypertension; they only control it. After withdrawal of the drug, BP will return to levels similar to those before treatment with medication, if all other factors remain the same. If antihypertensive therapy is to be terminated for some reason, the dosage should be gradually reduced, as abrupt withdrawal can cause rebound hypertension.

Drugs given to lower blood pressure act in various ways. The drug of choice varies according to the stage of hypertension (mild, moderate, or severe), other physical factors (especially other cardiac or renal complications), and effectiveness in individual cases. Frequently, antihypertensives are prescribed on a trial basis and then the dosage or medication is changed, and sometimes antihypertensives are combined for greater effectiveness and to reduce side effects. The health care practitioner must be observant of vital signs and side effects in order to assist the physician in the most effective treatment of hypertension on an individual basis.

Side effects of antihypertensives are common. The most common side effect of antihypertensives is *hypotension*, especially postural hypotension. Another side effect common to many of the antihypertensives is *bradycardia*. Exceptions include hydralazine, which can cause tachycardia.

Thiazide Diuretics

Most patients meeting the criteria for drug therapy should be started on thiazide-type diuretics, either alone or in combination with a drug from one of the other drug classes: ACE inhibitors, angiotensin receptor blockers, beta-blockers, or calcium channel blockers. Thiazide diuretics appear to be as effective as other antihypertensive agents and, in addition, are inexpensive. See Chapter 15 for a detailed discussion of these agents, especially Side effects, Contraindications or Cautions, and Interactions.

Beta-Adrenergic and Calcium Channel Blockers

Like thiazide diuretics, beta-adrenergic blockers such as propranolol (Inderal) and atenolol (Tenormin) are generally well tolerated and are suitable for initial therapy in some patients. Beta-blockers can benefit hypertensive patients with angina, postmyocardial infarction, ischemic heart disease, heart failure, certain arrhythmias, and diabetes.

Calcium channel blockers such as diltiazem (Cardizem) and nifedipine (Procardia) are an initial therapy option for hypertensive patients with diabetes or high coronary disease risk. They are more effective in treating African-American patients, older adults, and patients with higher pretreatment blood pressure readings. Based on historical data, *short-acting* calcium channel blockers should never be used to manage hypertension because of reports of increased risks of myocardial infarction and mortality.

Refer to the discussion under Antiarrhythmic Agents earlier in this chapter for more information on these agents.

Angiotensin-Converting Enzyme (ACE) Inhibitors (ACEIs)

Another class of antihypertensives are the angiotensin-converting enzyme (ACE) inhibitors, for example, captopril or enalapril. Inhibition of ACE lowers blood pressure by *decreasing vasoconstriction*; there are not significant changes in heart rate or cardiac output. ACEIs are first- or second-line agents in the treatment of hypertension and are excellent alone, but also effective and synergistic in combination with other antihypertensives, including diuretics and calcium channel blockers.

ACEIs are especially good choices for patients who also have other serious conditions, including those with heart failure, following myocardial infarction, when high coronary disease risk exists, diabetes, renal disease, and cerebrovascular disease. For example, ACEIs can be considered drugs of choice for hypertensive patients with nephropathy because they slow the progression of the renal disease. They are more effective in younger and white populations and less effective in black patients, unless given in higher doses or in combination with a diuretic.

Side effects of ACE inhibitors can include:

- ! Rash or photosensitivity
- Loss of taste perception
- Blood dyscrasias
- Renal impairment
- ! Severe hypotension
- ! Chronic dry cough or nasal congestion
- ! Hyperkalemia (monitor serum potassium levels periodically)

Contraindications or extreme caution with ACE inhibitors applies to:

- Collagen disease, for example, lupus or scleroderma
- Heart failure
- Angioedema
- Pregnancy, lactation, children

Interactions of ACE inhibitors apply to:

- Diuretics—potentiate hypotension; watch BP closely
- Vasodilators; watch BP closely
- Potassium-sparing diuretics and potassium supplements—hyperkalemia risk
- Nonsteroidal anti-inflammatory drugs (NSAIDs) and salicylates—antagonize effects of ACE inhibitors and increase deterioration of renal function in patients with compromised renal function
- Antacids—decrease absorption
- Digoxin—possible digitalis toxicity
- Lithium—risk of lithium toxicity

Angiotensin Receptor Blockers (ARBs)

Angiotensin receptor blockers (ARBs) are similar to ACE inhibitors (ACEIs) and are generally used as alternatives. They block the angiotensin receptor that causes vasoconstriction when stimulated by angiotensin II. ARBs such as losartan (Cozaar) and valsartan (Diovan) block the effects of angiotensin II, decreasing blood pressure without a marked change in heart rate.

Compared to ACEIs, ARBs are associated with a lower incidence of drug-induced cough, rash, and/or taste disturbances and are used in those patients who cannot tolerate ACEIs. Like the ACEIs, black patients experience a smaller antihypertensive response with the ARBs compared to other ethnic populations. The addition of a low-dose thiazide diuretic to an ARB significantly improves hypertensive efficacy. ARBs are also good choices for patients with other serious conditions, including those with heart failure, diabetes, and renal disease.

Side effects are relatively uncommon with ARBs and include dizziness, orthostatic hypotension, upper respiratory tract infections and hyperkalemia.

Contraindications or extreme caution with ARBs applies to:

Renal impairment

Heart failure

Pregnancy, lactation, children

Interactions with ARBs are similar to those seen with ACEIs.

OTHER ANTIHYPERTENSIVES

Antiadrenergic Agents

Methyldopa is a *central-acting* alpha-adrenergic agent which stimulates inhibitory receptors, thereby reducing peripheral resistance and lowering blood pressure. It is usually administered with a diuretic. Methyldopa is rarely used due to the availability of newer agents with a more favorable adverse side effect profile. It is the drug of choice, however, for chronic hypertension in pregnant women because of safety to the fetus.

Side effects of methyldopa can include:

- Hypotension and drowsiness

Anemia or leukopenia—rare

- GI symptoms, including nausea, vomiting, diarrhea, constipation, and sore tongue

Sexual dysfunction

Liver disorders

Nasal congestion

Contraindications or extreme caution with methyldopa applies to:

Liver disorders

Dialysis patients

Blood dyscrasias

Older adults

Interactions of methyldopa may occur with:

Levodopa (can cause CNS effects and psychosis)

Lithium

NSAIDs, tricyclic antidepressants, sympathomimetics (leads to hypertension)

Clonidine (Catapres), like methyldopa is a *central-acting* alpha-adrenergic agent, used mainly in the treatment of hypertension. It is available as an oral preparation, a transdermal system, and as an injection for epidural use. Clonidine has also been used successfully in a variety of other conditions including ADHD, nicotine/opiate withdrawal, vascular headaches, glaucoma, ulcerative colitis, Tourette's syndrome, and treatment of severe pain in cancer patients.

Prazosin (Minipress) is a *peripheral acting* alpha-adrenergic blocker used primarily to treat hypertension. Other agents in this class are used to treat benign prostatic hypertrophy (BPH). Treatment with alpha-adrenergic blockers once was considered potentially favorable for the management of hypertension in patients with BPH to target both blood pressure and BPH symptoms. However, a recent study determined that patients treated with the alpha-blocker doxazosin, when compared with those treated with the diuretic chlorthalidone, had an increased risk for stroke and heart failure. Therefore, hypertension should not be managed with an alpha-blocker alone, and BPH symptoms should be managed separately (see Chapter 15 for a discussion on the use of alpha-blockers in BPH).

Peripheral Vasodilator

Hydralazine, a peripheral vasodilator, is sometimes used in the treatment of moderate to severe hypertension, especially in patients with congestive heart failure, because it increases heart rate and cardiac output. The drug is generally used in conjunction with a diuretic and another hypotensive agent, for example, a beta-blocker. Recently, a fixed-dose combination therapy of isodorbide dinitrate and hydralazine (BiDil) was approved by the FDA for the treatment of heart failure in black patients.

Side effects of hydralazine can include:

- *Tachycardia* and palpitations
- Headache and flushing
- Orthostatic hypotension
- GI effects, including nausea, vomiting, diarrhea, and constipation
- Blood abnormalities
- Edema and weight gain

Contraindications with hydralazine include:

Systematic lupus erythematous (SLE)

Renal disease

Coronary artery disease, rheumatic heart disease

Pregnancy, usually (however, many regard hydralazine as the antihypertensive of choice during preeclampsia)

See Table 25-2 for a summary of the antihypertensives.

Table 25-2 Antihypertensives

GENERIC NAME	TRADE NAME	DOSAGE
Beta-Adrenergic Blockers		
atenolol	Tenormin	25–100 mg PO daily
carvedilol	Coreg	6.25–25 mg PO BID w/food
	Coreg CR	20–80 mg daily w/food (SR)[a]
metoprolol	Lopressor	100–400 mg PO daily in div. doses
	Toprol XL	50–100 mg PO daily (SR)
nebivolol	Bystolic	5–40 mg PO daily (also has vasodilatory properties)
propranolol	Inderal	160–480 mg PO daily in 2–3 div. doses
	Inderal LA[a]	80–160 mg PO daily (SR)
Calcium Channel Blockers		
amlodipine	Norvasc	2.5–10 mg PO daily
diltiazem	Cardizem CD	120–360 mg PO daily (SR)
	Cardizem LA	
	diltiazem SR	120–180 mg PO BID (SR)
nifedipine	Procardia XL	30–90 mg PO daily (SR)
	Adalat CC	
verapamil	Calan SR, Isoptin SR	120–240 mg PO 1–2 × per day (SR)
ACE Inhibitors		
benazepril	Lotensin	10–20 mg 1–2 × per day
captopril	Capoten	12.5–50 mg PO BID–TID ac
enalapril	Vasotec	5–20 mg PO BID
lisinopril	Prinivil, Zestril	5–40 mg PO daily
ramipril	Altace	2.5–20 mg PO 1–2 div. doses
trandolapril	Mavik	1–4 mg PO daily
Angiotensin Receptor Blockers		
losartan	Cozaar	25–100 mg PO 1–2 div. doses
olmesartan	Benicar	20–40 mg PO daily
telmisartan	Micardis	20–80 mg PO daily
valsartan	Diovan	80–320 mg PO daily

(*continued*)

Table 25-2 Antihypertensives—*continued*

GENERIC NAME	TRADE NAME	DOSAGE
Other Antihypertensives		
Antiadrenergic Agents		
clonidine	Catapres	0.1–1.2 mg PO daily in div. doses
	Catapres TTS	Weekly patch (delivers 0.1–0.3 mg per 24 h)
methyldopa		250 –500 mg PO 2–4 × per day
prazosin	Minipress	1–20 mg PO daily in 2–3 div. doses
Peripheral Vasodilator		
hydralazine		10–50 mg 2–4 × per day; IM, IV dose varies

[a]All extended release products (ER/SR) must be swallowed intact! Quick release of the medication can cause the blood pressure to drop suddenly, sending the patient into shock.
Note: This is only a representative list of the most commonly used drugs in this category. There are many others and many in combination with a diuretic.

PATIENT EDUCATION

For all antihypertensives, patients should be instructed regarding:

- Routinely monitoring blood pressure at home, keeping a log of their blood pressure readings, and sharing this information with their physician
- Immediate reporting of any adverse side effects, especially slow or irregular heartbeat, dizziness, weakness, breathing difficulty, gastric distress, and numbness or swelling of extremities
- Taking medication on time as prescribed by the physician; *not* skipping a dose or doubling a dose; *not* discontinuing the medicine, even if the patient is feeling well, without consulting the physician first
- Rising slowly from reclining position to reduce lightheaded feeling
- Taking care in driving a car or operating machinery if medication causes drowsiness (ask the physician, nurse, or pharmacist about the specific medication, since medicines differ and individual reactions differ; older people are more susceptible to this effect)
- Potentiation of adverse side effects by alcohol, especially dizziness, weakness, sleepiness, and confusion
- Reduction or cessation of smoking to help lower blood pressure
- Importance of lifestyle modifications, such as exercise, quitting smoking, limiting alcohol usage, and a healthy diet in control of blood pressure; following the physician's instructions regarding

appropriate diet for the individual, which may include a low-salt or low-sodium or weight-reduction diet if indicated

Avoiding hot tubs and hot showers, which may cause weakness or fainting

Mild exercise on a regular basis as approved by the physician

Always swallowing the extended-release products intact. Quick release of the medication into the system can cause the blood pressure to drop suddenly, causing loss of consciousness and possible shock.

Avoiding grapefruit juice while taking calcium channel blockers, which can increase the risk of hypotension and other adverse cardiac effects.

CORONARY VASODILATORS

Coronary vasodilators are used in the treatment of angina. When there is insufficient blood supply (**ischemia**) to a part of the heart, the result is acute pain. The most common form of angina is angina pectoris, chest pain resulting from decreased blood supply to the heart muscle. Obstruction or constriction of the coronary arteries which supply the heart muscle with oxygenated blood results in angina pectoris. Vasodilators are administered to dilate these blood vessels (thus decreasing myocardial oxygen demand) and stop attacks of angina or reduce the frequency of angina when administered prophylactically. Coronary vasodilators used in the treatment and prophylactic management of angina include nitrates, beta-blockers, and calcium channel blockers.

The nitrates used most commonly for relief of acute angina pectoris, as well as for long-term prophylactic management, are nitroglycerin and isosorbide (e.g., Isordil, Imdur). Nitroglycerin is available in several forms and can be administered in sublingual tablets allowed to dissolve under the tongue or a sublingual spray for relief of acute angina pectoris. If relief is not attained after a single dose during an acute attack, additional tablets may be administered at five-minute intervals, with *no more than three doses given in a 15-minute period*. If chest pain is not relieved or worsens 5 minutes after a dose, EMS should be activated because unrelieved chest pain can indicate an acute myocardial infarction.

Nitroglycerin is also available in timed-release capsules and tablets, and in an injectable formulation that must be diluted carefully according to the manufacturer's instructions for IV administration. Nitroglycerin tablets and capsules must be stored *only in glass containers* with tightly fitting metal screw tops away from heat. Plastic containers can absorb the medication, and air, heat, or moisture can cause loss of potency. Impaired potency of the SL tablets can be detected by the patient if there is an absence of the tingling sensation under the tongue common to this form of administration.

For long-term prophylactic management of angina pectoris, nitroglycerin is frequently applied topically as a transdermal system. One type of nitroglycerin that is absorbed through the skin is Nitro-Bid ointment, applied with an applicator-measuring (Appli-Ruler) paper. Usual dosage is 0.5–2 inches applied every eight hours. *Remove old paper first.* The ointment is spread lightly (not massaged or rubbed) over any hairless skin area, and the applicator paper is taped in place. Care must be taken to avoid touching the ointment when applying (accidental absorption through the skin of the fingers can cause headache). If nitroglycerin ointment is discontinued, the dose and frequency must be decreased gradually to prevent sudden withdrawal reactions. See Figure 9-1 in Chapter 9, Administration, for ointment application technique.

Another topical nitroglycerin product, which has longer action, is in transdermal form (e.g., Nitro-Dur). The skin patch is applied every 24 h (on in A.M./off 12 h later in the P.M.) to clean, dry, hairless areas of the upper arm or body. Do not apply below the elbow or knee. The sites should be rotated to avoid skin irritation and raw, scarred, or callused areas should be avoided. Patch dosage varies widely, from 0.1 to 0.8 mg per hour daily. *Check prescribed dosage carefully. Remove old patch.*

Another nitrate used for acute relief of angina pectoris and for prophylactic long-term management is isosorbide. It is available in SL tablets, regular-release tablets, and timed-release capsules and tablets. When using long-acting nitrates, a 12–14 h nitrate-free interval between the last dose of the day and the first dose of the following day is recommended to lessen the risk of nitrate tolerance.

Side effects of the nitrates can include:

- Headache (usually diminishes over time; analgesics may be given to alleviate pain)
- Postural hypotension, including dizziness, weakness, and syncope (*patients should be sitting during administration of fast-acting nitrates*)
- Transient flushing
- Blurred vision and dry mouth (discontinue drug with these symptoms)
- Hypersensitivity reactions, enhanced by alcohol, including nausea, vomiting, diarrhea, cold sweats, tachycardia, and syncope

Contraindications or extreme caution with nitrates applies to:

- Glaucoma
- GI hypermotility or malabsorption (with timed-release forms)
- Intracranial pressure
- Severe anemia
- Hypotension

Interactions of nitrates may occur with alcohol, which potentiates hypotensive effects. Phosphodiesterase (PDE) inhibitors such as sildenafil (Viagra), used for erectile dysfunction, are contraindicated in men taking

nitrates. The two drugs interact to cause a large, sudden, dangerous drop in blood pressure.

For long-term prophylactic treatment of angina pectoris, beta-blockers such as metoprolol (Lopressor), and calcium channel blockers, such as diltiazem (Cardizem) and verapamil (Calan), are frequently used (see Antiarrhythmic Agents for information on side effects, etc.).

PATIENT EDUCATION

Patients receiving coronary vasodilators (nitrates) should be instructed regarding:

- Administering fast-acting preparations (sublingual tablets or spray) while sitting down because the patient may become lightheaded
- Rising slowly from a reclining position
- Not drinking alcohol or taking PDE inhibitors while taking these medicines, which can cause a serious drop in blood pressure
- Using timed-release capsules or tablets to prevent attacks (they work too slowly to help once an attack has started)
- Taking timed-release capsules or tablets on an empty stomach with a full glass of water
- Allowing sublingual tablets, to dissolve under the tongue or in the cheek pouch and not chewing or swallowing them
- Repeating sublingual, tablets, or spray in 5–10 min for a maximum of three tablets or sprays (if no relief of chest pain or worsening within 5 min, activate EMS or if EMS unavailable report to the Emergency Department)
- Not discontinuing medication suddenly if administered for several weeks (dosage must be reduced gradually under physician's supervision)
- Sensations to be expected, including facial flushing, headache for a short time, lightheadedness upon rising too suddenly (if these symptoms persist or become more severe, or other symptoms occur, such as irregular heartbeat or blurred vision, notify the physician at once)
- Preventing attacks of angina by administering a sublingual tablet or spray before physical exertion or emotional stress (it is preferable to avoid physical or emotional stress when possible)
- See Chapter 9 for patient education regarding administration of nitroglycerin ointment or patch.

Please see Table 25-3 for a summary of coronary vasodilators.

Table 25-3 Coronary Vasodilators

GENERIC NAME	TRADE NAME	DOSAGE
Nitrates[a]		
nitroglycerin	Nitrostat tabs S.L.	1–3 tabs q5min × 3 max in 15 min PRN
	Nitrolingual spray	1–2 sprays (0.4–0.8 mg) SL q5min × 3 max in 15 min PRN
	caps E.R.	2.5–9 mg PO q8–12h
	Nitro-Bid oint 2%	1–2 inches q8h (while awake and at bedtime); unit dose foilpac equiv to ~ 1"
	Nitro-Dur, Others	1 transdermal patch to deliver 0.1–0.8 mg per hr daily, rotate site; on 12–14 h per off 10–12 h
	IV, premixed or sol for inj	IV dose varies
isorbide dinitrate		SL 2.5–5 mg × 3 max in 15–30 min
	Isordil	Prophylactic PO 10–40 mg BID–TID
	Dilatrate (SR)	PO 40 mg q8–12h
with hydralazine	BiDil	PO 1–2 tabs TID (for heart failure)
isosorbide mononitrate	Monoket, Ismo	10–20 mg PO BID (7 h apart) or TID at 8 AM, 1 PM, and 6 PM.
	Imdur (SR)	30–60 mg PO 1–2 × per day

[a]For prevention and treatment of angina pectoris
Note: Beta-blockers and calcium channel blockers are also administered prophylactically for angina pectoris, and can be given concurrently with the nitrates.

VASOCONSTRICTORS

Vasoconstrictors are adrenergic in action. Drugs such as norepinephrine (Levophed) constrict blood vessels, resulting in increased systolic and diastolic BP. These drugs, administered IV, are used mainly in the treatment of shock, short term only. Refer to Chapter 13 for a detailed discussion of these agents.

ANTILIPEMIC AGENTS

It is estimated that nearly 50% of Americans have elevated total blood cholesterol levels above 200 mg/dL—a key risk factor for coronary heart disease (CHD). Cardiovascular disease is the leading killer of men and women in the United States. High cholesterol can lead to arterial blockage, hardening of the arteries, blood clots, heart attack, or stroke and may even play a role in dementia.

Lipoproteins are responsible for transporting cholesterol and other fats through the blood stream. *Low-density lipoproteins* (LDLs; *bad cholesterol*) carry the largest amount of the cholesterol in the blood and are responsible for transporting and depositing it in arterial walls. *Very low-density lipoproteins* (VLDLs, triglycerides) are precursors of LDL and compose the largest proportion of lipids in the diet, adipose tissue, and the blood. *High-density lipoproteins (HDLs; "good cholesterol")* help transport LDL cholesterol from

the walls of the arteries through the bloodstream to the liver for excretion. An HDL level of below 40mg/dL is considered low and each 1mg/dL increase in HDL is associated with a 6% lower risk of cardiovascular disease.

LDL cholesterol is the primary target of treatment in clinical lipid management. The use of therapeutic lifestyle changes (TLC), including LDL-lowering dietary management (e.g., restriction of saturated fat/cholesterol intake, including fiber and soy protein in diet), weight control, appropriate exercise, and smoking cessation will achieve the therapeutic goal (LDL below 100 mg/dl) in many persons. If these measures are inadequate, drug therapy may be added. Six categories of **antilipemic agents** used to lower blood cholesterol levels are available: HMG-CoA reductase inhibitors (the *statins*), bile acid sequestrants, nicotinic acid (niacin), fibric acid derivatives, cholesterol absorption inhibitor, and omega-3 fatty acids.

Statins

HMG-CoA reductase inhibitors (*statins*) inhibit the enzyme for cholesterol synthesis. These agents are the most potent lipid-lowering medications available for monotherapy and are considered to be the first choice in managing high cholesterol. Statins (e.g., atorvastatin—Lipitor, simvastatin--Zocor) have been shown to be very effective in lowering LDL levels (up to 60%) and are modestly effective in reducing triglyceride levels and increasing HDL levels, thereby reducing cardiovascular morbidity and mortality. Statins are generally well tolerated.

Side effects of statins include:

Mild GI disturbances, headache, rash, fatigue

- Myalgia and muscle weakness
- Rarely, rhabdomyolysis (destruction of muscle tissue leading to renal failure)
- Elevated liver enzymes (periodic liver function tests are necessary)

Contraindications or extreme caution with statins applies to:

Hepatic or renal disease

Existing myalgia or muscle weakness

Pregnancy, breast-feeding, children

Interactions of certain statins with amiodarone, immunosuppressive drugs, erythromycins, azole antifungals, antiretroviral protease inhibitors, diltiazem, verapamil, *grapefruit juice*, or other antilipemic drugs (fibrates and niacin) increase risk of myopathy and renal failure.

