THE DIAGNOSIS AND MANAGEMENT OF AGITATION

Edited by **Scott L. Zeller, Kimberly D. Nordstrom** and **Michael P. Wilson**

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Medicine

The Diagnosis and Management of Agitation

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University Printing House, Cambridge CB2 8BS, United Kingdom

Cambridge University Press is part of the University of Cambridge.

It furthers the University's mission by disseminating knowledge in the pursuit of education, learning and research at the highest international levels of excellence.

www.cambridge.org
Information on this title: www.cambridge.org/9781107148123

First published 2017

Printed in the United Kingdom by Clays, St Ives plc

A catalogue record for this publication is available from the British Library

Library of Congress Cataloging-in-Publication Data
Names: Zeller, Scott L., editor. | Nordstrom, Kimberly, editor. | Wilson, Michael P., 1969– editor.
Title: The diagnosis and management of agitation / edited by Scott L. Zeller, Kimberly Nordstrom, Michael P. Wilson.
Description: Cambridge ; New York : Cambridge University Press, 2017. | Includes bibliographical references and index.
Identifiers: LCCN 2016046821 | ISBN 9781107148123 (hardback)
Subjects: | MESH: Psychomotor Agitation – diagnosis | Psychomotor Agitation – therapy | Acute Disease
Classification: LCC BF575.A35 | NLM WM 197 | DDC 152.4–dc23
LC record available at https://lccn.loc.gov/2016046821

ISBN 978-1-107-14812-3 Hardback

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Foreword

The Diagnosis and Management of Agitation marks the dawn of a new age in the management of acute psychiatric crises and emergencies. Medicine and society are in the midst of an international crisis on how to diagnose, treat, and coordinate care for the growing volume of patients with acute behavioral emergencies that commonly manifest with various forms of agitation. The editors – Scott L. Zeller, MD; Kimberly D. Nordstrom, MD, JD; and Michael P. Wilson, MD, PhD – are recognized visionaries and leaders in researching and teaching health care providers how to diagnose and treat psychiatric emergencies. They should be congratulated for their continued commitment to these psychiatric issues by creating the world's first textbook to help physicians, nurses, and mental health crisis workers appropriately treat the rapidly expanding number of patients with agitation.

Their publication of this unique work could not have come at a more critical time. We are in the midst of an international medical and societal crisis because of inadequate treatment facilities and providers to care for an unprecedented number of patients with acute behavioral emergencies that commonly present with agitation.

As a practicing emergency physician, I regularly care for adults and children with acute psychiatric decompensation and emergencies with agitation. Unfortunately, my colleagues and I are extremely frustrated by the inadequate treatment environment and options for these patients. These suffering patients arrive in our emergency departments with various degrees of agitation due to an acute psychiatric crisis, mental health decompensation, or other issues, often complicated by substance intoxication, withdrawal, or dependence. Although we want to diagnose and treat these patients immediately, we oftentimes do not have the space or personnel to properly treat them. This lack of staff and space resources directly leads to them being held in emergency departments – commonly against their will – in a queue awaiting psychiatric evaluation and initiation of treatment. If these patients are determined to need admission to a psychiatric facility, they are routinely subjected to waits of days or even weeks. When one considers that these patients and their families are in a very distressful psychiatric crisis, we have to acknowledge the inhumanity of this state of affairs. This is occurring throughout the United States, but, incredibly, I have learned from my international colleagues that this is a worldwide problem as well. Therefore, when I recently held the post of president of the American College of Emergency Physicians (ACEP), I created and chaired the steering committee for the Coalition on Psychiatric Emergencies Patients.

ACEP, the Emergency Nurses Association (ENA), the American Association for Emergency Psychiatry (AAEP), the National Council for Behavioral Health, the American Psychiatric Association, the National Alliance on Mental Illness (NAMI), the Depression and Bipolar Support Alliance (DBSA), and other national organizations convened in December 2014 to create and participate in a Coalition on Psychiatric Emergencies ("Coalition"). We emphatically agreed to take on this untenable situation of inadequate and fractured acute psychiatric care in this country and abroad.

The Coalition has been meeting and working regularly on many objectives. For example, it has been creating educational modules for emergency physicians and nurses on how to diagnose and begin treatment of psychiatric emergencies and agitation much sooner after

presentation than is now the status quo. The chapters in this textbook will give the Coalition much-needed guidance to create clinical guidelines and recommendations.

The editors of this textbook are all leaders in their respective fields and have created an incredibly well-researched and well-written resource for those of us on the front lines in our emergency departments, psychiatric units, hospital wards – indeed, anywhere agitation might be encountered. I personally have come to know the editors over the past couple of years as we have struggled together to eliminate the unacceptable disparity of care for psychiatric patients. Drs. Zeller, Nordstrom, and Wilson are dedicated and tireless advocates of correcting these inequities and putting international medicine on the right path to compassionately treat these patients and support their families. The Coalition has had the honor and benefit of enjoying their active participation in its activities.

Therefore, it will be unequivocally obvious that those who use this textbook will understand Drs. Zeller, Nordstrom, and Wilson's breadth and depth of knowledge in behavioral health emergencies and in the diagnosis and management of acute agitation. There are eighteen chapters in this book, by a team of international authors who provide the best overview on the diagnosis and treatment of agitation available today. For example, the most recent approaches to de-escalation, such as the results of Project BETA[1] (which has had an incredible impact on agitation care in the United States), are included. Agitation due to substance abuse is also extensively covered.