Bile Acid Sequestrants

Cholestyramine (Questran) and colesevelam (WelChol), which are not absorbed from the GI tract, bind bile acids in the intestine, interrupting the process by which bile acids are returned to the liver for reuse. Since bile acids are formed from cholesterol, sequestrants reduce total body cholesterol. Bile acid sequestrants can be used as monotherapy when moderate reductions in LDL are required or as add-on therapy to statins. They should not be used as a single agent in the presence of elevated triglycerides.

Side effects of bile acid sequestrants include:

- Constipation, gas, cramps, heartburn, nausea, anorexia, abdominal pain, and bloating (occurs frequently and may affect compliance)

  Colesevelam is administered at lower doses because of its higher bile-binding capacity and is associated with fewer GI adverse effects.

Contraindications for bile acid sequestrants include:

Biliary cirrhosis and obstruction

GI obstruction or fecal impaction

Interactions with bile acid sequestrants can reduce the absorption of many drugs, including antibiotics, cardiac glycosides, fat-soluble vitamins, thiazide diuretics, and thyroid hormones (administer at least one hour before or four hours after the bile acid sequestrants).

Nicotinic Acid (Niacin)

Nicotinic acid reduces hepatic synthesis of triglycerides and limits secretion of VLDLs by inhibiting the mobilization of free fatty acids from the peripheral tissues. It lowers serum total and LDL cholesterol and triglyceride levels and also raises HDL cholesterol levels. Niacin may be useful in combination with a statin in patients with diabetic dyslipidemia (abnormal levels of various blood lipid fractions).

Side effects of niacin can be troublesome and include:

- GI upset, blurred vision, fatigue
- *Skin flushing*, itching, and irritation (more common with immediate-release preparations; pretreatment with aspirin or ibuprofen can diminish cutaneous reactions)

  Glucose intolerance and hyperuricemia (higher doses)
- Hepatotoxicity (especially with sustained-release products)

Note
Regular- and extended-release formulations of niacin are not bioequivalent and are not interchangeable

Contraindications of niacin include:

Hepatic, gallbladder, or peptic ulcer disease, diabetes, glaucoma, or gout

Pregnancy and lactation (high doses); children (<10 years old)

Interactions of niacin with:

Antihypertensives and vasodilators potentiate hypotensive effects

Antidiabetic agents with loss of blood glucose control

Alcohol which worsens flushing

Fibric Acid Derivatives (Fibrates)

The fibrates fenofibrate (TriCor) and gemfibrozil (Lopid) possess minimal LDL reducing capacity but are especially effective in patients who have extremely high triglyceride levels, elevated VLDL levels, and in patients with combined forms of hyperlipidemia. They are a good choice for diabetics because they improve

glucose tolerance. The mechanism by which fibrates reduce triglycerides is poorly understood. Fibrates may be used in combination with other antilipemics, since these agents appear to be additive in lowering LDL and raising HDL cholesterol. Fibrates are generally well tolerated.

Side effects of fibrates can include:

- GI complaints (diarrhea, dyspepsia, nausea and vomiting, abdominal pain)
- Cholethiasis, jaundice, blood dyscrasias, myopathy

Hypersensitivity reactions, rarely

Increased risk of pulmonary emboli (PE)

Contraindications and cautions with fibrates include:

Gallbladder, hepatic, renal disease, or peptic ulcer

Pregnancy, lactation, and use in children

Interactions of fibrates with:

Oral anticoagulants and hypoglycemic agents (potentiate effects);

Statins to increase risk of serious muscle problems (use together only in the lowest effective doses and if benefits outweigh risks)

Ezetimibe is not advised—interaction studies pending

Cholesterol Absorption Inhibitor

Ezetimibe (Zetia) moderately reduces LDL by inhibiting intestinal absorption of both dietary and biliary cholesterol, blocking its transport in the small intestine. It can be taken simultaneously with a statin (Vytorin, a combination product), and the LDL-lowering effects of the two drugs are additive. Ezetimibe is generally well tolerated, with abdominal pain, back pain and arthralgia being reported. Patients with gallbladder disease and moderate to severe hepatic insufficiency should not take it.

Administer ezetimibe at least one and two hours before or two and four hours after administering antacids and bile acid sequestrants respectively. Avoid use with cyclosporine (increases serum concentrations of both drugs) and fibrates (combination not fully studied).

Preliminary results of a trial comparing Vytorin (ezetimibe/simvastatin) to Zocor (simvastatin) on reducing plaque build-up in blood vessels were recently released. Vytorin was not better than Zocor at reducing plaque build-up, but it was better at lowering LDL cholesterol. For now, experts recommend that healthcare providers continue to prescribe medication necessary to lower LDL cholesterol to target goals.

Omega-3 Fatty Acids

Omega-3 fatty acids include eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA), found in fatty cold-water fish, and alpha-linolenic acid (ALA), found in flaxseed, tofu, soybean oil, canola oil and nuts. There is good evidence that EPA and DHA prevent primary and secondary heart disease and reduce

triglycerides (as an adjunct to diet or simvastatin). The mechanism by which omega-3 fatty acids lower triglycerides (TG) is not clear, but may involve reduced TG biosynthesis, increased TG clearance, and competition with TG for the use of fatty acid substrates.

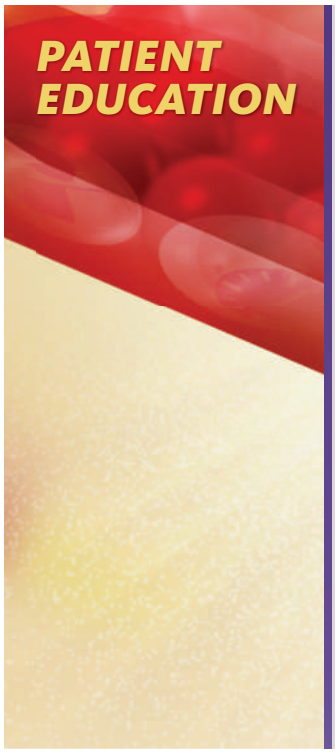
The best source of omega-3 fatty acids is fatty fish, like salmon, but fish oil capsules may be more convenient, especially if high doses are needed. A highly concentrated and purified form of omega-3 fatty acids is also available by prescription only as *Lovaza*. Fish oil can cause nausea, heartburn, or diarrhea. A fishy aftertaste can be reduced by refrigeration or freezing (Lovaza should not be frozen). Since omega-3 fatty acids inhibit platelet aggregation, caution is advised when used concurrently with anticoagulants, platelet inhibitors, and thrombolytic agents.

See Table 25-4 for a summary of antilipemic agents.

Table 25-4 Antilipemic Agents

GENERIC NAME	TRADE NAME	DOSAGE
Antilipemic Agents		
Statins		
atorvastatin	Lipitor	10–80 mg PO daily
lovastatin	Mevacor	20–80 mg PO at bedtime with food
pravastatin	Pravachol	10–80 mg PO at bedtime
rosuvastatin	Crestor	5–40 mg PO daily
simvastatin	Zocor	5–80 mg PO at bedtime
Bile Acid Sequestrants		
cholestyramine	Questran, Questran Light	4 g 1–2 × per day ac; mix powder with water, milk, or juice
colesevelam	Welchol	6 tabs (625 mg each) daily or 3 tabs BID w/ food and a full glass of water; max 7 tabs per day
Nicotinic Acid		
niacin	Niaspan, Slo-Niacin	Dose varies with response; take after meals or a snack
Fibric Acid Derivatives		
fenofibrate	Antara, Lofibra, Tricor	43–200 mg PO daily with food depending on formulation/manufacturer
gemfibrozil	Lopid	600 mg PO BID ac
Cholesterol Absorption Inhibitor		
ezetimibe	Zetia	10 mg PO daily
Omega-3 Fatty Acids		
fish oil (OTC)		3–6 grams per day
	Lovaza (Rx)	4 grams per day
Combinations		
atorvastatin/amlodipine	Caduet	PO daily; dose varies with response
ezetimibe/simvastatin	Vytorin	PO daily evening; dose varies with response
lovastatin/niacin	Advicor	PO daily bedtime w/ food; dose varies with response

Note: Other antilipemic agents are available. Some reduce triglycerides as well.



Patients on antilipemic therapy should be instructed regarding:

- Continuing diet (low-fat, low-cholesterol) and aerobic exercise
- Taking medicine with meals to reduce GI upset
- Reporting side effects to the physician immediately, *especially muscle pain, weakness, or bleeding*
- With cholestyramine, the importance of a high-fiber diet, and/or a stool softener, fat-soluble vitamin/folic acid supplements, and not taking other medication within four hours
- Expecting facial flushing with niacin
- Taking most statins in the evening (the body synthesizes most cholesterol at night)
- *Avoiding grapefruit juice* while taking statins; adverse effects potentiated, note other interactions
- The importance of regular liver function tests initially
- If all other factors remain the same, medication will probably need to be taken throughout the patient's lifetime. Sometimes diet and exercise will eliminate the need

ANTICOAGULANTS

Anticoagulants are divided into two general groups: coumarin derivatives and heparins. The action of these two classes is quite different. However, their purpose is the same: to prevent formation of clots or decrease the extension of existing clots in such conditions as venous thrombosis, stroke, pulmonary embolism, and coronary occlusion. Also, many patients with artificial heart valves, mitral valve disease, or chronic atrial fibrillation, or postsurgical patients (cardiac bypass, vascular surgery, and hip/knee replacement) receive anticoagulants to prevent embolism/thrombosis. Patients on anticoagulants, especially older patients, should be constantly observed for *bleeding complications*, such as cerebrovascular accidents (CVAs). The coumarin derivatives and heparin do not dissolve existing clots; they only interfere with the coagulation process preventing clot formation and/or propagation.

Warfarin

Warfarin (Coumadin) is administered *orally*. This medicine alters the synthesis of blood coagulation factors in the liver by interfering with the action of vitamin K. The *antidote for serious bleeding complications during warfarin therapy is prothrombin complex concentrate or fresh frozen plasma and vitamin K*. The action of warfarin is slower than that of heparin; therefore warfarin is generally used as follow-up for long-term anticoagulant therapy, although warfarin may be started at the same time as heparin.

The most commonly used laboratory method of monitoring therapy with coumarin derivatives is the International Normalized Ratio (INR). The INR serves as a guide in determining dosage. The observed variability in patient

response to warfarin may be due in part to *genetically* determined differences in drug distribution, drug target proteins, and drug metabolism. In the future, genotyping for warfarin therapy may aid in personalizing or tailoring of warfarin dosing.

Interactions of warfarin with *many* drugs have been reported. Concurrent administration of any other drug should be investigated, and the following drugs should be *avoided* if possible. Some of the drugs that may *increase* response to warfarin include:

Anabolic steroids

Alcohol (acute intoxication)

Proton pump inhibitors

All NSAIDs, including aspirin; thrombolytics

Tricyclic antidepressants; SSRIs

Thyroid drugs

Amiodarone, propafenone and quinidine

Many anti-infective agents

Many antilipemic agents

Acetaminophen (large daily doses or long duration)

Grapefruit juice, fish oil, vitamin E, many herbal supplements

Some of the drugs that may *decrease* response to coumarin derivatives include:

Alcohol (chronic alcoholism)

Barbiturates

Estrogen (including oral contraceptives)

Antiretroviral protease inhibitors

There are many other interactions with coumarin derivatives. *Always check before administering any other medicine.*

Heparin and Low-molecular Weight Heparins

There are two types of heparin: the standard or unfractionated type (UFH) and the low-molecular-weight heparins (LMWHs).

Heparin is not absorbed from the GI tract and the standard type (UFH) must be administered *intravenously* or *subcutaneously*. The LMWH type is usually only administered subcutaneously but may be given IV (not FDA-approved) as well. Heparin acts on thrombin, inhibiting the action of fibrin in clot formation. The *antidote for serious bleeding complications during heparin therapy is protamine sulfate*. When administered IV, the action of heparin is immediate. A *dilute flushing* solution of heparin is also used to maintain patency of indwelling venipuncture devices used to obtain blood specimens and of catheters used for arterial access (arterial lines). Be sure to check that it is a dilute flushing solution before injection, and not full-strength heparin. However, 0.9% sodium chloride (normal saline) injection alone is used to flush *peripheral* venipuncture devices, for example, PRN adapters.

Heparin is *not* normally used to flush these devices because of possible drug incompatibilities and laboratory test interferences.

Low-molecular-weight heparins (LMWHs) include enoxaparin (Lovenox) and dalteparin (Fragmin). Administered subcutaneously, enoxaparin and other LMWHs have a better bioavailability and produce a more predictable anticoagulant response than does UFH. At recommended doses, enoxaparin does not significantly affect platelet activity, INR, or activated partial thromboplastin time (aPTT). Monitoring of anticoagulant effect is not necessary, but periodic complete blood counts (CBCs), stool occult blood tests, and platelet counts are recommended during treatment. Unlike UFH, in the case of clinically significant bleeding, no agent fully reverses the activity of LMWHs although protamine has some activity and should be given for life-threatening bleeding along with packed red blood cells and fresh frozen plasma transfusions if indicated.

Enoxaparin was the first LMWH to be approved in the United States. It is currently approved for prevention of deep vein thrombosis (DVT) in patients undergoing hip or knee replacement or abdominal surgery, for the treatment of unstable angina and non–ST elevation myocardial infarction, and for the inpatient treatment of acute pulmonary embolism (PE). It is also used in the outpatient treatment of acute DVT not associated with pulmonary embolism and is combined with warfarin.

When heparin is administered subcutaneously, especially if the patient is discharged and the medication will be administered at home, be sure to stress *patient education*. See also Chapter 9, Subcutaneous Injection of Heparin.

Measurement of the activated aPTT is the most common laboratory test for monitoring heparin therapy. When long-term anticoagulant therapy is begun with warfarin, there is a short-term overlap period in which both heparin and warfarin are administered concurrently.

Interactions of heparins with other anticoagulants, aspirin and NSAIDs, platelet inhibitors, or with thrombolytic agents, for example alteplase (tPA), may increase the risk of hemorrhage.

Side effects of all anticoagulants can include:

- Major hemorrhage
- Thrombocytopenia
- Minor bleeding (e.g., petechiae, nosebleed, and bruising)
- Blood in urine (hematuria) or stools (melena)
- Osteoporosis with long term use

Contraindications and cautions with anticoagulants include:

GI disorders and ulceration of GI tract

Hepatic and renal dysfunction (dose adjustments may be needed with LMWHs)

Blood dyscrasias

Pregnancy (heparin can be used with caution as it does not cross the placenta)

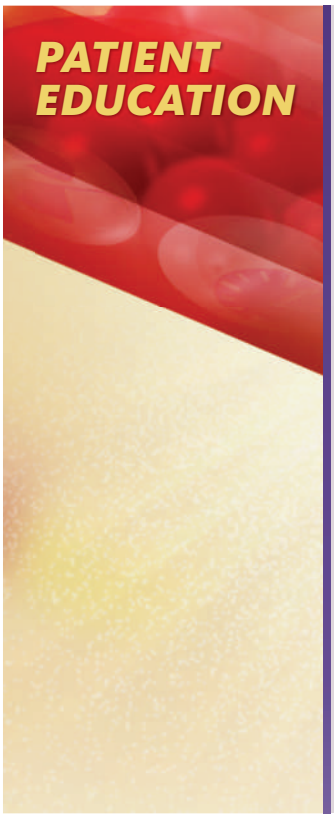
After stroke may increase risk of fatal cerebral hemorrhage

See Table 25-5 for a summary of the Anticoagulants.

Table 25-5 Anticoagulants

GENERIC NAME	TRADE NAME	DOSAGE
Anticoagulants		
warfarin	Coumadin, Jantoven	PO dose varies, based on PT/INR results
Unfractionated Heparin		
heparin		IV, subcu dose varies
Low-Molecular-Weight Heparins		
dalteparin	Fragmin	subcu, in fixed or body-weight-adjusted doses 1–2 × daily
enoxaparin	Lovenox	1–2 × daily subcu dose & duration varies
fondaparinux	Arixtra	pentasaccharide; daily subcutaneous dose varies

Note: Representative sample; many other products available.



It is very *important* that patients on anticoagulant therapy be instructed regarding:

- Daily observation of skin, gums, urine, and stools, and *immediate* reporting of any signs of bleeding
- Avoiding sports and activities that may cause bleeding
- *Immediate* reporting to the physician of any falls, blows, or injuries (internal bleeding is always a possibility)
- Special care with shaving (electric razor only) and with teeth brushing or dental floss
- Wearing an identification tag or carrying a card indicating use of anticoagulant
- *Immediate* reporting of severe or continued headache or backache, dizziness, joint pain or swelling, tarry stools, abdominal distention, vomiting of material resembling coffee grounds, or nosebleed
- *Avoid switching between brands and taking other medications without* the physician's approval, especially OTC aspirin, anti-inflammatory drugs, and antacids
- Avoiding alcohol

Note

Patients taking warfarin should be consistent in the amount of vitamin K-rich foods they eat daily in order to keep prothrombin levels stable. Large amounts of vitamin K–rich foods can counteract warfarin therapy. See Chapter 11, Vitamins and Minerals, for a list of foods containing vitamin K.

PLATELET INHIBITOR THERAPY

Platelet inhibitors prevent platelet clumping and are given as prophylactic therapy or as secondary prevention in patients with a history of recent stroke, recent MI, or established peripheral vascular disease. They are also used in the pharmacologic management of post-acute coronary syndrome (ACS), a spectrum of clinical conditions ranging from unstable angina and acute myocardial infarction, with or without ST-segment elevation. In addition to drug therapy, patients should be educated on modifying risk factors for coronary heart disease and stroke; that is, abstinence from all forms of tobacco, weight control, low-fat and low-cholesterol diet, and aerobic exercise on a regular basis.

Dipyridamole (Persantine)

Dipyridamole (Persantine) is a non-nitrate coronary vasodilator that inhibits platelet aggregation (clumping). When used alone, it is ineffective as an antithrombotic for patients with AMI, DVT or TIAs and therefore must be combined with other anticoagulant drugs. Dipyridamole is used with coumarin anticoagulants or aspirin in the prevention of postoperative thromboembolic complications of cardiac valve replacement.

Side effects of dipyridamole, usually transient, can include:

Headache, dizziness, weakness

Nausea, vomiting, diarrhea

Flushing, rash

Caution with older adults (more susceptible to orthostatic hypotension).

A combination of low-dose aspirin with extended-release dipyridamole (Aggrenox) is approved for stroke prophylaxis. Most adverse effects are mild and similar to those with either agent alone.

Aspirin

Because of its ability to inhibit platelet aggregation (clumping), aspirin has been studied extensively for use in the prevention of thrombosis. Aspirin therapy, usually 81–325 mg daily, has been used after myocardial infarction or recurrent transient ischemic attacks (TIAs) to reduce the risk of recurrence. Aspirin has also been used to reduce the risk of myocardial infarction in patients with unstable angina.

Aspirin therapy is not recommended for low risk patients because of an increased risk of hemorrhagic stroke associated with long-term aspirin therapy. Patients should be instructed not to start aspirin therapy without consulting a physician first. Because of *gastric irritation*, aspirin should be administered with food or milk. Film-coated tablets, enteric-coated tablets, and buffered aspirin preparations are available to reduce gastric irritation. Aspirin is **contraindicated** for anyone with bleeding disorders. See Chapter 19 for a description of other side effects, contraindications, and interactions.

Clopidogrel (Plavix)

Clopidogrel (Plavix) is an oral antiplatelet agent used to reduce atherosclerotic events (myocardial infarction, stroke, and vascular death) in patients with a history of recent stroke, recent MI, or established peripheral vascular disease. It is also used in combination with aspirin to prevent thrombosis of stents that are used to prop open diseased coronary arteries. Clopidogrel should be considered as an alternative in aspirin-intolerant or aspirin-failure patients.

Overall tolerability associated with use of clopidogrel appears to be similar to that of aspirin; however, GI bleeding may occur less often with clopidogrel. Conversely, clopidogrel is associated with higher rates of rash and diarrhea and possesses a slightly higher incidence of neutropenia than does aspirin, although severe neutropenia is rare with either drug. Just recently, a potentially new **drug interaction** was identified between clopidogrel and proton pump inhibitors (PPIs). Some reports suggest that use of certain PPIs may make clopidogrel less effective by inhibiting the enzyme that converts clopidogrel to the active form of the drug. There is currently no evidence that H2 blockers or antacids interfere with the antiplatelet activity of clopidogrel. Until further information is available, health care providers should re-evaluate the need for starting or continuing treatment with a PPI, including Prilosec OTC, in patients taking clopidogrel.

THROMBOLYTIC AGENTS

The body maintains a process to dissolve clots (fibrinolysis) after they have formed. Thrombolytic drugs (e.g., reteplase and alteplase) potentiate this process. **Thrombolytic agents**, given IV, reduce mortality when used as early as possible but within the first 12 hours after onset of acute myocardial infarction with ST-elevation (STEMI). Alteplase is also used to treat acute ischemic stroke (within 3 hours of the onset of stroke symptoms) and acute pulmonary embolism.

Administered in an ER or ICU setting, close monitoring of hemodynamics and vital signs is generally considered standard with thrombolytic therapy, particularly during the initial 24–48 h.

Intracranial hemorrhage is the most serious complication of thrombolytic therapy, but bleeding can occur at any site in the body. Bleeding occurs most commonly at access sites such as catheter insertion sites or venipuncture sites. Patients with preexisting coagulation problems, uncontrolled hypertension, severe chronic heart failure, and recent stroke are at the highest risk for developing bleeding complications during thrombolytic therapy.

Hemorrhage can result from concomitant therapy with heparin or other platelet-aggregation inhibitors. If severe bleeding occurs during therapy, the drug should be discontinued promptly. Rapid coronary lysis can result in the development of arrhythmias; however, they are generally transient in nature.

COLONY STIMULATING FACTORS (CSFs)

Colony stimulating factors (CSFs) are responsible for the regulation of hematopoiesis (production of blood cells) and certain activities of specific cell lines. All CSFs are products of recombinant technology. The **erythropoiesis-stimulating agents (ESAs)** such as epoetin alfa (Epogen or Procrit) are responsible for the regulation of the production and development of blood cells, normally in the bone marrow. Epoetin alfa stimulates the bone marrow to produce more red blood cells and is approved for treatment of anemia in chronic renal failure, human immunodeficiency virus (HIV) infection, and anemia associated with chemotherapy. It also reduces the need for blood transfusions in anemic patients scheduled to undergo certain kinds of surgery. Darbepoetin alfa (Aranesp) is a *second-generation* agent that is dosed less frequently than epoetin alfa.

Before initiating ESA therapy, supplemental iron is usually needed because adequate iron stores are necessary to incorporate iron into hemoglobin. Treatment of iron deficiency by regular use of iron improves erythropoiesis and response to ESA therapy.

Recently, the FDA updated safety information in the "Black Box" warning regarding the use of ESAs: use the lowest dose possible to gradually increase the hemoglobin (Hgb) concentration to avoid the need for transfusion; measure Hgb levels twice a week for two to six weeks after any dosage adjustment to ensure that Hgb has stabilized in response to the dose change, and withhold the dose of the ESA if the Hgb increase exceeds 12g/dL or rises by 1g/dL in any two week period.

Side effects of epoetin alfa (Epogen) include:

- ! Hypertension—especially in dialysis patients
- ! Flu-like symptoms

  GI effects

  Rash

  Chest pain
- ! Increased mortality, serious cardiovascular and thromboembolic events, and increased risk of tumor progression or recurrence when Hgb levels exceed 12g/dL

A **granulocyte colony-stimulating factor (G-CSF)**, filgrastim (Neupogen) is involved in the regulation and production of neutrophils in response to host defense needs. It lessens the severity of myelosuppression in cancer patients and has allowed chemotherapy dose intensification or maintenance of dose intensity.

Side effects of filgrastim include:

Bone pain is common

Headache

Dermatological reactions

See Table 25-6 for a summary of platelet inhibitors, thrombolytic agents, and colony stimulating factors.

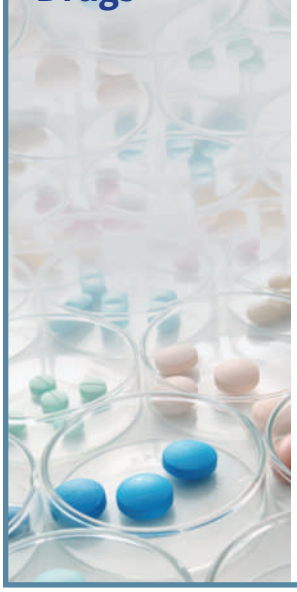
Table 25-6 Platelet Inhibitors, Thrombolytic Agents, and Colony Stimulating Factors

GENERIC NAME	TRADE NAME	DOSAGE
Platelet Inhibitors		
aspirin	Ecotrin, Ascriptin, others	81–325 mg PO daily
clopidogrel	Plavix	75 mg PO daily with or without food; 300 mg loading dose in ACS, usually with low dose aspirin
dipyridamole	Persantine	75–100 mg PO 4 × per day with warfarin or aspirin depending on indication
dipyridamole with aspirin	Aggrenox	1 cap PO BID
Thrombolytic Agents		
alteplase, t PA	Activase	IV bolus, then IV infusion
reteplase, r-PA	Retavase	IV bolus × 2 (30 min apart)
tenecteplase, TNK-tPA	TNKase	rapid IV bolus
Colony Stimulating Factors		
darbepoetin alfa	Aranesp	IV, subcutaneous dose varies
epoetin alfa	Epogen, Procrit	IV, subcutaneous dose varies
filgrastim, G-CSF	Neupogen	IV, subcutaneous dose varies

Note: Representative sample; many other products available.

CASE STUDY – A

Cardiovascular Drugs



Wilbur Worthington, a 65-year-old patient, has been treated in the hospital for cardiac arrhythmias with tachycardia. He will be discharged on Lanoxin and Calan and will need the following patient information.

1. Side effects of Lanoxin can include all of the following EXCEPT
   a. Double vision
   b. Headache
   c. Diarrhea
   d. Increased appetite
2. Older adults on Lanoxin are also more prone to the following EXCEPT
   a. Sedation
   b. Confusion
   c. Mental disorder
   d. Insomnia
3. The following drugs can increase risk of digoxin toxicity and arrhythmias EXCEPT
   a. Diuretics
   b. Antacids
   c. Quinidine
   d. Epinephrine
4. Calan does all of the following EXCEPT
   a. Dilates coronary arteries
   b. Increases heart contractions
   c. Blocks calcium
   d. Lowers blood pressure
5. Calan can have all of the following side effects EXCEPT
   a. Diarrhea
   b. Postural hypotension
   c. Bradycardia
   d. Vertigo

CASE STUDY – B

Homer Grange is diagnosed with hypertension and elevated cholesterol with increased LDL. The following information will be helpful.

1. The following antihypertensives can cause bradycardia EXCEPT
- a. Tenormin
- b. Procardia
- c. Hydralazine
- d. Methyldopa

2. The following advice would be appropriate EXCEPT
- a. Stop smoking
- b. Rise slowly
- c. Reduce salt intake
- d. Stop medicine when better

3. What medicine is often prescribed with antihypertensives?
- a. Antacids
- b. NSAIDs
- c. Diuretics
- d. Hypnotics

4. Lovastatin, an antilipemic, can cause all of the following EXCEPT
- a. Muscle cramps
- b. Edema
- c. Liver damage
- d. GI upset

5. Advice for patients taking statins should include all of the following EXCEPT
- a. Weight control
- b. Take medicine ac
- c. Low-fat diet
- d. Appropriate exercise

CHAPTER REVIEW QUIZ

Match the medication in the first column with the condition in the second column that it is used to treat. Conditions may be used more than once.

Medication	Classifications
1. _____ Isosorbide	**a.** Elevated cholesterol
2. _____ Zetia	**b.** Hypertension
3. _____ Lovenox	**c.** Angina
4. _____ Cardizem	**d.** Pulmonary emboli
5. _____ Zocor	**e.** Cardiac arrhythmia
6. _____ Plavix	**f.** Stroke prevention (platelet inhibitor)
7. _____ Crestor	
8. _____ Hydralazine	
9. _____ Quinidine	
10. _____ Procainamide	

Choose the correct answer.

11. Which one should be checked before administering digoxin?
    a. INR laboratory test **c.** Apical pulse
    b. Blood pressure **d.** Respirations
12. Which is not a toxic side effect of digoxin to be reported to the physician immediately?
    a. Nausea and vomiting **c.** Confusion
    b. Visual disturbances **d.** Tachycardia
13. Which is not a side effect of ACE inhibitors?
    a. Photosensitivity **c.** Dry cough
    b. Hypokalemia **d.** Hypotension
14. Which is not a side effect of beta-blockers, for example, Tenormin?
    a. Dizziness **c.** Confusion
    b. Insomnia **d.** Hyperglycemia
15. Which would not potentiate the hypotensive effect of beta-blockers, for example, Inderal?
    a. Isuprel **c.** Lasix
    b. Alcohol **d.** Tagamet
16. Which is not a side effect of calcium channel blockers, for example, Calan?
    a. Edema **c.** Vertigo
    b. Headache **d.** Tachycardia

17. Which is not a side effect of quinidine?
- **a.** Diarrhea
- **b.** Hypoglycemia
- **c.** Hypotension
- **d.** Bradycardia

18. Which is not an antihypertensive?
- **a.** Atenolol
- **b.** Hydrochlorothiazide
- **c.** Cholestyramine
- **d.** Verapamil

19. Which is not a side effect of nitrates?
- **a.** Postural hypotension
- **b.** Bradycardia
- **c.** Headache
- **d.** Flushing

20. Which is not a side effect of statins?
- **a.** Muscle pain
- **b.** Low liver enzymes
- **c.** GI distress
- **d.** Headache

21. Which drug, a fibrate, is the most effective single agent for lowering the triglyceride level?
- **a.** Questran
- **b.** Lipitor
- **c.** Lopid
- **d.** Zocor

22. Which is not a side effect of bile acid sequestrants, for example, Questran?
- **a.** Bloating
- **b.** Diarrhea
- **c.** Heartburn
- **d.** Nausea

23. Which is not a side effect of niacin?
- **a.** GI upset
- **b.** Low uric acid level
- **c.** Blurred vision
- **d.** Flushing

24. What is the antidote for bleeding problems with Coumadin?
- **a.** Protamine
- **b.** Vitamin K
- **c.** Persantine
- **d.** Procrit

25. What is the antidote for bleeding problems with heparin?
- **a.** Activase
- **b.** Vitamin K
- **c.** Plavix
- **d.** Protamine

Go to your StudyWARE™ CD-ROM and have fun learning as you play games and answer case study-related questions to help reinforce key concepts you learned in this chapter.

Go to your Study Guide and complete the review questions for this chapter.

Chapter 26

Respiratory System Drugs and Antihistamines

Objectives

Upon completion of this chapter, the learner should be able to

1. Describe uses of and precautions necessary with oxygen therapy
2. List medications used as smoking cessation aids and precautions for their use
3. Classify a list of respiratory system drugs according to action
4. List uses, side effects, and contraindications for bronchodilators and antitussives
5. Explain appropriate patient education for those receiving respiratory system drugs
6. Describe the action and uses of the antihistamines and decongestants
7. List the side effects, contraindications, and interactions of the antihistamines and decongestants
8. Define the Key Terms and Concepts

Key Terms and Concepts

Anticholinergics
Antihistamine
Antitussive
Asthma prophylaxis
Bronchodilator
Decongestants
Expectorant
Mucolytic
Rescue treatment
Smoking cessation aids
Sympathomimetic
Xanthine

Therapeutic measures for respiratory distress include oxygen, respiratory stimulants, bronchodilators, corticosteroids, mucolytics, expectorants, and antitussives.

OXYGEN

Oxygen is used therapeutically for hypoxia (insufficient oxygen supply to the tissues) and to decrease the workload of the heart and respiratory system, especially during distress. Some of the conditions for which oxygen is indicated are heart and lung diseases, carbon monoxide poisoning, and some central nervous system (CNS) conditions with respiratory difficulty or failure. Oxygen

may be administered by endotracheal intubation, nasal cannula, various masks, tents, and hoods.

Side effects of oxygen delivered at too high a concentration or for prolonged periods of time can include:

Hypoventilation, particularly with COPD (chronic obstructive pulmonary disease), may cause CO_2 retention and acidosis

Confusion

Changes in the alveoli of the lungs

Blindness (in premature infants)

See It In Action! Go to the StudyWARE™ CD-ROM to view a video on *Using Oxygen*.

Cautions apply to:

Patients with COPD (high O_2 concentrations may cause hypoventilation or apnea [cessation of breathing]).

Danger of fire when oxygen is used. Oxygen is not flammable but does support combustion. Smoking, matches, and electrical equipment that may spark (e.g., electric razors, hair dryers) are not allowed in rooms where oxygen is in use.

RESPIRATORY STIMULANTS

Respiratory stimulants include:

- Caffeine citrate in the treatment of neonatal apnea (see Chapter 20)
- Theophylline administered IV and orally to stimulate respiration in infants and patients with Cheyne-Stokes respiration

BRONCHODILATORS

Bronchodilators act by relaxing the smooth muscles of the bronchial tree, thereby relieving bronchospasm and decreasing the work of breathing. Bronchodilators are used in the symptomatic treatment of acute respiratory conditions such as asthma, as well as many forms of COPD. Classifications of bronchodilators include the sympathomimetics (adrenergics), the anticholinergics (parasympatholytics), and the xanthine derivatives.

Sympathomimetics

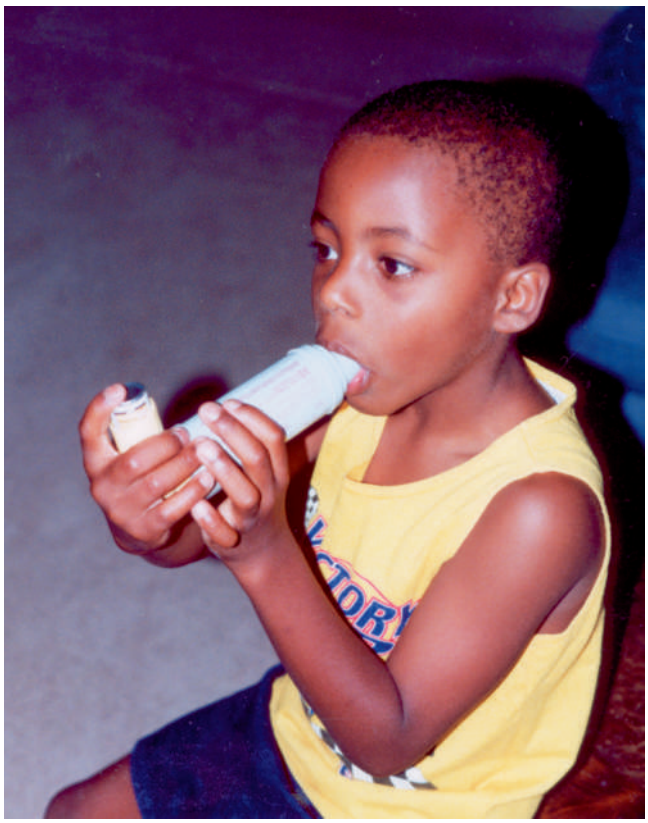
Sympathomimetics (adrenergics) are potent bronchodilators that increase vital capacity and decrease airway resistance. The adrenergics work on the smooth muscle in the lungs to cause relaxation. However, they also can affect the entire sympathetic nervous system. The adrenergics may produce serious side effects, and manufacturer's directions should be followed carefully regarding dosage and administration. The inhalation route of administration is preferred to minimize systemic adverse effects. Examples include albuterol, epinephrine, salmeterol, and others. The use of epinephrine as a bronchodilator in the treatment of asthma has largely been replaced by medications such as albuterol.

Metered Dose Inhalers

Metered dose inhalers (MDIs) remain popular due to ease of use, efficacy, and portability. In the past, all MDIs contained chlorofluorocarbon (CFC) as the propellant. Because of its detrimental effects on the ozone layer, the use of CFC was phased out by the end of 2008. Some manufacturers have reformulated their MDI to contain hydrofluoroalkane (HFA) as the propellant which has not been linked to depletion of the ozone layer and is nonflammable. Other manufacturers are discontinuing production of MDIs and utilizing dry-powder formulations instead. MDI's are frequently used and the use of a spacer or reservoir device assists in optimizing drug delivery within the lungs. See Figure 26-1.

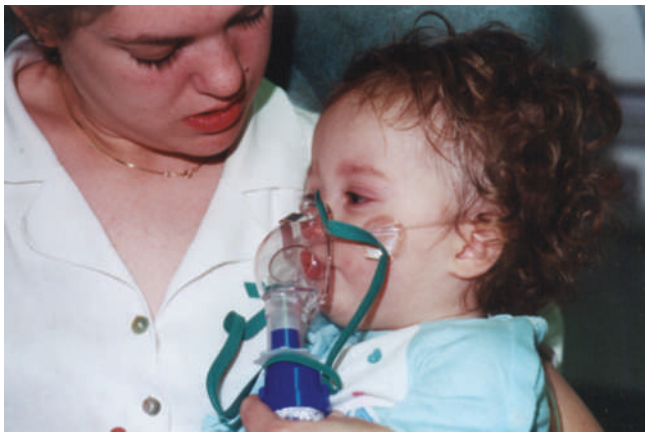
Breath-actuated inhalers provide medication (especially corticosteroids and long-acting beta$_2$ agonists) only under the pressure of inspiration, rather than through compression of the valve. This option is helpful for patients who are unable to coordinate inspiration with actuation of a conventional MDI. Unfortunately, the breath-actuated system, unlike the MDI, does not allow for use of a spacer and requires fast inhalation, which could be problematic in patients with severely diminished lung function.

Small volume nebulizers will create an aerosol mist of a drug solution that can then be inhaled into the lungs through a mouthpiece or a mask. The aerosol is created by either compressed air or oxygen gas and the optimal breathing pattern is a slow, deep breath with a sustained breath hold. See Figure 26-2.



Delmar/Cengage Learning

FIGURE 26-1 Child using an MDI with a spacer and a mouthpiece.



Delmar/Cengage Learning

FIGURE 26-2 Child receiving a small volume nebulizer (SVN) aerosol treatment with a mask.

See Table 26-1 for selected sympathomimetic products and dosages.

Side effects of the adrenergics include potentiation of theophylline effects with increased risk of toxicity, especially:

Gastrointestinal (GI)—nausea, vomiting, decreased appetite

- CNS stimulation—nervousness, tremor, dizziness
- Cardiac irregularities—tachycardia, palpitations, arrhythmias, angina

(Levalbuterol [Xopenex], an isomer of albuterol, and may cause less cardiac stimulation than albuterol, however this is controversial)

- Hypertension
- Hyperglycemia

Cautions for the adrenergics apply to:

First administration, which should be observed by medical personnel for hypersensitivity reactions

Contacting physician if decreased effectiveness occurs

Close monitoring, if administering oral inhaled adrenergics with other oral inhaled bronchodilators, for cardiovascular effects.

Patients on nonselective beta-blocking drugs (Inderal) will have a significant decrease in the effectiveness of adrenergic drugs.

Patients with cardiovascular or kidney disorders, diabetes, seizure disorders, or hyperthyroidism.

Due to a prolonged onset of action, long-acting beta$_2$ agonists (such as salmeterol) should not be used to treat an acute asthma attack or bronchospasm; these are indicated only for asthma prophylaxis. A short-acting beta$_2$ agonist (such as albuterol) should be available for **rescue treatment** of acute attack; warn patients that increasing use of rescue inhalers is a sign of deteriorating asthma control. In addition, long-acting beta$_2$ agonists have been associated with an increased risk of severe asthma exacerbations and asthma-related deaths.

Anticholinergics

Anticholinergics *(parasympatholytics)*, for example Atrovent, achieve bronchodilation by decreasing the chemical that promotes bronchospasm. Anticholinergics block the parasympathetic nervous system and can cause drying of pulmonary secretions. Adequate hydration should be encouraged to avoid mucus plugging. Inhaled anticholinergics are first-line therapy for COPD once symptoms become persistent. See Table 26-1 for dosage and other product names.

Side effects of anticholinergics can include:

- Cardiac effects—changes in heart rate, palpitations
- CNS stimulation—headache, drowsiness, dizziness, confusion, agitation
- Thickened secretions and mucus plugging; metallic taste

Cautions: Anticholinergics are not indicated for patients with unstable cardiac status, history of heart attacks, glaucoma, drug sensitivity, or prostatic hypertrophy.

Tiotropium (Spiriva), which is structurally similar to ipratropium (Atrovent), is administered daily in a Dry Powdered Inhaler (DPI) (vs. three to four times daily for ipratropium). It is more efficacious than ipratropium and may lead to a reduction in the use of sympathomimetics for rescue therapy.

Xanthines

The **xanthine** derivative theophylline, listed in Table 26-1, relaxes the smooth muscle of the bronchial airways and pulmonary blood vessels, and may possess anti-inflammatory actions. Xanthines are no longer a first-line treatment due to the modest clinical effectiveness, need for serum monitoring, their many adverse effects, and drug interactions. Because different individuals metabolize xanthines at different rates, appropriate dosage must be determined by carefully monitoring the patient's response, tolerance, and blood concentrations. For faster absorption, oral forms may be taken with a full glass of water on an empty stomach. To reduce gastric irritation, take with meals.

Theophylline is generally reserved for patients with COPD who do not respond or cannot take inhaled long-acting bronchodilators. When used, xanthines are usually administered as sustained-release formulations with other respiratory system drugs such as adrenergics and anticholinergics.

Side effects of theophyllines can be mild, or severe with acute toxicity including:

- GI distress—nausea, vomiting, epigastric pain, abdominal cramps, anorexia, or diarrhea
- CNS stimulation—nervousness, insomnia, irritability, headache, tremors, seizures (can be fatal)

- ! Cardiac effects—palpitation, tachycardia, arrhythmias, *especially with rapid IV administration*
- Urinary frequency (mild diuresis)
- ! Hyperglycemia

Caution when administering theophylline applies to:

- Cardiovascular, kidney, pulmonary, or liver dysfunction
- Diabetes, peptic ulcer, or glaucoma
- Children and older adults—more prone to toxicity
- IV injection—*must be done slowly*—see cardiac side effects
- Patients undergoing influenza immunization or who have influenza
- Pregnancy and lactation

Interactions occur with:

- Cimetidine, allopurinol, erythromycins, quinolones, oral contraceptives, calcium channel blockers, and beta-blockers, which increase theophylline levels
- Smoking, barbiturates, phenytoin, and rifampin, which decrease theophylline effectiveness

PATIENT EDUCATION

Patients taking bronchodilators (e.g., adrenergics, anticholinergics, or the xanthines) should be instructed regarding:

- Following the written directions on the package very carefully regarding dosage and administration because of the danger of serious side effects
- Proper technique for inhaler use
- Watching closely for cardiac irregularities or CNS stimulation (e.g., nervousness, tremor, dizziness, confusion, headache), and reporting these symptoms to the physician immediately
- Other side effects possible with adrenergics and xanthines, for example gastric distress, insomnia, or hyperglycemia
- Drinking adequate fluids to prevent mucus plugging, especially with anticholinergics
- Avoiding any new medications, including over-the-counter (OTC) drugs, without consulting the physician first, because of the danger of serious complications; many interactions are possible
- Avoiding changing brands of medicine without consulting the physician or pharmacist

See Table 26-1 for a summary of the sympathomimetic, anticholineric, and xanthine bronchodilators.

Table 26-1 Bronchodilators

GENERIC NAME	TRADE NAME	DOSAGE
Sympathomimetics		
Short-acting Beta$_2$ Agonists (rescue medications)		
albuterol sulfate	Proair HFA, Proventil HFA, Ventolin HFA	MDI, 1–2 puffs (90–180 mcg) q4–6h
		Inhal sol 2.5 mg q4–6h
		Oral soln, Tabs 2–4 mg q6–8h
	Vospire ER	Tabs ER 4–8 mg q12h
levalbuterol	Xopenex	Inhal sol 0.63 mg q6h–1.25 mg q8h; max 3.75 mg per day
	Xopenex HFA	MDI, 1–2 inhal (45–90 mcg) q4–6h
Long-acting Beta$_2$ Agonists (maintenance medications)*		
formoterol	Foradil Aerolizer	Powder for inhal, 12 mcg (contents of 1cap) q12h
salmeterol	Serevent Diskus	Powder for inhal, 1 puff q12h
Other		
epinephrine	Adrenalin	IM/Subcu 1:1000 sol 0.3–0.5 mL; Watch dose carefully!
Anticholinergics		
Short-acting		
ipratropium bromide	Atrovent HFA	MDI, 1–2 puffs (17–34 mcg) TID-4 × per day
	Atrovent	Inhal soln, 1 unit dose (500 mcg/ 2.5 mL NS)
		TID-4 × per day
		Nasal sol 0.03–0.06%, 2 sprays each nostril TID-4 × per day (up to 4 days)
ipratropium/albuterol (combination of anticholinergic and sympathomimetic)	Combivent	MDI, 2 puffs 4 × per day
	DuoNeb	Neb sol 1 vial (3 mL) 4 × per day
Long-acting		
tiotropium	Spiriva	Powder for oral inhal, 18 mcg daily
Xanthines		
theophylline	RTU infusion in D_5W	Dosage based on response and drug levels
	Elixophyllin	Elixir, 80 mg per 15 mL
	Uniphyl	Tabs ER, 200–600 mg daily
	Theo-24	Caps ER, 100–400 mg daily

***Note:** Due to delayed onset of action, long-acting beta$_2$ agonists should never be used to treat an acute attack. This is a representative list. Other products are available.

CORTICOSTEROIDS

Synthetic corticosteroids are used to relieve inflammation, reduce swelling, and suppress symptoms in acute and chronic reactive airway disease (asthma and some COPDs). Inhaled corticosteroids are considered a preferred drug therapy in long-term management of persistent asthma of various severities. Corticosteroids should be administered systemically (oral and injectable forms) for short-term "bursts" during exacerbations and occasionally at the beginning of treatment until symptoms are controlled. Inhaled corticosteroids are best employed on a regular, long-term, daily scheduled basis to prevent symptoms and may be administered by dry powder for inhalation, MDI, or aerosol. Inhaled corticosteroids have less systemic side effects than oral or injectable administration.

Nasal corticosteroids are increasingly considered first-line therapy for most *noninfectious* types of rhinitis and should be started before symptoms occur and taken regularly throughout the period of exposure. Aerosol preparations seem to be more irritating to the nasal mucosa. Aqueous preparations may drip into the throat, resulting in reduced deposition of drug in the nasal mucosa.

Side effects of inhaled corticosteroids

- Throat irritation and dry mouth

  Hoarseness

  Coughing, dysphonia (hoarseness)
- Oral fungal infections—patient should be encouraged to rinse mouth with mouthwash or water after administration
- Increased susceptibility to pneumonia

Contraindications and extreme caution with corticosteroids include:

Viral, bacterial, or fungal infections

Hypertension or congestive heart failure

Diabetes

Hypothyroidism or cirrhosis

Renal failure

See Chapter 23 for further information about corticosteroids and see Table 26-2 for a summary of corticosteroids.

Table 26-2 Corticosteroids

GENERIC NAME	TRADE NAME	DOSAGE
Corticosteroids (inhaled and intranasal)		
beclomethasone	QVAR HFA	MDI, 1–2 puffs (40 or 80 mcg per puff) BID
	Beconase AQ	Spray 1–2 inhal each nostril daily–BID
budesonide	Pulmicort Flexhaler	Powder for inhal, 180–360 mcg BID
	Pulmicort Respules	Neb susp, 0.25–1 mg daily or BID; indicated for children ≤ 8 yrs old
	Rhinocort Aqua	Aerosol 1–4 inhal each nostril daily (32 mcg per spray)
w/ formoterol	Symbicort	MDI, 2 puffs (80/4.5, 160/4.5) BID
fluticasone	Flovent HFA	MDI, 2–4 puffs BID (88–880 mcg)
	Flonase	Spray 1 inhal each nostril BID or 2 inhal daily
w/ salmeterol	Advair Diskus (100/50, 250/50, 500/50)	Powder for inhal, 1 inhal q12h
	Advair HFA (45/21, 115/21, 230/21)	MDI, 2 puffs q12h
nometasone	Asmanex Twisthaler	Powder for inhal, 220 mcg BID or 440 mcg qPM
	Nasonex	Spray 2 inhal each nostril daily (50 mcg per spray)
triamcinolone	Nasacort AQ	Inhaler, 2 inhal each nostril daily

This is a representative list. Other products are available.

ASTHMA PROPHYLAXIS

Leukotriene Inhibitors

Zafirlukast (Accolate) and montelukast (Singulair) are oral leukotriene receptor antagonists for **asthma prophylaxis** and treatment of chronic asthma. Leukotriene receptor antagonists primarily help to control the inflammatory process of asthma caused by leukotriene production, thus helping to prevent asthma symptoms and acute attacks. Montelukast can be used in children as young as two years old and has fewer drug interactions compared to zafirlukast.

Side effects of Singulair include:

- Headache
- Dizziness
- Nausea or dyspepsia
- Pain
- Fatigue
- Respiratory infections and fever

Contraindications/precautions include:

- Hepatotoxicity (zafirlukast)
- Pregnancy or lactation

Children under age 12 (zafirlukast)

Do not use to treat acute episodes of asthma

Drug interactions occur with:

Aspirin (increased levels of zafirlukast)

Erythromycin and theophylline (decreased levels of zafirlukast)

Warfarin and zafirlukast (increased prothrombin time)

Phenobarbital and rifampin (decreased levels of montelukast)

Mast Cell Stabilizers

The rupture or degranulation of mast cells and the subsequent spilling of their chemical mediator contents cause an inflammatory response that can lead to asthma. Stabilizing the mast cell membrane has anti-inflammatory actions that modify the release of mediators from mast cells and eosinophils.

A prophylactic for asthma, cromolyn was one of the first classified mast-cell stabilizers. Cromolyn has no value in the treatment of acute attacks of asthma. It has also been used in the prevention of exercise-induced bronchospasm. Cromolyn is available as an aerosol or solution for inhalation or a nasal solution (to treat seasonal allergic rhinitis). To be effective, the manufacturer's directions must be followed carefully.

Side effects of cromolyn can include:

- Throat irritation, cough, bronchospasm
- Nose burning, stinging, sneezing with nasal solution
- Nausea or headache

Caution applies to:

Those with cardiovascular disorders

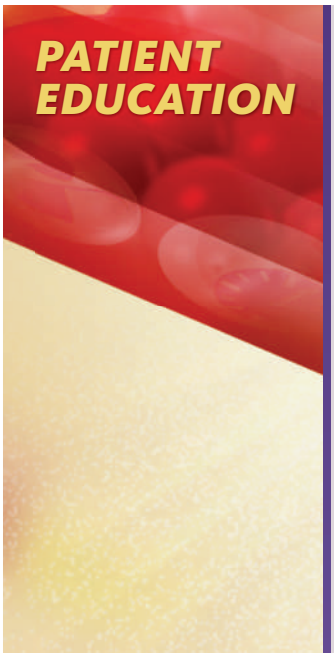
Proper use on a regular schedule

See Table 26-3 for a summary of asthma prophylaxis.

Table 26-3 Asthma Prophylaxis Agents

GENERIC NAME	TRADE NAME	DOSAGE
Asthma Prophylaxis and Treatment of Chronic Asthma		
Mast Cell Stabilizers		
cromolyn sodium		Inhal sol, 20 mg per treatment 4 × per day
		MDI 2 puffs 4 × per day
	Nasalcrom	Inhaler, 1 spray each nostril TID–4 × per day
Leukotriene Inhibitors		
montelukast	Singulair	Tabs 10 mg qPM
		Chew tabs, 4–5 mg qPM
zafirlukast	Accolate	Tabs 10–20 mg BID on empty stomach

This is a representative list. Other products are available.



Patients treated with inhaled corticosteroids or the asthma prophylaxis agents should be instructed regarding:

- Proper technique for inhaler use
- Side effects to expect, such as throat irritation, dry mouth, and cough, and with products administered nasally, for example cromolyn, nose burning, stinging, or sneezing are possible
- Complications of inhaled corticosteroids without proper precautions, for example, oral fungal infections. Patient should be encouraged to rinse mouth with mouthwash or water after treatment and to always rinse and air dry equipment after use
- Administering bronchodilator before corticosteroid when the two inhaled medications are ordered at the same time
- Reporting side effects to the physician, especially respiratory distress
- The importance of not smoking

MUCOLYTICS AND EXPECTORANTS

Mucolytics, such as acetylcysteine, decrease the hypersecretion of and liquefy pulmonary secretions. Thick secretions can be a problem in patients with obstructive lung disease, but there is little evidence that thinning or increasing the clearance of secretions improves symptoms and are generally not recommended for routine care. **Expectorants**, such as guaifenesin and others listed in Table 26-4, increase secretions, reduce viscosity, and help to expel sputum but like mucolytics offer no clinical benefit and are not recommended for patients with obstructive lung disease. Adequate fluid intake is important to maintain euvolemia (normal fluid volume) but excessive fluid intake is of no value. Guaifenesin is commonly combined in cough syrups for symptomatic management of productive ("wet") coughs associated with upper respiratory tract infections, bronchitis, pharyngitis, influenza, measles, or coughs provoked by sinusitis but evidence of benefit is lacking. Expectorants should not be used for self-medication or persistent or chronic coughs such as that associated with smoking or COPD. A persistent cough may be indicative of a serious condition. If cough persists for more than a week or is recurrent, or accompanied by a fever, a physician should be consulted.

Side effects of the expectorants are infrequent, usually not serious at recommended doses, and can include:

- Nausea and vomiting, diarrhea
- Runny nose
- Drowsiness, dizziness, and headache

Contraindications or caution with expectorants applies to:

- Patients with persistent or chronic cough
- Some asthmatics (prone to bronchospasm)

Patients with cardiovascular disease and hypertension, diabetes, glaucoma, hyperthyroidism, and prostatic hypertrophy, especially with combination products

Pregnancy or lactation

See Table 26-4 for a summary of the mucolytics and expectorants.

Table 26-4 Mucolytics and Expectorants

GENERIC NAME	TRADE NAME	DOSAGE
Mucolytic		
acetylcysteine	(Mucomyst)*	Neb soln, 3–5 mL 20% sol (diluted) or 6–10 mL 10% sol (undiluted) 3–4× per day; give short acting bronchodilator 10–15 min prior to dose
Expectorants		
guaifenesin	Mucinex	ER tabs 600–1200 mg, daily-bid; do not crush
	Robitussin	Sol 2–4 tsp q 4h as needed

Note: Guaifenesin is frequently combined with other drugs, for example, antihistamines, decongestants, and antitussives in OTC cough syrups.
*Brand name no longer marketed, but name is still commonly used.

The safety of OTC cough and cold preparations in the pediatric population is of great concern owing to reports of severe adverse reactions and deaths in infants and children. In October 2007, the FDA's Nonprescription Drugs and Pediatric Advisory Committee found there was no proof that these medications eased cold symptoms in children, while there were rare reports that they have caused serious harm. At that time, many manufacturers voluntarily removed from the market cough and cold products labeled for use in infants and babies.

In October of 2008, the FDA supported manufacturers of nonprescription cough and cold medicines for children voluntary modification of package labeling to state, "Do not use in children under 4 years of age." In addition to product labeling changes, new child-resistant packaging and measuring devices for the products are being introduced. With the changing status of cough and cold medications, the health care practitioner should thoroughly assess each patient's use of similar products (both OTC and Rx) to avoid duplication of therapy and the potential for inadvertent overdose. A web site (www.otcsafety.org/Parents) is available for parents seeking information on the use of these medicines in children.

ANTITUSSIVES

Antitussives are medications to prevent coughing in patients not requiring a productive cough. Coughing, a reflex mechanism, helps eliminate secretions from the respiratory tract. A dry, nonproductive cough can cause fatigue,

insomnia, and, in some cases, pain to the patient (e.g., pleurisy and fractured ribs). Most antitussives produce cough suppression by acting centrally on the cough center located in the brainstem. Cough suppressants are divided into narcotic preparations such as codeine and hydrocodone and non-narcotic preparations such as dextromethorphan.

Codeine, a *narcotic antitussive*, is widely used as a cough suppressant due to its reduced incidence of side effects (respiratory depressant action and bronchial constriction) at antitussive doses as compared to morphine. In some states, codeine is available as an OTC cough medication. Hydrocodone, another narcotic cough suppressant, has slightly greater antitussive activity compared to codeine but is more sedating.

Nonnarcotic antitussives (e.g., dextromethorphan) are used more frequently because they do not depress respirations, do not cause dependence, and have few side effects at recommended doses. Benzonatate (Tessalon), chemically related to the local anesthetic tetracaine, suppresses cough peripherally by anesthetizing receptors in the alveoli of the lungs, the bronchi, and the pleura; it also acts centrally like the other antitussives. Diphenhydramine (Benadryl), a first-generation antihistamine, is also used as a cough suppressant and is described in detail later in this chapter.

Many prescription and over-the-counter cough and cold formulations are available that combine several drugs, for example, antitussives with expectorants, antihistamines, and decongestants to treat two or more simultaneous symptoms. Combination formulations should be used only if the corresponding symptom is present. Combination products should not be given in addition to a different product with the same active ingredient.

Patients should be cautioned to seek advice from a healthcare professional familiar with each ingredient. Some ingredients are contraindicated in certain conditions. For example, antitussives and antihistamines would make it more difficult to expel secretions and thereby worsen conditions such as pneumonia and COPD. Products containing decongestants can cause serious adverse side effects in those with cardiovascular or thyroid conditions.

Side effects of antitussives can include:

- Respiratory depression (large doses or excessive use)
- Constipation
- Urinary retention with narcotic antitussives
- Sedation and dizziness
- Nausea and vomiting

Contraindications for antitussives apply to:

- Addiction-prone patients (refer also to discussion on dextromethorphan abuse by adolescents in Chapter 20)
- Asthma; COPD
- Use with other CNS depressants (refer to Chapter 19 for opioid interactions)

Caution with antitussives with children can include:

Some CNS side effects, behavioral disturbances, respiratory depression reported, especially large doses

Ester-type anesthetic (e.g., tetracaine) hypersensitivity with *benzonatate*

Interactions with dextromethorphan can include:

Triptans used for migraine headache

Monoamine oxidase inhibitors (MAOIs) resulting in "serotonin syndrome" (applies to benzonatate as well)

The SSRIs fluoxetene and paroxetine (reduce dextromethorphan dose)

Memantine (Namenda)

The American College of Chest Physicians practice guidelines do not recommend the use of cough suppressants in coughs associated with upper respiratory infection (URI) because of their limited efficacy. It is recommended that patients experiencing a cough associated with the common cold or postnasal drip associated with a URI use a first-generation antihistamine and a decongestant to treat cough.

See Table 26-5 for a summary of the antitussives.

Table 26-5 Antitussives

GENERIC NAME	TRADE NAME	DOSAGE	COMMENTS
Narcotic			
codeine w/ guaifenesin	Tussi-Organidin NR, Cheratussin AC	Sol or tabs 10–20 mg q4–6h	Any cough medicine containing a controlled substance is not for extended use; can develop physical dependence and tolerance; watch for side effects
hydrocodone w/ homatropine[a]	Hydromet, Hycodan	Syrup or tabs 5 mg q4–6 h	
w/ chlorpheniramine	Tussionex	ER Susp, 5 mL q12h	
Nonnarcotic			
benzonatate	Tessalon	Caps 100–200 mg tid	Related to tetracaine; Swallow caps whole
dextromethorphan w/ guaifenesin	Delsym	ER susp, 10 mL (60 mg) q12h	Note interactions
	Robitussin DM	Sol 10–20 mg q4h or Sol 30 mg q6–8h	
diphenhydramine	Benadryl	Caps 25 mg q4–6h	Antihistamine with anticholinergic effects, especially drying

[a]Anticholinergic agent added in subtherapeutic amounts to some hydrocodone products in order to discourage deliberate overdosage.

Patients taking antitussives should be instructed regarding:

- Read and carefully follow the directions on the product label
- Starting with a low dose of antitussive and increasing the dose only if cough suppression does not occur
- Caution with those operating machinery because of sedative effect

ANTIHISTAMINES

Antihistamines, such as diphenhydramine (Benadryl), competitively antagonize the histamine$_1$ receptor sites. Through this action, the antihistamines combat the increased capillary permeability and edema, inflammation, and itch caused by sudden histamine release.

Antihistamines are not curative, but provide *symptomatic relief of allergic symptoms caused by histamine release*. They are also used as adjunctive treatment of anaphylactic reactions after the acute symptoms (e.g., laryngeal edema and shock) have been controlled with epinephrine and corticosteroids.

Antihistamines are used to treat the symptoms of allergies (e.g., rhinitis, conjunctivitis, and rash). However, when antihistamines are used to reduce nasal secretions in the common cold, the consequent thickening of bronchial secretions may result in further airway obstruction, especially in those with COPD and asthma.

Some antihistamines are used in the symptomatic treatment of vertigo associated with pathology of the middle ear or in the prevention and treatment of motion sickness (see Chapter 16).

H_1-blockers are grouped into two categories: the first-generation agents and the second-generation agents.

Side effects of the first-generation antihistamines are anticholinergic in action and include:

- ! Drying of secretions, especially of the eyes, ears, nose, and throat
- ! Sedation, dizziness, and hypotension, especially in older adults
- Muscular weakness and decreased coordination
- Urinary retention and constipation
- Visual disorders
- ! Paradoxical excitement, insomnia, and tremors, especially in children
- GI—nausea, vomiting, anorexia
- Nasal irritation, epistaxis with nasal spray

Contraindications or extreme caution with first-generation antihistamines applies to:

- COPD and asthma
- Persons operating machinery or driving a car

Older adult patients (extended half life with sedation)

Cardiovascular disorders

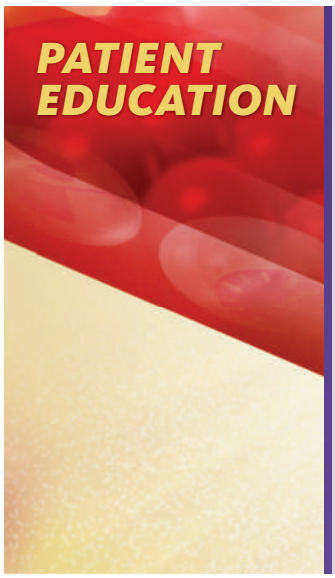
Benign prostatic hypertrophy (BPH)

Infants, pregnancy, and lactation

Seizure disorders

Interactions of first-generation antihistamines may occur with:

Potentiation of CNS depression with tranquilizers, analgesics, hypnotics, alcohol, and muscle relaxants



Patients taking first-generation antihistamines should be instructed regarding:

- Avoiding frequent or prolonged use of antihistamines, which may cause increased bronchial or nasal congestion and dry cough
- NOT using antihistamines to sedate children; manufacturers are making voluntary label changes that warn parents not to use the product with the intention of making a child sleepy
- No self-medication (check with the physician first) in those with COPD or cardiovascular disorders, BPH, older adults, and children
- Caution with those operating machinery because of sedative effect
- Not mixing with alcohol or any other CNS depressant drugs

The *second-generation antihistamines* include fexofenadine (Allegra) and loratadine (Claritin). These drugs are *selective* histamine receptor antagonists and have fewer CNS effects, for example, less sedation, and no anticholinergic effects compared to the first-generation antihistamines. Although these agents cause little or no sedation, it is important to note that the incidence of sedation is not zero. They are used to provide symptomatic relief of seasonal allergic rhinitis, for example, hay fever. The second-generation antihistamines are not effective in the treatment of cough.

Side effects of second-generation antihistamines, usually mild, can include:

Headache, dizziness, fatigue, drowsiness

Dry mouth, pharyngitis

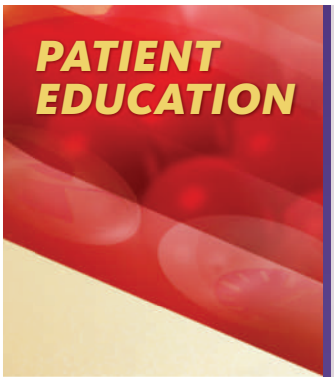
Contraindications or caution with second-generation antihistamines apply to:

Asthma

Renal and hepatic impairment

Driving or operating machinery

Pregnancy or lactation, use in neonates



Patients taking second-generation antihistamines should be instructed regarding:

- Avoiding any other drug, including OTC, without consulting physician first
- Reporting symptoms such as fainting, dizziness, or palpitations to physician immediately
- Using caution with driving or operating machinery until you know how these drugs affect you

DECONGESTANTS

Several adrenergic drugs, for example, phenylephrine (Neo-Synephrine) or pseudoephedrine (Sudafed), act as **decongestants**. These drugs constrict blood vessels in the respiratory tract, resulting in shrinkage of swollen mucous membranes and helping to open nasal airway passages. However, these drugs, both oral and nasal, should be used only on a short-term basis because rebound congestion may occur within a few days. Decongestants are frequently combined with antihistamines, analgesics, caffeine, and/or antitussives. Many of these products are available over the counter and, by combining several drugs, the possibility of adverse side effects is increased, especially without adequate medical supervision.

As mentioned in Chapter 20, the Combat Methamphetamine Epidemic Act of 2005 (which took effect in 2006) banned over-the-counter (OTC) sales of ingredients commonly used to make methamphetamine. Psuedoephedrine (PSE), a popular and effective oral nasal decongestant, was the primary target of the Act. PSE can now only be stored and sold in limited quantities under special conditions ("behind the counter") by pharmacies.

Side effects of decongestants can include:

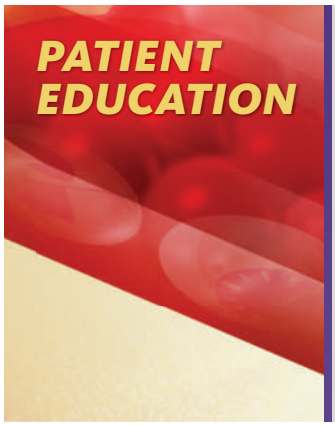
- Anxiety, nervousness, tremor, seizures
- Palpitations, hypertension, headache, cerebral hemorrhage
- Reduced cardiac output and reduced urine output
- Burning, stinging, sneezing, and dryness with nasal preparations

Contraindications or extreme caution with decongestants applies to:

- Cardiovascular disorders
- Hyperthyroid or diabetes
- Older adults—especially those with glaucoma or BPH
- Pregnancy or lactation

Interactions may occur with:

- Potentiation of adverse side effects with other adrenergics, ergot, tricyclics, MAOIs



Patients taking decongestants should be instructed regarding:

- Using decongestants for only a few days (3 days for nasal; 7 days for oral) to avoid rebound congestion
- Avoiding when cardiac or thyroid conditions or diabetes are present
- Discontinuing with side effects such as nervousness, tremor, palpitations, or headache
- Avoiding combining with any other medications without consulting physician

See Table 26-6 for a summary of the antihistamines and decongestants

Table 26-6 Antihistamines and Decongestants

GENERIC NAME	TRADE NAME	DOSAGE
First Generation Antihistamines		
azelastine (Rx)	Astelin, Astepro	1–2 sprays per nostril BID
chlorpheniramine	Chlor-Trimeton, Aller-Chlor	Elix 2 mg/5 mL q4–6h
		Tabs 4 mg q4–6h
		ER Caps, Tabs 8 mg TID –12 mg BID
clemastine	Tavist Allergy	Tabs 1.34–2.68 mg BID–TID
diphenydramine (Rx/OTC)	Diphenhist	Elix 25–50 mg q4–6h
	Benadryl Allergy	Tabs 25–50 mg q4–6h
	Benadryl	IM or IV 10–50 mg q4–6h
Second Generation Antihistamines		
certrizine	Zyrtec	Syrup, tabs 5–10 mg per day
desloratadine (Rx)	Clarinex	Syrup, tabs 5 mg daily
fexofenadine (Rx)	Allegra	Susp, tabs 30–60 mg BID, 180 mg per day
levocetirazine (Rx)	Xyzal	Soln, tabs 2.5–5 mg per day
loratadine	Claritin, Alavert	Syrup, tabs 10 mg daily
Decongestants		
oxymetazoline	Afrin, Visine L.R.	Sol 2–3 of 0.025% – 1–2 of 0.05% sprays, drops q12h
phenylephrine	Neo-Synephrine	Sol 0.125%–1% 2–3 drops/sprays q4h; Tabs 10 mg q4–6h
	Sudafed PE	
pseudoephedrine	Sudafed	Sol or tabs 30–60 mg q4–6h
		Tabs ER 120 mg q12h or 240 mg q24h

Rx = available by prescription only; Rx/OTC=availability depends on product labeling.
Note: This is a representative list. Many prescription and OTC drugs have combinations of antihistamines and/or decongestants and/or antitussives.

Patients taking respiratory system drugs should be instructed regarding:

- Care in taking medications only as prescribed and required; do not give children medicine labeled only for adults
- Avoiding combining respiratory system drugs with other prescription or OTC drugs or alcohol, which could potentiate CNS stimulation or depression, resulting in serious adverse side effects
- Choose OTC cough and cold medications with child-resistant safety caps; only use measuring devices that come with the product or those made for measuring medicine
- Avoiding self-medication when cardiac, thyroid, or CNS conditions are present
- Benefit from desensitization therapy and air-conditioned environmental control for patients with allergic conditions
- Avoiding air pollution (e.g., smoke-filled rooms)
- Exercises (e.g., swimming) that increase lung capacity and help reduce the necessity for medication
- Proper use of inhalers when prescribed (see administration with inhalers in Chapter 9)
- Not crushing, chewing, or breaking extended-release preparations; swallow whole

SMOKING CESSATION AIDS

Cigarette smoking is the leading cause of preventable disease and death in the United States. Most smokers fail to quit on their first try, and after experiencing how difficult quitting is, many will never try again. All smoking-cessation medications have been shown to help twice as many smokers quit versus quitting "cold turkey" when used properly and in conjunction with nonpharmacologic therapies.

Smoking cessation aids (Table 26-7), including Nicorette gum, Commit lozenges, the Nicoderm CQ patch, and the Nicotrol inhaler, help to lessen withdrawal symptoms by slowly lowering the level of nicotine in the body. They let the smoker focus on breaking the social habits of nicotine, and participation in a behavior modification program for smoking cessation, without battling the withdrawal symptoms at the same time.

Bupropion is an oral antidepressant drug (Wellbutrin) that is also prescribed as an aid to smoking cessation (marketed as Zyban). Zyban is also indicated for use in combination with nicotine patches for treating the symptoms of smoking cessation. (Refer to Chapter 20 for information on bupropion.)

Side effects of smoking cessation aids (which could also be related to nicotine withdrawal symptoms) can include:

- Mechanical problems with chewing gum, especially if patient has dentures
- Cardiac irritability
- Chewing too fast—may cause lightheadedness, nausea, heartburn, vomiting, throat and mouth irritation

Cautions with smoking cessation aids apply to:

Patients with dental problems that might be exacerbated by chewing gum

Drug abuse and/or overdependence

Overdosage

Pregnancy and lactation

Severe cardiovascular disease

Patients should be warned not to smoke

Varenicline

Varenicline (Chantix) is a prescription-only partial nicotine receptor agonist-antagonist given orally, and indicated for adults as an aid in smoking cessation. It alleviates the symptoms of nicotine craving and withdrawal through its agonist activity while inhibiting the effects of repeated nicotine exposure by its antagonist activity, thus eliminating the pleasurable feelings associated with smoking. Mild to moderate nausea and vomiting are the most common side effects, occurring in nearly one-third of patients. To date, no clinically significant drug interactions have been identified.

There have been recent reports of serious neuropsychiatric symptoms, such as changes in behavior, agitation, depressed mood, suicidal ideation and behavior associated with varenicline. There is some controversy as to whether these were caused by complications due to nicotine withdrawal or by the drug itself. The safety and efficacy of varenicline in patients with serious psychiatric disorders such as schizophrenia, bipolar, and major depression has not been established. Patients and caregivers should be aware of the need to monitor for these symptoms and report them immediately to the patient's physician.

Table 26-7 Smoking Cessation Aids

GENERIC NAME	TRADE NAME	DOSAGE
nicotine	Nicorette	1 piece of gum (2 or 4 mg) whenever urge to smoke up to 24 pieces per day for up to 12 weeks
	Commit	1 lozenge (2 or 4 mg) after waking up; no more than 5 loz in 6hrs / 20 loz per day for up to 12 weeks
	Nicoderm CQ	lst dose 21 mg patch per day, 6 wks
		2nd dose 14 mg patch per day, 2 wks
		3rd dose 7 mg patch per day, 2 wks
	Nicotrol inhaler (Rx)	24–64 mg (6–16 cartridges) daily up to 12 wk, then gradual reduction in dose last 6–12 wks
bupropion	Zyban (Rx)	Tabs, SR 150 mg daily × 3d, then 150 mg BID for 7–12 wk for up to 6 months maintenance; start 1–2 wks before quit date
varenicline	Chantix (Rx)	Tabs, 1 mg BID, following a 1-week titration for 12 wks with additional 12-week course if needed

Rx=available by prescription only.

CASE STUDY – A

Respiratory Medications

Fred Jefferson, a 68-year-old man with a history of COPD, complains of increased shortness of breath and nasal congestion. His Theo-24 prescription ran out last week and was not refilled. He has been using an albuterol inhaler more frequently without relief, and also taking an OTC decongestant for a week.

1. Decongestants can cause all of the following EXCEPT
- a. Rebound congestion
- b. Frequency
- c. Tremor
- d. Nervousness

2. Side effects of Theo-24 can include the following EXCEPT
- a. GI distress
- b. Nervousness
- c. Sedation
- d. Frequency

3. The following statements are true of albuterol EXCEPT
- a. CNS stimulant
- b. Avoid with decongestants
- c. Dilates bronchioles
- d. Can be used PRN q2h

4. Side effects of albuterol can include the following EXCEPT
- a. Palpitations
- b. Dizziness
- c. Sedation
- d. Tremor

5. Side effects of decongestants can include the following EXCEPT
- a. Anxiety
- b. Insomnia
- c. Headache
- d. Hypotension

CASE STUDY – B

Respiratory Medications

Mae Wright, a 70-year-old asthmatic, began using a Flovent HFA inhaler a week ago. Today, she complains of a thick white coating on her tongue. She has also been taking OTC Benadryl for a runny nose and fever.

1. Inhaled corticosteroids are used for all of the following EXCEPT:
- a. Chronic asthma
- b. Some COPD
- c. Some URI
- d. Acute asthma

2. Side effects of Flovent HFA can include the following EXCEPT
- a. Rash
- b. Oral fungal infections
- c. Dry mouth
- d. Hoarseness

3. What should Ms. Wright be reminded to do after using her Flovent HFA inhaler?
- a. Hold her breath for one minute
- b. Rinse mouth with mouthwash
- c. Rest for several minutes
- d. take shallower breaths

4. Antihistamines are used to treat all of the following EXCEPT
- a. Rhinitis
- b. Conjunctivitis
- c. Rash
- d. Asthma

5. Side effects of first-generation antihistamines, e.g., Benadryl, can include all of the following EXCEPT
- a. Dizziness
- b. Mucus plugs
- c. Urinary frequency
- d. Sedation

CHAPTER REVIEW QUIZ

Match the medication in the first column with the condition in the second column that it is used to treat. Conditions may be used more than once.

Medication		Condition
1. _____	Allegra	**a.** Bronchospasm (anticholinergic)
2. _____	Commit	**b.** Chronic asthma
3. _____	Guaifenesin	**c.** Asthma (adrenergic)
4. _____	Xopenex	**d.** Asthma (prophylactic)
5. _____	Spiriva	**e.** Allergies
6. _____	Tessalon	**f.** Smoking cessation
7. _____	Cromolyn sodium	**g.** Bronchitis (unproductive cough)
8. _____	Accolate	
9. _____	Zyban	

Choose the correct answer.

10. All of the following are possibilities with inhalers EXCEPT:
a. Increased systemic effects **c.** Breath-actuated
b. Dry powder formulations **d.** Metered-dose

11. Adrenergic bronchodilators, for example albuterol, could cause all of the following side effects EXCEPT:
a. Nervousness **c.** Hypertension
b. Hypoglycemia **d.** Tachycardia

12. Anticholinergic bronchodilators, for example Atrovent, could cause all of the following side effects EXCEPT:
a. Dried secretions **c.** Bradycardia
b. Confusion **d.** Dizziness

13. Singulair is appropriate for all of the following EXCEPT:
a. Asthma prophylaxis **c.** Young children
b. MDI inhalations **d.** Chronic asthma

14. Patient education for inhaled corticosteroid treatment would include all of the following EXCEPT:
a. Rinse equipment after **c.** Expect dry mouth
b. Use before a bronchodilator **d.** Rinse mouth after

15. The following statements are true about quaifenesin, found in many cough syrups, EXCEPT:
a. Can cause runny nose **c.** Increases secretions
b. Helps expel sputum **d.** Stops the cough

16. The following statements are true of Claritin, EXCEPT:
- **a.** For allergies
- **b.** Less sedation
- **c.** For rhinitis
- **d.** For asthma

17. Decongestants should only be used short term. Which of the following is NOT a decongestant?
- **a.** Benadryl
- **b.** Afrin
- **c.** Neo-Synephrine
- **d.** Sudafed

18. Antitussives frequently contain controlled substances. Which one of the following medicines is available OTC?
- **a.** Hycodan
- **b.** Delsym
- **c.** Tussionex
- **d.** Tussi-Organidin NR

19. Cough and cold medications containing antihistamines are only appropriate when the cause of the cough is
- **a.** Asthma
- **b.** Allergic rhinitis
- **c.** Emphysema
- **d.** Smoking

20. Nicorette would be an appropriate treatment for one with which condition?
- **a.** Arrhythmia
- **b.** Dentures
- **c.** Pregnancy
- **d.** COPD

Go to your StudyWARE™ CD-ROM and have fun learning as you play games and answer case study-related questions to help reinforce key concepts you learned in this chapter.

Go to your Study Guide and complete the review questions for this chapter.

Chapter 27

Drugs and Older Adults

Objectives

Upon completion of this chapter, the learner should be able to

1. List at least 15 drugs that are inappropriate for older adults
2. Describe four factors that may lead to cumulative effects in older adults
3. Name at least five categories of drugs that frequently cause adverse side effects in older adults
4. List at least 10 drugs that can cause mental problems in older adults
5. Describe the dangers and side effects associated with NSAID therapy
6. List side effects and cautions for gastrointestinal (GI) drugs
7. Explain patient education for nonsteroidal anti-inflammatory drugs (NSAIDs) and GI drugs
8. Describe patient education for all patients on long-term drug therapy
9. List the responsibilities of health care personnel in preventing complications of drug therapy
10. Define the Key Terms and Concepts

Key Terms and Concepts

Absorption
Beers List drugs
Cumulative effects
Distribution
Excretion
Mental impairment
Metabolism
Motor impairment
Polypharmacy

Today, people are living longer and are taking more medications. Prescribing of medications is the most common intervention that older adult patients experience. Consequently, there has also been an increase in serious complications resulting from adverse drug reactions. It has been estimated that more than 200,000 adults over the age of 60 are hospitalized yearly as the result of adverse drug effects. In 2000, it was estimated that medication-related problems (MRPs) caused 106,000 deaths annually.

MRPs can be mistaken for what is often considered a normal consequence of aging or for progression of disease. Cognitive impairment and behavioral changes are frequently the result of drug therapy. Therefore, it is imperative that members of the health care community work together to reverse this dangerous trend.

The aging process is an individualized matter. Because of genetic or environmental factors or good health practices, for example, exercise, healthy diet, and mental stimulation, some older adults may not feel or appear particularly different. However, we need to realize that there are gradual changes in body composition and organ function as we grow older. These changes can affect the reaction to drugs and make the individual more sensitive to a wide variety of medications.

A study by Harvard Medical School researchers looked at medicines prescribed for individuals over 65 years of age. The panel of experts in geriatrics and pharmacology found "a disturbingly high level of potentially inappropriate prescribing for older adults. Over the course of one year, almost one quarter of older Americans were unnecessarily exposed to potentially hazardous prescribing."

CUMULATIVE EFFECTS OF DRUGS

Complex changes of aging involve both anatomic and physiological factors that affect how drugs are processed in the body (see Chapter 3). The four processes that drugs undergo in the body—that is, **absorption**, **distribution**, **metabolism** (biotransformation), and **excretion**—are all altered as the body ages. The end result of this slowed process can be exaggerated responses to medications, changes in drug levels, increased susceptibility to drug-drug interactions, and a 3- to 10-fold risk of adverse drug reactions compared with younger individuals.

Cumulative effects of drugs in older adults can be due to:

Inadequate absorption—slowed GI motility, reduced fluid intake, and/or relative achlorhydria (lack of stomach acid)

Impaired distribution—circulatory dysfunction, less muscle and more fat

Slower metabolism—hepatic dysfunction

Impaired excretion—renal dysfunction, constipation, or poor exchange of gases in the lungs

Absorption

As we age, several things happen to our GI tract. Not only does the gastric motility decrease, but gastric acid production diminishes, increasing the gastric pH, causing a more alkaline environment, which affects the absorption process. Many older adults also take medication that reduces gastric acid, for example, Zantac or Prilosec (See Chapter 16, Gastrointestinal Drugs).

Antacids are also used frequently by older adults. Calcium, magnesium, and aluminum form insoluble and nonabsorbable complexes that are passed out of the body in the feces. Some of the drugs that are affected by antacids are quinolone antibiotics, tetracycline, iron salts, ketoconazole, and isoniazid. Therefore, it is recommended that these, and certain other drugs as well, not be taken within two hours of taking antacids.

Decreased gastric motility, especially when taking anticholinergic drugs, for example, the tricyclic antidepressants or the antispasmodics, can cause

adverse effects. Gastric slowing will lead to increased time for other drugs to be dissolved and absorbed.

Absorption by other routes of administration may be affected as well. Aging skin atrophies and becomes thinner, potentially impairing transdermal drug absorption of patches and gels because of reduced blood flow to the skin. Muscle mass may be significantly decreased in some older adult patients, which may alter drug absorption of IM and subcutaneous injections.

Distribution

Once drugs are absorbed and enter the circulation, many of them bind to proteins. Albumin is the principal protein used to bind drugs. As we age, the liver produces less albumin, especially in conditions such as malnutrition, cancer, diabetes, surgery, burns, and liver disease. This allows more of the drug to be unbound (free) to reach receptor sites and therefore have a greater than expected response.

Phenytoin (Dilantin) is an example of a drug that responds quite noticeably to drops in plasma albumin levels. Older adults need to be monitored frequently with laboratory studies, especially with symptoms such as sleepiness, confusion, nystagmus, diplopia, and ataxia. Other drugs that are highly protein-bound include warfarin, aspirin, naproxen, diazepam, and valproic acid (Depakote). When any of these drugs are used in the older adult, the best advice is to start at the lowest effective dose and increase slowly to avoid adverse effects. The frequency of administration may also need to be decreased.

Because the older adult has less body water, drugs that are water soluble, such as digoxin, ethanol, lithium, morphine, and theophylline may become concentrated and cause adverse reactions, with additive effects over time. Smaller doses would be needed to avoid potential toxicity.

Metabolism

The liver serves as a major site for drug metabolism. As we age, the mass of functional liver tissue and blood flow to the liver decreases. The ability of the liver to break down drugs declines, and drugs remain in the body longer. Repeated dosing can result in the accumulation of the drug and increases the risk for toxicity. Some drugs that can produce toxic effects when poorly metabolized are caffeine, diazepam, chlordiazepoxide, lidocaine, theophylline, meperidine, hydromorphone, warfarin, phenytoin, diphenhydramine, and propranolol.

! *Long-acting benzodiazepines* have been implicated in falls and hip fractures. These drugs build up with repeated administration and cause *side effects*, such as daytime sedation, dizziness, lethargy, and ataxia. Therefore, it is safer to use *shorter-acting sedatives*, for example lorazepam (Ativan) in doses no higher than 2 mg, and hypnotics, such as zolpidem (Ambien).

Omeprazole (Prilosec) and cimetidine (Tagamet) inhibits liver enzymes from breaking down the long-acting benzodiazepines and prolongs the drug's duration of action. It may be preferable to use other PPIs or H_2 blockers such as pantoprazole (Protonix) or ranitidine (Zantac), rather than omeprazole.

Excretion

In the older adult, kidney size, blood flow, and glomerular filtration all decrease, resulting in a decline in creatinine clearance. Illnesses such as hypertension, heart failure, and diabetes add to the age-related loss and further reduce creatinine clearance. Consequently, drug by-products normally eliminated through the kidneys can accumulate, with toxic effects. For example, metformin (Glucophage), poses increased risks of adverse reactions (including lactic acidosis) to older adults with impaired renal function. Other oral antidiabetic agents such as nateglinide (Starlix) and pioglitazone (Actos) may be better alternatives.

Nephrotoxic drugs, such as the aminoglycosides, can prove particularly dangerous to older people with reduced renal function. Acute renal failure and irreversible damage to the eighth cranial nerve (auditory and vestibular branches) are possible.

Older adults are more likely to have adverse drug reactions to *anticholinergics*. (See Chapter 13.) The resulting *side effects* are blurred vision, confusion, disorientation, dry mouth, dry eyes, constipation, palpitations, worsening of glaucoma, and urinary retention. Men with prostate problems are at extreme risk for acute urinary retention.

Drugs that produce ***significant*** *anticholinergic* effects include:

- Antipsychotic agents, such as the phenothiazines chlorpromazine (Thorazine), fluphenazine, thioridazine (Mellaril), and perphenazine (Trilafon)
- Antidepressants, such as tricyclics, amitriptyline (Elavil), doxepin (Sinequan), imipramine (Tofranil), and nortriptyline (Pamelor)
- Antiparkinson agents, such as benztropine (Cogentin) and trihexyphenidyl (Artane)
- Antispasmodics, such as dicyclomine (Bentyl) and hyoscyamine (Levsin)
- Antihistamines, such as diphenhydramine (Benadryl) and promethazine (Phenergan)

There are many other classes of medications (SSRIs, some atypical antipsychotics, H_2 blockers, certain cardiovascular drugs, corticosteroids, etc.) that exhibit subtle anticholinergic activity that becomes more pronounced in the older adults. Because the increase in the amount of a drug circulating in the system is often gradual, the consequences of an "overdose" may not be recognized. Family, friends, and even patients themselves may conclude that their symptoms are just due to "aging."

While age-related physiologic changes affect how older adults process and tolerate medications, pharmaceutical research is frequently focused on younger individuals, while older adults are often excluded from or underrepresented in clinical trials. The study results may be inappropriately extrapolated to other populations with negative outcomes.

An example of this was a study in which spironolactone was found to reduce mortality in clinical trial patients who were around 60 years old. When this finding was extrapolated to the general population, where most patients with

heart failure are older than 75 years, there was an increase in hyperkalemic deaths and no change in heart failure hospitalizations. Some medicines that are perfectly safe for a 30-year-old person may produce unexpected results in a person over age 50 or 60. An example is *digoxin (Lanoxin)*. An older person still on the same dose that was appropriate 10 or 20 years earlier may experience *side effects* such as loss of appetite, weakness, personality changes, nightmares, confusion, or even hallucinations. In addition, digoxin can interact with many other drugs, sometimes slowing clearance of the drug from the system, which could result in cumulative effects, including possible dangerous arrhythmias.

POTENTIALLY INAPPROPRIATE MEDICATION USE IN OLDER ADULTS

A group of physicians led by Dr. Mark Beers conducted a national survey of geriatrics experts in 1991 to determine the most *inappropriate* drugs for ambulatory nursing home residents and adults 65 or older. Medications were considered inappropriate if there was evidence in the literature to substantiate that the risk of drug use outweighed the clinical benefit when alternative therapy was available. The results of this survey came to be called *The Beers List* (**Beers List drugs**).

The Beers study was updated and revised by another panel of experts and the results were published in 2003 in *The Archives of Internal Medicine under the title, Updating the Beers Criteria for Potentially Inappropriate Medication Use in Older Adults*. A selective summary of the results from both of these studies can be found in the following Table 27-1. The complete article with rationale is available for download free of charge from www.archinternmed.com.

Table 27-1 Potentially Inappropriate Medications for Older Adults

Adults over 65 should avoid these drugs completely because they are either ineffective or pose unnecessarily high risk for older adults and safer alternative is available, unless noted otherwise.

GENERIC NAME	TRADE NAME	COMMENTS
Sedative-Hypnotics		
long-acting benzodiazepines—Prolonged daytime effects: sedation, dizziness, ataxia; confusion, falls, fractures, respiratory depression in COPD		
chlordiazepoxide	Librium, Limbitrol, Librax	
clorazepate	Tranxene	
diazepam	Valium	
flurazepam	Dalmane	
meprobamate	Miltown	
short-acting benzodiazepines—Avoid long-term use; risk of falls, can be habit forming.		
alprazolam	Xanax	No dose greater than 2 mg; do not exceed daily max
lorazepam	Ativan	No dose greater than 3 mg; do not exceed daily max
oxazepam	Serax	No dose greater than 60 mg; do not exceed daily max
temazepam	Restoril	No dose greater than 15 mg; do not exceed daily max
triazolam	Halcion	No dose greater than 0.25 mg; do not exceed daily max

(*continued*)

Table 27-1 Potentially Inappropriate Medications for Older Adults—*continued*

GENERIC NAME	TRADE NAME	COMMENTS
Antidepressants		
amitriptyline	Elavil	Anticholinergic and sedative effects
buproprion (in seizure disorder)	Wellbutrin	May lower seizure threshold
doxepin	Sinequan	Anticholinergic and sedative effects
fluoxetine (used daily)	Prozac	Long half-life; potential for agitation, anorexia, insomnia; Safer alternatives
Antipsychotics		
haloperidol	Haldol	Doses >3 mg per day should be avoided due to EPS[a] potential (patients with known psychotic disorders may receive higher doses)
olanzapine (in obesity)	Zyprexa	Increased appetite, weight gain
thioridazine	Mellaril	Avoid doses >30 mg per day due to EPS[a] potential (unless known psychotic disorder)
Antihypertensives		
hydrochlorothiazide	Esidrix, HydroDIURIL	Avoid >50 mg doses; may precipitate gout attack in patients with gout
methyldopa	Aldomet	Bradycardia, depression
nifedipine (short- acting)	Adalat, Procardia	Hypotension, constipation
propranolol	Inderal	Other beta-blockers offer less CNS penetration
reserpine	Serpasil	Potential for CNS adverse effects and orthostatic hypotension.
clonidine	Catapres	Potential for CNS adverse effects and orthostatic hypotension.
Antiarrhythmic		
digoxin	Lanoxin	doses >0.125 mg per day (except for atrial arrhythmias); toxicity due to reduced renal clearance
disopyramide	Norpace	May induce heart failure in older adults Anticholinergic; better alternatives
NSAIDs		
indomethacin	Indocin	Other NSAIDs cause less CNS and GI toxic reactions than these drugs
ketorolac	Toradol	GI bleeding
Oral Hypoglycemics		
chlorpropamide	Diabinese	Prolonged hypoglycemia; causes SIADH[b]
Analgesics		
meperidine	Demerol	May cause confusion, dependency, falls, fractures
propoxyphene	Darvon	Better alternative, for example, morphine
	Darvocet N	No better than acetaminophen, has narcotic adverse CNS effects potentiated in older adults
pentazocine	Talwin	More CNS effects (confusion, hallucinations) than other opioids

Table 27-1 Potentially Inappropriate Medications for Older Adults—*continued*

GENERIC NAME	TRADE NAME	COMMENTS
Platelet Inhibitors		
dipyridamole	Persantine	Only avoid short-acting due to orthostatic hypotension; ER acceptable
Histamine-2 Blockers		
cimetidine	Tagamet	Avoid doses >900 mg per day; confusion and other CNS adverse effects; interaction with warfarin
Anti-infective		
nitrofurantoin	Macrodantin	Potential for renal impairment Safer alternatives available
Antihistamines—*Nonanticholinergic* antihistamines are preferred for older adults (see Chapter 26 *Respiratory Drugs*)		
chlorpheniramine	Chlor-Trimeton	All of these drugs have anticholinergic effects; use short-term only for conditions other than allergies
diphenhydramine	Benadryl, Tylenol PM	
hydroxyzine	Vistaril, Atarax	
promethazine	Phenergan	
Estrogens		
oral	Premarin, others	Breast, endometrial cancer; not cardioprotective
Decongestants		
oxymetazoline	Afrin, Dristan, others	May produce elevation of blood pressure; concern with insomnia due to CNS stimulant effects; concern with urinary retention in bladder outflow obstruction. Avoid daily use >2 wk
phenylephrine	Neo-Synephrine	
pseudoephedrine	Sudafed	
Iron		
ferrous sulfate	Feosol	Avoid doses >325 mg per day; constipation without increased iron absorption
Antispasmodics—Avoid long-term use; potential for toxicity greater than potential benefit		
hyoscyamine	Cytospaz, Levsin, Levsinex	All of these have anticholinergic effects; worsened cognition and behavioral problems in dementia
belladonna alkaloids	Donnatal and others	
dicyclomine	Bentyl	
oxybutynin	Ditropan	Problems may be lessened but still present with sustained release forms
tolterodine	Detrol	Problems may be lessened but still present with sustained release forms
Muscle Relaxants—All cause anticholinergic adverse side effects; sedation, cognitive impairment		
cyclobenzaprine	Flexeril	
orphenadrine	Norflex	
methocarbamol	Robaxin	
carisoprodol	Soma	
Antiemetics		
trimethobenzamide	Tigan	Poor efficacy; can cause EPS[a]

[a]EPS, extrapyramidal side effects
[b]SIADH, syndrome of inappropriate antidiuretic hormone secretion.

DRUGS THAT MAY CAUSE MENTAL IMPAIRMENT

Many medications can cause mental problems in older people. One government study found that more than 150,000 older adults had experienced *serious mental impairment either caused or worsened by drugs*. Many medications can have CNS *side effects*, such as anxiety, depression, confusion, disorientation, forgetfulness, hallucinations, nightmares, or impaired mental clarity, *especially in older adults*. Some drugs that can cause **mental impairment** in older adults include:

amitryptiline	Haldol	Sinequan
Benadryl	Inderal	Tagamet
Bentyl	Lopressor	Tegretol
chlorpromazine	methyldopa	Tenormin
Cogentin	Pamelor	thioridazine
Corgard	Phenergan	Timoptic
Dalmane	prednisone	Tofranil
Dilantin	Pro-Banthine	trazodone
Ditropan	prochlorperazine	trihexyphenidil
Donnatal	Reglan	Xanax
Halcion	Sinemet	

Other CNS drugs also impair mental function. This is a representative list. In addition, all antipsychotics can cause tardive dyskinesia and/or parkinsonism. Alcohol can also potentiate adverse effects of many drugs.

Many CNS drugs and antihypertensives can also cause dizziness or **motor impairment**, which increases the risk of falls. These drugs can also impair sexual functioning, reducing the quality of life for some older adults.

NONSTEROIDAL ANTI-INFLAMMATORY DRUGS

Many older people suffer from arthritis and take over-the-counter non steroidal anti-inflammatory drugs (NSAIDs), frequently without adequate supervision. Anyone taking NSAIDs should be cautioned about the real danger of serious complications. Every year there are over 70,000 hospitalizations and more than 7,000 deaths from drug-induced bleeding ulcers or perforations. Particularly in older adults, there may be no warning signs of pain and the first symptoms of trouble may be a “silent” bleed that could lead to fatal GI hemorrhage.

In addition, memory loss, confusion, and other mental status changes can occur in the older adult patient taking NSAIDs that is not seen in younger patients. Patients and health care practitioners may attribute memory loss to dementia and not drug therapy.

Side effects of NSAIDs and corticosteroids (e.g., prednisone) can include:

- Indigestion, heartburn, abdominal pain
- Nausea, vomiting, and anorexia
- Flatulence, diarrhea, or constipation
- Silent ulceration (no symptoms of GI problems)

Other possible side effects of NSAIDs (including aspirin):

- Prolonged bleeding time
- Liver toxicity and kidney dysfunction
- Hypertension; exacerbation of heart failure
- Bronchospasm (especially with asthma)
- Visual or hearing problems (e.g., tinnitus)

The NSAID and COX-2 inhibitor Celebrex, has less potential for gastric problems, GI bleeding, or other bleeding problems than the other nonselective NSAIDs. However, more data are needed to confirm this.

Studies have indicated *increased risk of cardiovascular problems* (thrombotic events, MI, and stroke) with the use of some COX-2 inhibitors no longer marketed. Consultation with the physician should include consideration of whether the benefits of Celebrex outweigh the potential risks.

Misoprostol (Cytotec) is sometimes given for the prevention of NSAID-induced gastric ulcers, but may cause severe diarrhea. The use of PPIs may decrease the risk of GI bleeding associated with NSAIDs.

PATIENT EDUCATION

Patients receiving NSAID therapy should be instructed regarding:

- Administration with food
- Not exceeding dosage prescribed by physician
- Not taking aspirin, alcohol, or any other drugs at the same time because they may potentiate GI or bleeding problems
- The possibility of "silent" bleeding
- Reducing dosage of NSAIDs and substituting acetaminophen for pain, if possible, at least part of the time
- Trying exercise and heat for pain control, as approved by physician

See Chapter 21 for a list of NSAIDs and interactions.

GI problems, for example indigestion, heartburn, and constipation, are frequent complaints of older adults. Consequently, a common practice is the taking of over-the-counter (OTC) remedies without adequate awareness of potential side effects or implications.

PATIENT EDUCATION

Patients receiving GI medicines should be instructed regarding:

- Side effects of antacids, including constipation (with aluminum or calcium carbonate products), diarrhea (with magnesium antacids); acid rebound, belching, or flatulence (with calcium carbonate)
- Avoiding prolonged use (no longer than two weeks) of OTC antacids without medical supervision because of the danger of masking symptoms of GI bleeding or GI malignancy
- Avoiding taking antacids within two hours of any other drug because of numerous interactions (see Chapter 16)
- Antiulcer drugs, for example Tagamet, can lead to mental confusion, especially in older adults.
- Avoiding frequent use of strong cathartics, which can lead to laxative dependence and loss of normal bowel function. Instead, increase fluids and high-fiber diet and regular bowel habits. If laxatives are necessary, use bulk laxatives (e.g., psyllium) or stool softeners.

POLYPHARMACY

Individuals at any age, but especially older adults, may be the victims of **polypharmacy**, that is, excessive use of drugs or prescriptions or many drugs given at one time (see Figure 27-1). Polypharmacy increases the risk of dangerous interactions, with potentially serious adverse side effects. Health care practitioners should take every opportunity to educate their patients

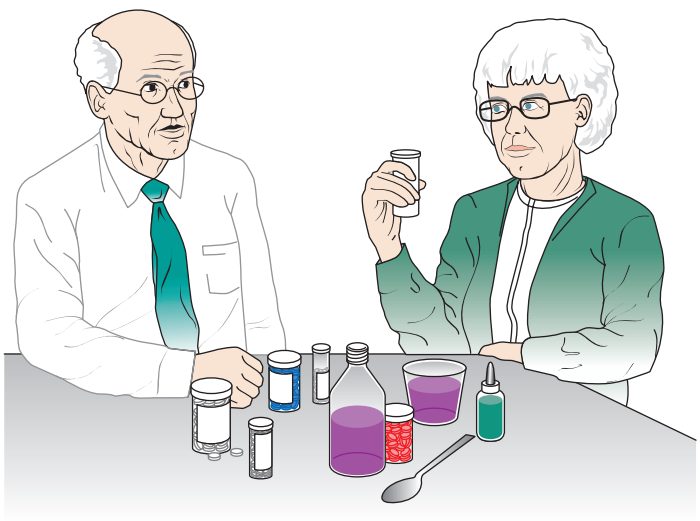


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FIGURE 27-1 Polypharmacy. "My internist prescribed the red pill, my cardiologist the white one, my allergist the blue one, and the ophthalmologist the eyedrops. I have medicines for arthritis, angina, indigestion, insomnia, constipation, and glaucoma."

regarding their medicines, the purpose for them, possible side effects, potential dangers, and interactions between medicines. Anyone receiving medicines should be monitored on an ongoing basis to determine continuing effectiveness and possible cumulative or adverse effects. Medicines should be reviewed regularly to determine feasibility of reducing dosage, possibly substituting a more effective or safer medicine, or discontinuing some of the medicines.

PATIENT EDUCATION

Older patients should be instructed regarding:

- Making a list of *all* medicines (with dosage). Include pain medicine, eye drops, OTC medicines, vitamins and herbal remedies, and topical medications. This list should be carried in wallet and/or be readily available at all times.
- The purpose for their medicines, side effects, best time to take each medication, and interactions
- Asking the pharmacist for easy to hold and easy to open medication containers
- Reporting side effects to physician immediately
- The importance of seeing their physician on a regular basis, every six months to a year or more often, to reevaluate the need for and effectiveness of the drug
- Not stopping the medicine or changing the dose without consulting the physician. Abrupt withdrawal can be dangerous with some medicines.
- Asking the physician to prescribe a generic or less expensive alternative if the cost of the medicine is prohibitive. Sometimes social service departments can assist the patient in securing expensive medicines that are imperative to the patient's health.
- If there is a problem with remembering to take medicines, ask the pharmacist to recommend a pillbox organizer or other memory aids.
- Not taking another person's medication even if you think it is the same as yours.
- If you use one or more physicians and/or pharmacies, be sure all parties are informed of any issues.

All health care practitioners must be aware of their responsibilities in preventing complications of drug therapy in patients of any age, but especially the old and the very young, who are more vulnerable. The following guidelines should be helpful:

- Educate yourself, your patients, and their families regarding adverse side effects, cumulative effects, and interactions.

- With each newly prescribed drug, note diagnoses, allergies, and other medications.
- Monitor long-term drug use for effectiveness and physiological or mental changes. Do periodic laboratory tests as appropriate (e.g., digoxin levels).
- *Question* any inappropriate medicine or dosage. You have a moral, ethical, and legal responsibility to do what is best for the patient.
- Document all adverse side effects, calls to the physician, and action taken.

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CASE STUDY – A

Drugs and Older Adults

Harry Washington, a 75-year-old man, has a diagnosis of hypertension, angina, arteriosclerosis, GERD (gastroesophageal reflux disease), colitis, and BPH. He is receiving Lanoxin, Inderal, Xanax, Lopressor, Pepcid, and Halcion.

1. He is at risk for cumulative effects with his diagnoses and the following conditions EXCEPT
   a. Impaired excretion
   b. Hepatic dysfunction
   c. Circulatory dysfunction
   d. Increased GI motility
2. Side effects of Lanoxin can include the following EXCEPT
   a. Confusion
   b. Weakness
   c. Palpitations
   d. Anorexia
3. All of the drugs he is taking have the potential for causing mental impairment, depression, or confusion EXCEPT
   a. Inderal
   b. Xanax
   c. Lopressor
   d. Pepcid
4. All of the drugs he is taking have the potential for causing weakness or dizziness EXCEPT
   a. Lanoxin
   b. Halcion
   c. Pepcid
   d. Xanax
5. Serious interactions with toxicity are possible with his drugs and the following EXCEPT
   a. Antihistamines
   b. Antacids
   c. Alcohol
   d. Analgesics

CASE STUDY – B

Drugs and Older Adults

Grace Grey, an 83-year-old resident of a nursing home, has a diagnosis of arthritis, diabetes, organic brain syndrome, and gastritis. Her medicines include prednisone, Naprosyn, chlorpropamide, Haldol, Tagamet, Ditropan, Metamucil, and prochlorperazine PRN.

1. Side effects of corticosteriod and/or NSAIDs can include all of the following conditions EXCEPT
   a. GI distress
   b. Incontinence
   c. Bleeding
   d. Ulcers
2. Her medicines that could cause confusion include the following EXCEPT
   a. Chlorpropamide
   b. Tagamet
   c. Ditropan
   d. Prochlorperazine
3. Haldol can cause all of the following EXCEPT
   a. Confusion
   b. Depression
   c. Weakness
   d. Diarrhea
4. Which oral antidiabetic agent is contraindicated for older adults?
   a. Micronase
   b. Tolbutamide
   c. Chlorpropamide
   d. Glucotrol
5. Which is the only laxative that should be taken daily?
   a. Dulcolax
   b. Mineral oil
   c. Milk of Magnesia
   d. Metamucil

Note A Comprehensive Review Exam for Part II can be found at the end of the text following the Summary.

CHAPTER REVIEW QUIZ

Choose the correct answer.

1. Polypharmacy can result in the following EXCEPT:
   a. Better patient compliance **c.** Overdose
   b. More medication errors **d.** Dangerous interactions
2. Older adults should be instructed to do all of the following EXCEPT:
   a. Use pillbox organizer **c.** List medicines
   b. Stop medications abruptly **d.** Report problems
3. Older adults should be cautioned that adverse effects of NSAIDs are potentiated when taking with the following EXCEPT:
   a. Aspirin **c.** Food
   b. Alcohol **d.** Prednisone
4. Cumulative effects of drugs in older adults can be due to:
   a. Increased GI motility **c.** Inadequate absorption
   b. Higher metabolism **d.** Improved renal function
5. Which problem of many nursing home residents is not potentiated by anticholinergic medications?
   a. Blurred vision **c.** Constipation
   b. Urinary frequency **d.** Confusion
6. Which one of these is an appropriate medication to treat arthritis pain for older adults?
   a. Indocin **c.** Acetaminophen
   b. Toradol **d.** Darvon
7. Which one of these is an appropriate medication to treat allergies in older adults?
   a. Benadryl **c.** Chlor-Trimeton
   b. Claritin **d.** Vistaril
8. Which one of these is an appropriate pain medication for older adults after surgery?
   a. Morphine **c.** Demerol
   b. Darvon **d.** Talwin
9. Which one of these anti-infectives should *not* be used to treat urinary infections in older adults?
   a. Macrodantin **c.** trimethoprim
   b. Keflex **d.** Biaxin
10. Which one of these antihypertensives would not be prefered to treat older adults?
    a. Cozaar **c.** Inderal
    b. Calan **d.** Tenormin
11. Which of these cardiac drugs is *least* appropriate for older adults?
    a. Norpace **c.** Procardia XL
    b. Vasotec **d.** Hydralazine
12. Which one of these is an appropriate antidepressant to treat older adults with no history of seizure disorder?
    a. Prozac **c.** Sinequan
    b. Amitriptyline **d.** Wellbutrin

13. Which statement is *not* true of Tagamet?

a. Prolongs drug effects
b. Inhibits liver enzymes
c. Speeds metabolism
d. Possible CNS effects

14. Which statement is *not* true of short-acting sedatives, for example, Xanax?

a. Can be habit forming
b. Short-term use only
c. Dosage limited
d. Long half-life

15. Which statement is *not* true of antispasmodics, for example, Ditropan?

a. Short-term use only
b. Cholinergic effects
c. Potential toxicity
d. Long-acting preferable

Go to your StudyWARE™ CD-ROM and have fun learning as you play games and answer case study-related questions to help reinforce key concepts you learned in this chapter.

Go to your Study Guide and complete the review questions for this chapter.

Summary

The health care professional has a great responsibility in the administration of medications and when advising others regarding drug therapy. As the older adult population increases and many more new drugs are developed and prescribed, more knowledge is required regarding cumulative effects and interactions. Moral, ethical, and legal issues of drug therapy are raised with increasing frequency. Therefore, it is imperative that the health care practitioner keep abreast of changes in drug therapy practices. Complete knowledge and good judgment are necessary for effective administration and adequate patient education.

The following guidelines should prove useful for safe drug therapy:

- Always research new drugs before administration to determine side effects, interactions, and cautions.
- Always check to make sure that you are administering the drug to the correct patient by whatever system your institution utilizes. If the patient is wearing a wrist band, this must always be checked.
- Assess the patient before administration for allergies, general condition, and possible contraindications, and after administration for results and adverse effects.
- Question any inappropriate drugs, dosages, or possible interactions.
- Responsibilities of drug administration and medication errors are discussed further in Chapter 7.
- Reduce the risk of medication errors by checking the spelling of each medicine very carefully. Many drug names look and/or sound alike but act differently.
- Check the patient's diagnosis to be sure the medication is appropriate.

Comprehensive Review Exam for Part 1

1. Drug standards regulate all of the following factors in drug preparation EXCEPT
   a. Strength
   b. Purity
   c. Color
   d. Quality
2. All of the following facts are true of the Pure Food and Drug Act EXCEPT
   a. For consumer protection
   b. Listed approved drugs
   c. Set minimal standards
   d. Passed in 1776
3. The Food and Drug Administration regulates all of the following drug factors EXCEPT
   a. Prescription labeling
   b. Shape of tablet
   c. Effectiveness
   d. Safety
4. Which of the following drugs is *not* a controlled substance?
   a. Marijuana
   b. Valium
   c. Codeine
   d. Benadryl
5. Which statement is *not* true of controlled drugs?
   a. Listed by schedule
   b. No limitations on refills
   c. May cause dependence
   d. Sometimes illegal
6. Which is *not* a good source of drug information?
   a. PDR
   b. USP/DI
   c. Drug package insert
   d. News magazine
7. Which statement is true of the generic name of a drug?
   a. Assigned by drug company
   b. Written in capital letters
   c. Common name
   d. Same as trade name
8. The term OTC refers to drugs:
   a. Often times controlled
   b. Requiring prescription
   c. For sale to anyone
   d. Officially certified
9. Which of the following conditions is *not* commonly listed as a *contraindication* for drug administration?
   a. Obesity
   b. Allergy
   c. Pregnancy
   d. Lactation
10. Before giving a new drug, you must know all of the following EXCEPT
    a. Interactions
    b. Contraindications
    c. Side effects
    d. Usual price
11. An antibiotic with *photosensitivity* listed as a side effect could cause
    a. Deafness
    b. Sunburn
    c. Blindness
    d. Kidney damage
12. Which is *not* a source of drugs?
    a. Minerals
    b. Inert gases
    c. Animals
    d. Laboratory

13. Which is *not* a process that drugs go through in the body?
a. Tolerance
b. Distribution
c. Metabolism
d. Excretion

14. Which of the following patient characteristics is not a factor affecting the processing of drugs in the body?
a. Weight
b. Age
c. Mental state
d. Skin color

15. Drug toxicity from cumulative effects may result from all of the following EXCEPT
a. Low metabolism
b. Poor circulation
c. High blood pressure
d. Kidney malfunction

16. Which term does *not* describe an adverse or unexpected result from a drug?
a. Idiosyncrasy
b. Anaphylaxis
c. Placebo effect
d. Teratogenic effect

17. Which route of administration is used most often?
a. Topical
b. Sublingual
c. Injection
d. Oral

18. Which is *not* a form of parenteral administration?
a. Inhalation
b. Rectal
c. Dermal patch
d. Injection

19. Which type of medication can be crushed and mixed with food to facilitate administration?
a. Timed-release capsule
b. Lozenge
c. Film-coated tablet
d. Enteric-coated tablet

20. Which is *not* a topical form of administration?
a. Ointment
b. Intradermal
c. Eyedrops
d. Vaginal cream

21. Which is the most rapid form of administration?
a. PO
b. IV
c. IM
d. subcu

22. Which is the least accurate system for measuring medication?
a. Metric
b. Apothecary
c. Household
d. Standard

23. Which is the most frequently used system for measuring medicine?
a. Apothecary
b. Metric
c. Household
d. Standard

24. Medication orders must contain all of the following EXCEPT
a. Dosage
b. Route
c. Medication name
d. Patient's address

25. The prescription blank for a controlled substance must contain all of the following EXCEPT
a. Physician's DEA number
b. Name of drug company
c. Frequency
d. Number of refills

26. Which type of equipment is least accurate in measuring medicine?
a. Medicine cup
b. Minim glass
c. Teaspoon
d. Syringe

27. Responsibilities of the health care practitioner include all of the following EXCEPT
a. Patient education
b. Current information
c. Judgment
d. Prescribing

28. Which is *not* appropriate action after administration of medication?
a. Assessment
b. Research concerning meals
c. Evaluation
d. Documentation

29. Which is the *least* helpful information in dispensing medication?
a. Allergies
b. Handicaps
c. Health history
d. Patient's occupation

30. If a medication error is made, all of the following actions are required EXCEPT
a. Report to physician
b. File incident report
c. Note on patient record
d. Apologize to patient

31. Before giving any medicine, it is essential to review the five Rights of Medication Administration, including all of the following EXCEPT
a. Right amount
b. Right drug
c. Right drug company
d. Right time schedule

32. Documentation of a controlled drug given PRN for pain requires all of the following EXCEPT
a. Note on narcotic record
b. Note of trade name
c. Note of effectiveness
d. Note on patient record

33. Which is *not* used for administration by the gastrointestinal route?
a. Nasogastric tube
b. Oral inhaler
c. Rectal suppository
d. Timed-release capsule

34. Which is *not* an advantage of the oral route over other routes?
a. Speed
b. Safety
c. Economy
d. Convenience

35. If a medication is ordered PO and the patient is NPO, which action is *most* appropriate?
a. Give medication by injection
b. Give medication rectally
c. Omit medication and note on chart
d. Consult the person in charge

36. Oral medications are usually best administered with which fluid?
a. Fruit juice
b. Milk
c. Water
d. Hot tea

37. When preparing cough syrup, which is the most appropriate action?
a. Shake the bottle
b. Dilute with liquid
c. Hold bottle label side down
d. Hold medicine cup at eye level

38. Which of the following is *not* required for administration of rectal suppository?
a. Lubricant
b. Privacy
c. Bed elevated
d. Disposable glove

39. Which parenteral route is *least* likely to be used for systemic effects?
a. Transdermal
b. Topical
c. Sublingual
d. Inhalation

40. Which route has the slowest action?
a. Transcutaneous
b. Inhalation
c. Sublingual
d. Injection

41. After instilling eyedrops, which is the most appropriate action?
a. Rub eyelid vigorously
b. Press inner canthus
c. Close eyelid quickly
d. Discard eyedropper

42. Which is *not* appropriate for intradermal injection?
a. Tuberculin syringe
b. 21-gauge, 1-inch needle
c. Wheal formation on skin
d. 0.1–0.2 mL solution

43. Which is *not* true of intramuscular injections?
a. Skin held taut
b. 1½-inch needle usual
c. 45-degree angle of needle
d. Can be Z-track

44. Which one of these intramuscular injection sites is used for infants?
a. Dorsogluteal
b. Ventrogluteal
c. Deltoid
d. Vastus lateralis

45. Before administering medication via NG tube, which step should be taken to verify placement?
a. Inject 10 mL water
b. Attach NG to suction
c. X-ray abdomen
d. Check pH of gastric juice

46. What is the first step to take if a two-year-old swallows several children's aspirin tablets?
a. Administer ipecac
b. Give activated charcoal
c. Call Poison Control
d. Give 8 oz of milk

47. If there is doubt about the type of poison, toxicology tests will be done on all of the following EXCEPT
a. Urine
b. Stool
c. Blood
d. Emesis

48. Which group is *least* at risk of accidental poisoning?
a. Infants
b. Older adults
c. Healthy adults
d. Dementia patients

49. Patient education to prevent poisoning includes all of the following advice EXCEPT
a. Label all medications and poisons
b. Discard medications in toilet
c. Always read medicine labels
d. Keep medications at bedside

Calculate the correct dosage for administration in the following problems. Label your answers. Remember that syringes are not marked in fractions; therefore, when computing dosages for administration, you must convert all fractions to decimals and round off to one decimal place.

50. You are to give 7,500 units of heparin Subcu. The vial is labeled 10,000 units/mL. How many milliliters should you give?

51. You are to give 10 mL of guaifenesin cough syrup with codeine. The bottle is labeled 10 mg of codeine in 5 mL of cough syrup. How much codeine would the patient receive in each prescribed dose?

52. The medicine bottle label states that the strength of each tablet in the bottle is 0.25 mg. The physician has ordered that the patient is to receive 0.5 mg. How many tablets should you give?

53. The physician has ordered 20 mg of meperidine to be given. On hand is medication containing 50 mg/mL. How many milliliters should you give?

54. To convert pounds to kilograms (kg), you would divide the number of pounds by what number?

Comprehensive Review Exam for Part 2

1. Deficiency of potassium may result in
- a. Diarrhea
- b. Petechiae
- c. Cardiac arrhythmias
- d. GI bleeding

2. Who would be *least* likely to require vitamin or mineral supplements?
- a. Executive secretary
- b. Nursing mother
- c. Adolescent
- d. Alcoholic

3. The following statements are true of vitamin C EXCEPT
- a. Destroyed by heat
- b. Unstable with antacids
- c. Found in citrus fruits
- d. Large supplements helpful

4. Which condition will slow absorption of topical medication?
- a. Heat
- b. Moisture
- c. Macerated skin
- d. Callused skin

5. The following statements are true of resistance to antibiotics EXCEPT
- a. Caused by too frequent use
- b. Caused by incomplete treatment
- c. Decreased with use of combination drugs
- d. Decreased with use of antacids concurrently

6. All of the following drugs are used in the initial treatment program for tuberculosis EXCEPT
- a. Isoniazid
- b. Rifampin
- c. Fluconazole
- d. Pyrazinamide

7. Unless ordered otherwise, antibiotics are best administered:
- a. With fruit juice
- b. With antacids
- c. 1 h ac
- d. ½ h pc

8. Allergic hypersensitivity can be manifested in all of the following ways EXCEPT
- a. Diarrhea
- b. Rash
- c. Hives
- d. Anaphylaxis

9. Which of the following would be most likely to develop a penicillin reaction?
- a. Premature infant
- b. Cancer patient
- c. Diabetic
- d. Allergic asthmatic

10. The following statements are true of atropine EXCEPT
- a. Used as a mydriatic
- b. Used as a cycloplegic
- c. Treatment for glaucoma
- d. Can cause blurred vision

11. The following statements are true of corticosteroid ophthalmic ointment EXCEPT
- a. Can delay healing
- b. Used short term
- c. Anti-inflammatory
- d. Used for infections

12. The following instructions are appropriate for those taking loop diuretics, for example, Lasix or Bumex, EXCEPT
- a. Avoid alcohol
- b. Report rash
- c. Take at bedtime
- d. Limit exposure to sun

13. The following side effects are possible with thiazide diuretics EXCEPT
a. Hypokalemia
b. Hypoglycemia
c. Increased uric acid
d. Muscle weakness

14. The thiazides are used to treat all of the following conditions EXCEPT
a. Hypertension
b. Congestive heart failure
c. Gout
d. Edema

15. Which term does *not* describe a purpose for antineoplastic drugs?
a. Cytotoxic
b. Analeptic
c. Palliative
d. Remission

16. Which is *not* a frequent side effect of antineoplastic drugs?
a. Jaundice
b. Diarrhea
c. Ulcers of mucosa
d. Nausea and vomiting

17. Which side effect is *not* associated with atropine?
a. Diaphoresis
b. Confusion
c. Blurred vision
d. Urinary retention

18. Which side effect is *not* associated with epinephrine?
a. Palpitations
b. Lethargy
c. Tachycardia
d. Tremor

19. Which is *not* an action of cholinergic drugs?
a. Increased peristalsis
b. Lowered intraocular pressure
c. Reduced salivation
d. Bladder contraction

20. Drugs that can cause mental impairment in older adults include all of the following EXCEPT
a. Tagamet
b. Naprosyn
c. Benadryl
d. Ditropan

Jim J. is admitted to the emergency room with a history of insecticide poisoning (cholinergic action). Questions 21 and 22 relate to Jim's situation:

21. Jim's symptoms might include all of the following EXCEPT
a. Facial flushing
b. Diaphoresis
c. Diarrhea
d. Nausea

22. His treatment would most likely include which drug?
a. Prostigmin
b. Adrenalin
c. Atropine
d. Isuprel

23. Which statement is *not* true of Lomotil?
a. Slows peristalsis
b. Contains atropine
c. Has drying effect
d. Used for food poisoning

24. Which laxative would be used for chronic constipation?
a. Milk of Magnesia
b. Dulcolax
c. Senokot
d. Metamucil

25. Which medication is *not* an antiemetic?
a. Phenergan
b. Imodium
c. Dramamine
d. Compazine

26. The most likely prescription for frequent gas pains is:
a. Milk of Magnesia
b. Colace
c. Simethicone
d. Metamucil

27. Which statement is *not* true of the nonsteroidal anti-inflammatory drugs?
a. Alleviate pain of arthritis
b. Raise prostaglandin levels
c. Used long term sometimes
d. Reduce joint swelling

28. Which drug is *not* a muscle relaxant?
a. Robaxin
b. Valium
c. Naprosyn
d. Flexeril

29. Which is *not* a likely side effect with opioid analgesics?
a. Constipation
b. Tachycardia
c. Urinary retention
d. Blurred vision

30. Which drug does *not* potentiate the CNS depression effect of analgesics and hypnotics?
a. Alcohol
b. Antihistamines
c. Corticosteroids
d. Muscle relaxants

31. Which is the most common side effect of prolonged use of haldoperidol (Haldol)?
a. Hypertension
b. Diarrhea
c. Diaphoresis
d. Parkinsonism

32. Which statement is *not* true of the tricyclic antidepressants?
a. Rapidly effective
b. Cause dry mouth
c. Tranquilizing effect
d. Anticholinergic action

33. Which statement is *not* true of the minor tranquilizers?
a. For psychosomatic disorders
b. Relieve nausea and vomiting
c. May cause photosensitivity
d. Useful long term

34. Adjuvant drugs that can enhance analgesic effect when combined with opioids include all of the following EXCEPT
a. Neurontin
b. Effexor
c. Tegretol
d. Tofranil

35. All of the following have GI bleeding as a possible side effect EXCEPT
a. Ibuprofen
b. Prilosec
c. Prednisone
d. Naprosyn

36. Which medication is used to treat febrile convulsions in children?
a. Dilantin
b. Depakote
c. Zarontin
d. Phenobarbital

37. Which is a purpose of the anticonvulsants?
a. Reduce seizures
b. Sedate the patient
c. Cure epilepsy
d. Treat parkinsonism

38. Which is *not* an antiparkinsonian drug?
a. Cimetidine
b. Cogentin
c. Sinemet
d. Symmetrel

39. Which condition is *not* treated with estrogen?
a. Female hypogonadism
b. Prostatic cancer
c. Threatened abortion
d. Atrophic vaginitis

40. Which condition is *not* treated with testosterone?
a. Enuchoidism
b. Androgen deficiency
c. Cryptorchidism
d. Metastatic breast cancer
e. Prostate cancer

41. Which is *not* a possible side effect of corticosteroids?
a. Delayed healing
b. Peptic ulcer formation
c. Reduced resistance to infection
d. Hypoglycemia

42. Midazolam (Versed), a preoperative medication, can cause all of the following EXCEPT
a. Slow respiration
b. Tachycardia
c. Amnesia
d. Sedation

43. The following statements are true of isoproterenol (Isuprel) EXCEPT
a. May cause hypoglycemia
b. May cause palpitations
c. May be given sublingually
d. Is a sympathomimetic

44. The following statements are true of codeine used as an antitussive EXCEPT
a. May depress respirations
b. Useful with COPD
c. May be addictive
d. Controlled substance

45. Which of the following respiratory drugs would not have tachycardia as a possible side effect?
a. Albuterol
b. Atrovent
c. Theophylline
d. Singulair

46. Which is *not* a symptom of hypoglycemia?
a. Tremor
b. Dry skin
c. Irritability
d. Confusion
e. Drowsiness

47. Which is *not* a symptom of hyperglycemia?
a. Polyuria
b. Dehydration
c. Lethargy
d. Sweating
e. Excessive thirst

48. Which antihistamine is *least* likely to cause sedation?
a. Benadryl
b. Phenergan
c. Chlor-Trimeton
d. Claritin

49. All of the following might be a symptom of digitalis toxicity EXCEPT
a. Cardiac arrhythmia
b. Blurred vision
c. Urinary retention
d. GI disturbance

50. Which of the following antihypertensives is *least* likely to cause bradycardia?
a. Procardia
b. Inderal
c. Apresoline
d. Catapres

Glossary

A

Abbreviations. Symbols used for medication orders.

Absence epilepsy. Absence of convulsions characterized by a sudden 10–30 second loss of consciousness with no falling; formerly called petit mal.

Absorption. Passage of a substance through a body surface into body fluids or tissues.

Acetylcholine. Chemical mediator of nerve impulses in the parasympathetic system.

Action. A description of the cellular changes that occur as a result of a drug.

Addiction. Physical and/or psychological dependence on a substance, especially alcohol or drugs, with use of increasing amounts (tolerance) and withdrawal reactions.

Adjunct. Addition to the course of treatment to increase the efficacy.

Adjuvant. A drug added to a prescription to hasten or enhance the action of a principle ingredient.

Adrenal. Glands located adjacent to the kidneys that secrete hormones called corticosteroids.

Adrenergic. Sympathomimetic drug that mimics the action of the sympathetic nervous system.

Adsorbent. Substance that leads readily to absorption.

Adverse effects. Harmful unintended reactions to a drug.

Adverse reaction. A list of possible unpleasant or dangerous secondary effects, other than the desired effect.

Albuminuria. Albumin (proteins) in urine.

Allergic reaction. Response of the body resulting from hypersensitivity to a substance (e.g., rash, hives, and anaphylaxis).

Alopecia. Loss or absence of hair.

Alpha-blockers. Drugs that block the alpha-1 receptors found in smooth muscle in the bladder neck and prostate, causing them to relax.

Alzheimer's disease. Dementia characterized by a devastating, progressive decline in cognitive function, followed by increasingly severe impairment in social and occupational functioning.

Aminoglycosides. Drugs used in combination with other antibiotics that treat many infections caused by gram-negative and gram-positive bacteria.

Amnesia. Loss of memory.

Ampule. Glass container with drug for injection, must be broken at the neck to withdraw drug in solution.

Analeptic. A drug used to stimulate the central nervous system, especially with poisoning by CNS depressants.

Analgesic. Medication that alleviates pain.

Anaphylaxis. Allergic hypersensitivity reaction of the body to a foreign substance or drug. Mild symptoms include rash, itching, and hives. Severe symptoms include dyspnea, chest constriction, cardiopulmonary collapse, and death.

Androgens. Male hormones that stimulate the development of male characteristics.

Angina pectoris. Severe chest pain resulting from decreased blood supply to the heart muscle.

Angiogenesis. Development of new blood vessels.

Anorexia. Loss of appetite.

Antacid. Agent that neutralizes gastric hydrochloric acid.

Antagonism. Opposing action of two drugs in which one decreases or cancels out the effect of the other.

Antiandrogen. A gonadotropin-releasing hormone analog that is used to treat prostate cancer.

Antiarrhythmic. Drug that controls or prevents cardiac irregularities.

Anticholinergic. Drug that blocks the action of the parasympathetic nervous system.

Anticoagulants. Medications used to prevent formation of clots or decrease the extension of existing clots in such conditions as venous thrombosis, pulmonary embolism, and coronary occlusion.

Anticonvulsants. Medication used to reduce the number and/or severity of seizures in patients with epilepsy.

Antidepressant. Medication used to treat patients with various types of depression; sometimes called mood elevators.

Antidiabetic. Medication to lower blood glucose levels in those with impaired metabolism of carbohydrates, fats, and proteins.

Antidiarrhea. Medication that reduces the number of loose stools.

Antidote. Substance that neutralizes poisons or toxic substances.

Antiemetic. Drug that prevents or treats nausea, vomiting, or motion sickness.

Antiflatulent. Symptomatic treatment of gastric bloating or GI gas pain.

Antifungal. Medication used in the treatment of candidal and other specific susceptible fungi.

Antiglaucoma drugs. Medications used to lower intraocular pressure.

Antihistamines. Medications that provide symptomatic relief of allergic symptoms caused by histamine release.

Antihypertensives. Medications used in the treatment and management of all degrees of hypertension.

Anti-infective. Medication used in the treatment of infections; includes antibiotics, antifungals, and antivirals.

Anti-inflammatory. Medication used to relieve inflammation.

Antilipemic. Drug that lowers the serum cholesterol and low-density lipoproteins (LDLs) and increases the high-density lipoproteins (HDLs).

Antimuscarinics. Drugs that block cholinergic stimuli at muscarinic receptors. A type of anticholinergic. Also called parasympatholytics.

Antineoplastic. Agent that prevents the development, growth, or spreading of malignant cells.

Antioxidant. Agent that prevents or inhibits oxidation or cell destruction in damaged or aging tissues. A compound that fights against the destructive effects of free radical formation.

Antiparkinsonian drugs. Medications used in the treatment of Parkinson's disease to relieve symptoms and maintain mobility, but do not cure the disease.

Antipruritic. Products applied topically to alleviate itching.

Antipsychotic. Major tranquilizers used to relieve symptoms of psychoses or severe neuroses; sometimes called neuroleptics.

Antipyretic. Medication to reduce fever.

Antiseptic. Substances that inhibit the growth of bacteria.

Antispasmodics. Medications used to reduce the strength and frequency of contractions of the urinary bladder and to decrease gastrointestinal motility.

Antithyroid. Medication used to relieve the symptoms of hyperthyroidism in preparation for surgical or radioactive iodine therapy.

Antituberculosis agents. Medications used to treat asymptomatic infection, and to treat

active clinical tuberculosis and prevent relapse.

Antitussive. Medication that suppresses coughing.

Antiulcer. Drug that reduces gastric acid secretion, or that acts to prevent or treat gastric or duodenal ulcers.

Antiviral. Medications used to treat viruses, for example, HIV and herpes.

Anxiolytics. Antianxiety medications (tranquilizers) used for the short-term treatment of anxiety disorders, neurosis, some psychosomatic disorders, and insomnia.

Apnea. Cessation of breathing.

Appropriate. Reasonable under the circumstances for a specific patient.

Arteriosclerosis. A common arterial disorder characterized by thickening and loss of elasticity of the arterial walls, resulting in a decreased blood supply, especially to the cerebrum and lower extremities.

Ascites. The abnormal accumulation of fluid in the pleura or peritoneal cavity.

Asthma treatment. Medications used for prophylaxis and treatment of chronic asthma. Bronchodilators are used for acute asthmatic attacks.

Asymptomatic. No evidence of clinical disease.

Ataxia. Defective muscular coordination, especially with voluntary muscular movements (e.g., walking).

Atherosclerosis. A type of arteriosclerosis characterized by yellowish plaques of cholesterol, lipids, and cellular debris in the walls of large and medium-sized arteries, resulting in reduced circulation, the major cause of coronary heart disease, such as angina pectoris or myocardial infarction.

Atypical antipsychotics. A newer class of antipsychotics with less potential for adverse effects, such as extrapyramidal symptoms and tardive dyskinesia.

Autonomic. Automatic, self-governing, or involuntary nervous system.

B

Bactericidal. Destroying bacteria.

Bacteriostatic. Inhibiting or retarding bacterial growth.

Beta-blocker. Drug that blocks the action of the sympathetic nervous system.

Biotransformation. Chemical changes that a substance undergoes in the body.

Bipolar disorder. Manic-depressive mental disorder in which the mood fluctuates from mania to depression.

Blood dyscrasia. A condition in which any of the blood constituents are abnormal or are present in abnormal quantity.

BPH. Benign prostatic hypertrophy.

BPH therapy. Drug used to reduce prostate size and associated urinary obstruction and manifestations in patients with BPH.

Bradycardia. Abnormally slow heartbeat.

Bradykinesia. Abnormally slow movement.

Broad spectrum. Antibiotic effective against a large variety of organisms.

Bronchodilators. Medications that relax the smooth muscles of the bronchial tree, thereby relieving bronchospasm and increasing the vital capacity of the lungs.

Buccal. In the cheek pouch.

C

C & S. Culture and sensitivity test to identify a causative infectious organism and the specific medicine to which it is sensitive.

Cachexia. Condition of malnutrition and wasting in chronic conditions such as some malignancies or AIDS.

Calculus. Stone.

Carbonic anhydrase inhibitors. Drugs that reduce the hydrogen and bicarbonate ions and have a diuretic effect (increasing the excretion of fluids from the body through the urine).

Cardiac glycosides. Medication used primarily in the treatment of heart failure.

Cardiotonic. Increasing the force and efficiency of contractions of the heart muscle.

Cardioversion. Correcting an irregular heartbeat (arrhythmia). Usually accomplished by electrical shock (e.g., defibrillation).

Catecholamines. Mediators released at the sympathetic nerve endings (e.g., epinephrine and norepinephrine).

Cautions. Precautions; steps to take to prevent errors.

Cephalosporins. Semisynthetic antibiotic derivatives produced by a fungus.

Cheilosis. Reddened lips with cracked corners.

Chemical dependency. Condition in which alcohol or drugs have taken control of an individual's life and affect normal functioning.

Chemotherapy. Chemicals (drugs) with specific and toxic effects upon disease-producing organisms.

Cholelithiasis. The presence of gallstones in the gallbladder.

Cholinergic. Parasympathomimetic drug that mimics the action of the parasympathetic nervous system.

Classification. Broad subcategory for drugs that affect the body in similar ways.

Clone. A copy.

Clonic. Spasm marked by alternate contraction (rigidity) and relaxation of muscles.

Coanalgesic. Nonopioid analgesic drugs that are combined with opioids for more effective analgesic action in relief of acute or chronic pain (e.g., NSAID or acetaminophen).

Coenzyme. Enzyme activator.

Comorbidities. Other serious conditions existing concurrently with the one under discussion.

Concomitant. Taking place at the same time.

Concurrent. Existing at the same time.

Contraceptives. Medications used for birth control.

Contraindication. Condition or circumstance that indicates that a drug should not be given.

Controlled substance. Drug controlled by prescription requirement because of the danger of addiction or abuse.

Conversion. Changing from one system of measurement to another.

COPD. Chronic obstructive pulmonary disease.

Coronary vasodilators. Medications used in the treatment of angina. See Vasodilator.

Corticosteroids. Hormones secreted by the adrenal glands that act on the immune system to suppress the body's response to infection or trauma; medications given for their anti-inflammatory and immunosuppressant properties.

COX-2 inhibitors. Anti-inflammatory drugs that do not inhibit clotting and cause fewer gastric problems and less GI bleeding than other NSAIDs.

Cryptorchidism. Undescended testicles.

Cumulative effect. Increased effect of a drug that accumulates in the body.

Cushing's syndrome. Excessive production or administration of adrenal cortical hormones, resulting in edema, puffy face, fatigue, weakness, and osteoporosis.

Cutaneous. Pertaining to skin.

Cycloplegic. Drug that paralyzes the muscles of accommodation for eye examinations.

Cytotoxic. Destroys cells.

D

Decongestants. Drugs that constrict blood vessels in the respiratory tract, resulting in shrinkage of swollen mucous membranes and opened nasal airway passages.

Deficiency. Lacking adequate amount.

Demulcent. Medication used topically to protect or soothe minor dermatological conditions such as diaper rash, abrasions, and minor burns.

Dependence. Acquired need for a drug after repeated use; may be psychological with craving and emotional changes or physical with body changes and withdrawal symptoms.

Digitalization. The process of establishing the correct therapeutic dose of digitalis for maintaining optimal functioning of the heart without toxic effects.

Diplopia. Double vision.

Direct toxicity. Drug that results in tissue damage; may or may not be permanent.

Distribution. Circulation of drugs, after absorption, to the organs of the body.

Diuretic. Medication that increases urine excretion.

Documentation. Recording medication given to a patient on the patient's medical record, including the dose, time, route, and location of injections.

Dosage. Amount of drug given for a particular therapeutic or desired effect.

Dosage calculation. Using mathematical computation to determine the correct dosage to administer when a dosage ordered differs from the dose on hand.

Drug. Chemical substance taken into the body that affects body function.

Drug abuse. The use of a drug for other than therapeutic purposes.

Drug Enforcement Administration (DEA). A bureau of the Department of Justice that enforces the Controlled Substances Act.

Drug form. The type of preparation in which a drug is supplied.

Drug interactions. Response that may occur when more than one drug is taken. The combination may alter the expected response of each individual drug.

Drug processes. Four biological changes that drugs undergo within the body.

Drug standards. Federally approved requirements for the specified strength, quality, and purity of drugs.

Dry Powdered Inhaler (DPI). A self-generating device that forms a fine mist from a powdered drug solution that can then be inhaled using a fast, deep breath into the respiratory system.

Dyskinesia. An impairment of the ability to execute voluntary movements, frequently an adverse effect of prolonged use of some medications, for example, phenothiazines.

Dyslipidemia. Abnormal levels of various blood lipid fractions.

Dysmenorrhea. Painful menstruation

Dysphagia. Difficulty in swallowing.

Dysphonia. Difficulty speaking or hoarseness

Dystonic reaction. Spasm and contortion, especially of the head, neck, and tongue, as an adverse effect of antipsychotic medication.

E

Effects of drugs. Physiological changes that occur in response to drugs.

Emetic. Agent that induces vomiting.

Emollient. Medication used topically to protect or soothe minor dermatological conditions, such as diaper rash, abrasions, and minor burns.

Endocrine. Internal secretion (hormone) produced by a ductless gland that secretes directly into the bloodstream.

Endogenous. Produced or originating within a cell or organism.

Endorphin. Endogenous analgesics produced within the body.

Enteric coated. Tablet with a special coating that resists disintegration by the gastric juices and dissolves in the intestines.

Enuresis. Urinary incontinence; bed-wetting.

Epidural anesthesia. Local anesthetic solution injected into the epidural space just outside the spinal cord.

Epilepsy. A recurrent paroxysmal disorder of brain function characterized by sudden attacks of altered consciousness, motor activity, or sensory impairment.

Epistaxis. Nosebleed.

Estrogens. Female sex hormones responsible for the development of female secondary sexual characteristics; medications used for many conditions.

Eunuchism. Lack of male hormone, resulting in high-pitched voice and absence of beard and body hair.

Euphoria. Exaggerated feeling of well-being and elation.

Euthyroid. Normal thyroid function.

Excretion. Elimination of by-products of drug metabolism from the body, essentially through the kidneys, some from the intestines and lungs.

Exogenous. Originating outside the body or an organ or produced from external causes.

Expectorants. Drugs that increase secretions, reduce viscosity, and help to expel sputum.

Extrapyramidal. Disorder of the brain characterized by tremors, parkinsonlike symptoms, dystonic twisting of body parts, or tardive dyskinesia, sometimes associated with prolonged use of antipsychotic drugs and some other CNS drugs.

F

Fat-soluble. Vitamins A, D, E, and K.

Flatulence. Excessive gas in the digestive tract.

Follicle-stimulating hormone (FSH). Hormone that stimulates development of ovarian follicles in the female and sperm production in the testes of the male.

Food and Drug Administration (FDA). A department of Health and Welfare that enforces the provisions of the Federal Food, Drug, and Cosmetic Act and amendments of 1951 and 1965.

Free radicals. Unbound compounds that attack and damage the cells or initiate growth of abnormal cells, resulting in conditions such as cancer or atherosclerosis.

G

Gastric tube administration. Medication administered through a tube in the abdomen to the stomach.

Gastroesophageal reflux disease (GERD). A backward flow of gastric secretions into the esophagus causing inflammation and discomfort. GERD is treated with drugs to accelerate gastric emptying.

Gastroparesis. Partial paralysis of the stomach.

Generic name. General, common, or nonproprietary name of a drug.

GERD. Gastroesophageal reflux disease.

Gingivitis. Inflammation of the gums characterized by redness, swelling, and tendency to bleed.

Glaucoma. Abnormal condition of the eye with increased intraocular pressure (IOP) due to obstruction of the outflow of aqueous humor.

Glossitis. Inflammation of the tongue.

Glycosuria. Sugar in the urine.

Goiter. Enlargement of the thyroid gland.

Gout. Form of arthritis in which uric acid crystals are deposited in and around joints.

Grand mal seizures. A form of epilepsy characterized by loss of consciousness, falling, and generalized tonic, followed by clonic contractions of the muscles.

Gray List. List of inappropriate drugs for nursing home residents based on a national survey of geriatric experts.

Gynecomastia. Enlargement of breast tissue in males.

H

HAART. Highly active antiretroviral therapy for HIV infections.

Hematological. Concerned with the blood and its components.

Hematopoiesis. Production of blood cells, normally in bone marrow.

Hematuria. Blood in the urine.

Hepatotoxicity. Damage to the liver as an adverse reaction to certain drugs.

Herbs. Any product intended for ingestion as a supplement to the diet.

Heterocyclics. Second-generation cyclic antidepressants with very different adverse effect profiles.

Homeostasis. Body balance, state of internal equilibrium.

Hormone replacement therapy (HRT). Estrogen with or without progestin used for osteoporosis prevention and treatment.

Hyperalimentation. The intravenous infusion of a hypertonic solution containing all of the necessary elements to sustain life. Usually infused through a subclavian catheter into the superior vena cava.

Hypercalcemia. Abnormally high blood calcium.

Hyperglycemia. Abnormally high blood glucose.

Hyperkalemia. Abnormally high potassium in the blood can lead to cardiac arrhythmias.

Hyperlipidemia. High lipid levels in the blood.

Hyperosmotic. Laxative to draw water from the tissues and stimulate evacuation.

Hyperpyrexia. Extreme elevation of body temperature.

Hypersensitivity. Allergic or excessive response of the immune system to a drug or chemical.

Hypertriglyceridemia. High triglyceride level in the blood.

Hyperuricemia. Abnormal amount of uric acid in the blood.

Hypnotic. Drug that promotes sleep.

Hypoglycemia. Abnormally low blood glucose.

Hypokalemia. Abnormally low blood potassium; can lead to cardiac arrhythmias.

Hypotensive. Antihypertensive; medication used in the treatment of hypertension.

Hypothyroidism. Diminished or absent thyroid function.

Hypoxia. Deficiency of oxygen.

I

Idiopathic. Condition without a known cause.

Idiosyncratic. Unusual reaction to a drug, other than expected.

Immunosuppressive. Decreasing the production of antibodies and phagocytes and depressing the inflammatory reaction.

Indications. List of conditions for which a drug is meant to be used.

Infiltration anesthesia. Local anesthetic solution injected into the skin, subcutaneous tissue, or mucous membranes of the area to be anesthetized.

Ingestion. To take into the body by mouth through swallowing.

Inhalation therapy. Medications administered through a metered dose inhaler, small-volume nebulizer, dry powder inhaler, or intermittent positive pressure breathing apparatus.

Interactions. Actions that occur when two or more drugs are combined, or when drugs are combined with certain foods. See Drug interactions.

Intra-articular (intracapsular). Injected into the joint.

Intradermal (ID). Injected into the layers of the skin.

Intramuscular (IM). Injected into the muscle.

Intrathecal. Injection into the spinal canal.

Intravenous (IV). Injected into the vein.

Ischemia. Holding back of the blood; local deficiency of blood supply due to obstruction of circulation to a part (e.g., heart or extremities).

K

Keratolytic. An agent that promotes loosening or scaling of the outer layer of the skin.

Korsakoff's psychosis. Disorder characterized by polyneuritis, disorientation, mental deterioration, and ataxia with painful foot drop, usually associated with chronic alcoholism.

L

Lability. State of being unstable or changeable.

Lacrimation. Discharge of tears.

Laxatives. Drugs that promote evacuation of the intestine.

Legend drug. Available only by prescription.

Leukopenia. Abnormal decrease in white blood cells, usually below 5,000.

Local. Affecting one specific area or part.

Local anesthetic. Medication administered to produce temporary loss of sensation or feeling in a specific area.

Lozenge (troche). Tablet that dissolves slowly in the mouth for local effect.

Luteinizing hormone (LH). Hormone that works in conjunction with FSH to induce secretion of estrogen, ovulation, and development of corpus luteum.

Luteotropic hormone (LTH). Hormone that stimulates the secretion of progesterone by the corpus luteum and secretion of milk by the mammary gland.

M

Macrolides. Drugs used in many infections of the respiratory tract, for skin conditions such as acne, or for some sexually transmitted infections when the patient is allergic to penicillin.

Medication orders. The physician's prescription for administration of a drug; contains six parts.

Megadose. Abnormally large dose.

Melena. Blood in the stool.

Mental impairment. Decreased mental function in older adults frequently caused or worsened by drugs.

Metabolism. Physical and chemical alterations that a substance undergoes in the body.

Metered Dose Inhaler (MDI). A canister containing a propellant used to deliver a fine mist (aerosol) of a drug into the respiratory system. Often used with a spacer device or reservoir to increase the effectiveness of drug delivery.

Metric system. International standard for weights and measures.

Minerals. Chemical elements occurring in nature and in body fluids.

Miotic. Drugs that cause the pupil to contract.

Mixed seizure. Having more than one type of seizure.

Monoclonal antibodies. Chemotherapy designed to target only cancer cells, thereby sparing normal tissues.

Mortar and pestle. Glass cup with glass rod used to crush tablets.

Mucolytic. Medication that liquefies pulmonary secretions.

Myalgia. Tenderness or pain in the muscles.

Mydriatic. Drug that dilates the pupil.

Myelosuppression. Inhibiting bone marrow function.

Myopathy. Abnormal condition of skeletal muscle.

N

Nasogastric tube administration. Medication administered through a tube inserted through the nose and extending into the stomach.

Nebulizer (vaporizer). Apparatus for producing a fine spray or mist for inhalation.

Neoplasms. New growth or tumor.

Nephropathy. Disease of the kidneys.

Nephrotoxicity. Damage to the kidneys as an adverse reaction to certain drugs.

Neuropathy. Any disease of the nerves.

Neurotoxicity. Having the capability of harming nerve tissue.

Neurotransmitters. Substances that travel across the synapse to transmit messages between nerve cells.

Neutropenia. Abnormally small number of neutrophil leukocytes in the blood.

Nosocomial. Hospital-acquired infection.

NSAID. Nonsteroidal anti-inflammatory drug.

Nystagmus. Involuntary rhythmic movements of the eyeball.

O

Objective. Referring to symptoms observed or perceived by others.

Oligospermia. Deficient sperm production.

Onychomycosis. Toenail fungus.

Oophorectomy. Excision of an ovary.

Opioids. Analgesics, controlled substances, whose action is similar to opium in altering the perception of pain; can be natural or synthetic.

Opportunistic infections. Infections that occur because the immune system is compromised.

Oral medications. Medication administered by mouth.

Orphan drug. A drug or biological product for the diagnosis, treatment, or prevention of a rare disease or condition, that is, one affecting less than 200,000 persons in the United States, or greater than 200,000 persons where the cost of developing the drug is probably not recoverable in the United States.

Osmotic agents. Medications used to reduce intracranial or intraocular pressure.

Osteomalacia. Softening of the bones due to inadequate calcium and/or vitamin D.

Osteoporosis. Softening of the bone seen most often in older adults, especially postmenopausal women.

Osteoporosis therapy. Medications used to prevent or treat osteoporosis by increasing bone mineral density.

Ototoxicity. Damage to the eighth cranial nerve resulting in impaired hearing or ringing in the ears (tinnitus); adverse reaction to certain drugs.

Overdose. A higher than normal amount sufficient to cause toxicity.

Over-the-counter drug (OTC). Medication available without a prescription.

Oxytocin. Hormone that stimulates the uterus to contract, thus inducing childbirth.

P

Palliative. Referring to alleviation of symptoms, but not producing a cure.

Paradoxical. Opposite effect from that expected.

Paraphilia. A psychosexual disorder in which unusual or bizarre imagery or acts are necessary for realization of sexual excitement.

Parasympatholytics. Anticholinergics; medications that decrease the chemical that promotes bronchospasm.

Parenteral. Any route of administration not involving the gastrointestinal tract (e.g., injection, topical, and inhalation).

Paresthesia. Numbness, tingling, or a "pins and needles" feeling, especially in extremities.

Parkinson's disease. A chronic neurological disorder characterized by fine, slowly spreading muscle tremors, rigidity and weakness of muscles, and shuffling gait.

Pedophilia. Sexual attraction to children.

Pellagra. A disease caused by deficiency of niacin (nicotinic acid), characterized by skin, gastrointestinal, mucosal, neurological, and mental symptoms.

Penicillins. Antibiotics produced from certain species of a fungus.

Perioral. Around the mouth.

Peripheral. Away from the center. Usually refers to the extremities.

Peripheral nerve block. Local anesthetic solution injected into or around nerves or ganglia supplying the area to be anesthetized.

Pharmacology. The study of drugs and their origin, nature, properties, and effects on living organisms.

Photosensitivity. Increased reaction, e.g., burn, from brief exposure to sun or ultraviolet lamp.

Physiological dependence. Physical adaptation of the body to a drug and withdrawal symptoms after abrupt drug discontinuation.

Phytoestrogen. A plant substance with estrogen-like properties.

Placebo. Inactive substance given to simulate the effect of another drug; physical or emotional changes that occur reflect the expectations of the patient.

Placebo effect. Relief from pain as the result of suggestion without active medication.

Platelet inhibitor. A drug that inhibits platelet aggregation (clumping) to prevent clots.

Poison. Substance that is taken into the body by ingestion, inhalation, injection, or absorption that is toxic and can cause illness, injury, or death.

Polypharmacy. Excessive use of drugs or prescription of many drugs given at one time.

Postherpetic neuralgia. Nerve pain following an episode of shingles.

Potentiation. Increased effect; action of two drugs given simultaneously is greater than the effect of the drugs given separately.

Precautions. List of conditions or types of patients that warrant closer observation for specific side effects when given a drug.

Prevention of medication errors. Rules to follow to avoid making mistakes.

Priapism. Prolonged penile erection.

Prodrug. A newly developed group of chemicals that exhibit their pharmacological activity after biotransformation.

Progesterone. Hormone responsible for changes in uterine endometrium in the second half of the menstrual cycle in preparation for implantation of the fertilized ovum, development of maternal placenta after implantation, and development of mammary glands; medication with several uses.

Progestins. Synthetic drugs that exert progesterone-like activity.

Proliferation. Rapid reproduction.

Proportion. Two ratios that are equal.

Prototype. Model or type from which subsequent types arise (e.g., an example of a drug that typifies the characteristics of that classification).

Pruritis. Itching.

Psychomotor epilepsy. Also known as temporal lobe epilepsy because of the area in the brain that is involved; characterized by temporary impairment of consciousness, confusion, loss of judgment, and abnormal acts, even crimes and hallucinations, but no convulsions.

Psychotropic. Any substance that acts on the mind.

Q

Quinolones. Drugs used in adults for the treatment of some infections of the urinary tract, lower respiratory tract, gastrointestinal tract, skin, bones, and joints.

R

Ratio. A relationship between two numbers.

Rectal medications. Medication in suppository or liquid form administered as a retention enema.

Refractory. A disorder resistant to treatment.

REM. Rapid eye movement, or dream phase of sleep.

Reporting. Notifying the FDA of serious adverse events or product quality problems associated with medications (MEDWATCH).

Resistance. An organism's lack of response to antibiotics when they are used too often or treatment is incomplete.

Responsibility. Duty to administer drugs safely and accurately.

Reye's Syndrome. Complication following acute viral infections in those under 18 years of age, characterized by rash, vomiting, and confusion about 1 week after the onset of a viral illness. May lead to respiratory arrest. Aspirin may induce Reye's syndrome when administered to children or adolescents with viral infections.

Rhabdomyolysis. An acute, sometimes fatal disease characterized by destruction of muscle leading to renal failure.

"Rights" of medication administration. Guidelines for giving medication that include the right medication, right amount, right time, right route, right patient, and right documentation.

Route of delivery. The way that drugs are taken into the body.

S

Scurvy. A vitamin C deficiency disease usually resulting from lack of fresh fruits and vegetables in diet. Symptoms include ulcerated gums and mouth, loose teeth, muscle cramps and weakness, poor healing, and bruising.

Sedatives. Controlled substances used to promote sedation in smaller doses and to promote sleep in larger doses.

Selective distribution. Affinity or attraction of a drug to a specific organ or cells.

Selective Serotonin Reuptake Inhibitors (SSRI). Antidepressants that block the reabsorption of the neurotransmitter serotonin, thus helping to restore the brain's chemical balance.

Skeletal muscle relaxants. Medication used to treat some musculoskeletal disorders associated with pain, spasm, abnormal contraction, or impaired mobility.

Small Volume Nebulizer (SVN). Device that creates a fine mist of a drug solution using a gas source (aerosolization). The aerosol is then inhaled via a mouthpiece or mask.

Smoking cessation aids. Medications used to slowly lower the level of nicotine while the patient participates in a behavior modification program for smoking cessation.

Somogyi effect. Hyperglycemic rebound, usually a result of frequent overdoses of insulin, which causes an accelerated release of glucagon.

Sources of drugs. Five ways that the drugs are obtained.

Spinal anesthesia. Local anesthetic solutions injected intrathecally (into the subarachnoid space of the spinal canal) either in the lumbar region or lower (saddle block), depending on the area to be anesthetized.

Status epilepticus. Continual attacks of convulsive seizures without intervals of consciousness.

STD. Sexually transmitted diseases.

Stevens–Johnson Syndrome. A severe, sometimes fatal inflammatory disease affecting children and young adults, characterized by ulcers on the skin and mucous membranes, fever, and painful joints.

Stomatitis. Inflammation of the mucous membranes of the mouth.

Subcutaneous (subcu, SC, or SubQ). Beneath the skin.

Subjective. Perceived by the individual, not observable by others.

Sublingual (SL). Under the tongue.

Sulfonamides. Anti-infectives used in combinations with other drugs to slow the development of resistance; used in treatment of urinary tract infections, enteritis, and opportunistic infections of AIDS.

Sulfonylurea. Oral antidiabetic drug for treatment of type II diabetes.

Superinfection. A new infection with different resistant bacteria or fungi. Usually associated with certain types of antibiotic therapy.

Supplement. Any product intended for ingestion as an addition to the diet.

Sympathomimetic. Adrenergic drug that mimics the action of the sympathetic nervous system.

Syncope. A brief lapse in consciousness; fainting.

Synergism. Action of two drugs working together for increased effect.

Synthetic. Prepared in the laboratory by artificial means.

Systemic. Affecting the whole body or system.

T

Tachycardia. Abnormally fast heartbeat.

Tachypnea. Abnormal rapidity of respiration.

Tardive dyskinesia (TD). Slow, rhythmical, stereotyped, involuntary movements such as tics.

Temporal lobe epilepsy. See Psychomotor epilepsy.

Teratogenic effect. Effect of a drug administered to the mother that results in abnormalities in the fetus.

Testosterone. Male hormone; medication used for replacement therapy and other uses.

Tetracyclines. Broad-spectrum antibiotics used in the treatment of infections caused by rickettsia, chlamydia, or some uncommon bacteria.

Thrombocytopenia. Abnormal decrease in number of blood platelets.

Thrombolytic agents. Medications used to dissolve clots after they have formed.

Timed-release capsules (sustained-release (SR) or extended-release (ER)). Capsules containing many small pellets that are dissolved over a prolonged period of time.

Tinnitus. Ringing in the ears.

Tocolysis. Suppression of uterine contractions in preterm labor.

Tolerance. Decreased response to a drug after repeated dosage; greater amounts of the drug are required for the same effect.

Tonic. Muscular tension resulting in *extension* of the trunk and extremities, sometimes followed by synchronous *contractions* of the muscles (clonic spasm).

Topical. Applied to a specific area for a local effect to that area only (e.g., applied to skin or mucous membranes).

Topical anesthesia. Application of a local anesthetic directly to the surface of the area to be anesthetized.

Toxicity. Condition resulting from exposure to a poison or a dangerous amount of a drug.

Toxicology. Study and detection of toxic substances, establishing treatment and methods of prevention of poisoning.

Trade name. Name by which a pharmaceutical company identifies its product; brand name.

Transcutaneous. Across the skin, as in transdermal medication delivery to the body by slow absorption through the skin.

Transdermal (transcutaneous) delivery system. Patch containing the medicine is applied to the skin; the drug is absorbed through the skin over a prolonged period of time.

Tricyclics. Antidepressants that elevate the mood, have a mild sedative effect, and increase appetite.

U

Unilateral seizures. Affect only one side of the body.

Uricosuric. Promoting urinary excretion of uric acid.

Urinary analgesic. Medication used to relieve burning, pain, and discomfort in the urinary tract mucosa.

Urinary anti-infectives. Drugs used for initial or recurrent urinary tract infections caused by susceptible organisms, usually bacteriostatic instead of bactericidal.

Urticaria. Hives.

V

Variables. Factors that affect the speed and efficiency of drugs processed by the body.

Vasoconstrictor. Drug that narrows blood vessels resulting in increased blood pressure; used in the treatment of shock.

Vasodilator. A drug that expands the walls of the blood vessels, improving blood flow and resulting in a lowering of blood pressure.

Verify. Confirm the result of calculations with another professional, such as an instructor.

Vertigo. Dizziness, lightheadedness.

Vial. Glass container with rubber stopper that must be punctured with a needle to withdraw a drug solution or to reconstitute a drug in powdered form.

W

Water-soluble. B-complex vitamins and vitamin C.

Wernicke's syndrome. Mental disorder characterized by loss of memory, disorientation, and confusion, usually associated with old age or chronic alcoholism.

Withdrawal. Cessation of administration of a drug, especially a narcotic or alcohol, to which a person has become physiologically and/or psychologically addicted; withdrawal symptoms vary with the chemical used.

X

Xanthines. Medications that indirectly increase the chemical that causes bronchodilation; also respiratory stimulant to increase the ventilatory drive.

Xerophthalmia. Dryness of the eyes.

Xerostomia. Dryness of the mouth.

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