The authors' wisdom and insights will drive physicians, nurses, and our mental health colleagues to diagnose more promptly and initiate treatment within minutes rather than days. They and the Coalition know that this will significantly lessen the probability of current interminable and inhumane delays in emergency departments and acute care facilities.

Let me conclude by thanking the editors and authors for their dedication and passion for caring for patients with acute psychiatric illness. This textbook is a seminal treatise on how we should rapidly and accurately make a correct diagnosis followed by the prompt initiation of treatment. This will ideally be done in a non-chaotic caring and healing environment, with the patient quickly moving on to adequate follow-up inpatient or outpatient facilities.

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[1] Overview of Project BETA: Best Practices in Evaluation and Treatment of Agitation Garland H Holloman, Jr, MD, PhD* and Scott L Zeller, MD† *West J Emerg Med.* 2012 Feb; 13(1): 1–2. doi: 10.5811/westjem.2011.9.6865 PMCID: PMC3298232

Preface

Since the start of this project, we have been asked again and again, "You're creating a book just on agitation?" Well… yes, we are. Let's go back a little. In 2010, the American Association for Emergency Psychiatry began a project to create consensus guidelines on agitation, more specifically, Best Practices for the Evaluation and Treatment of Agitation, also known as Project BETA. By this time, Scott Zeller was well known as an emergency psychiatrist and scholar but Mike and Kimberly were newer to the field. The three of us met during the project, with Scott as the project lead. We became fast friends and natural collaborators. Since that time we have been teaching colleagues the BETA principles, nationally and internationally. During our travels we have found that physicians in emergency medicine and psychiatry have the same questions and concerns around agitation, no matter the country in which they practice. These questions have led to more papers and lectures.

One major concept that unites the three of us is around the humane treatment of those who are agitated. We must reframe the all-too-common perception that agitated individuals are an "enemy" worthy of coercion, containment, and perhaps, even punishment. Too many health care personnel see agitation as an "us versus them" situation. What we all need to understand is that our patients, in an episode of agitation, are not bad people even though they might be using profanity, making threatening statements, posturing, or even becoming physical. It is important for us to reframe the idea that the person is "bad" to the concept that the person is *suffering* from a bad disease state. When we approach these conditions with compassion rather than coercion, with understanding rather than immediate restraints, and with collaboration rather than force, we will most often find safer, better outcomes for our patients, staff, and all those around us.

With all of this in mind, we thought it was time to focus our efforts in a way to address all the major topics of agitation: chemical and biological etiology, medical workup, social impact, prehospital care, psychological and pharmacological interventions, and treatment of special populations.

We hope you enjoy reading this book as your questions about agitation are answered.

Chapter 1

Agitation: Where We're Going, Where We've Been

Scott L. Zeller

Introduction

For a condition as pervasive and impactful as agitation, it has historically been surprisingly under-researched. Current estimates suggest that anywhere between 1.7 million and 7 million episodes of agitation – defined as "excessive motor activity associated with a feeling of inner tension" by the American Psychiatric Association (APA) (APA, 2013) – are encountered in US hospitals and emergency settings each year (Zeller and Rhoades, 2010; Talsma, 2014). The number of patients with agitation dwarfs the numbers of many other, better-researched emergency medical presentations.

However, not until the relatively recent past have scholars conducted even basic studies involving the treatment of agitation. Perhaps this is because it was assumed that there could only be one treatment for agitation episodes – namely, contain the individuals, physically restrain them to a bed or gurney, and inject them with powerful sedative medications, a method that has come to be known as "restrain and sedate." To many clinicians, this method of treatment was good enough. These patients were seen as frightening, dangerous, perhaps even malevolent individuals who needed to be subdued so that all others in the area could be kept safe. Any coercive treatment, the thinking went, was appropriate and something that these patients had brought upon themselves. Since it was accepted dogma among mental health clinicians that serious psychosis would take weeks of treatment to resolve, they saw no compelling reason not to "snow" the patients with medications and keep them obtunded until they could be securely transferred to an inpatient hospital bed.

It is not as if agitation is a new concept. One can find descriptions of psychomotor "agitation" in the medical literature going back to the early 1950s (Kliess, 1951; Prior and Lawrance, 1952). There are even articles documenting the use of lithium in 1953 and 1955 (Duc and Maurel, 1953; Teulie et al., 1955) and chlorpromazine in 1955 (Rettig, 1955) for the treatment of agitation. However, most historic considerations of agitation have been more about which medication works best as part of the "restrain and sedate" approach, and little emphasis has been placed on other considerations such as diagnosis, treatment sequelae, and patient experience, until the past twenty years.

A confluence of emerging research focusing on agitation with a major media spotlight on poor care for acute psychiatric patients began in the late 1990s, leading to major attention on the treatment of agitation. Perhaps the first noteworthy and influential research of this era was a landmark head-to-head study by Battaglia and colleagues (Battaglia, 1997) that compared existing pharmacologic treatments for agitation – intramuscular antipsychotics and benzodiazepines – and determined that the combination treatment of haloperidol and lorazepam was superior to either agent used individually. However, the most powerful

change in the way agitation was viewed came about as the result of a 1999 broadcast of the CBS News program *60 Minutes II* (Kohn, 1999).

60 Minutes II Program Leads to New Guidelines

During the late 1990s, increasing scrutiny began to be paid to the use (and misuse) of physical restraints on psychiatric patients. Although it had first published restraint standards in 1984, the Joint Commission on Accreditation of Healthcare Organizations (JCAHO) stepped up its focus when it formed the Restraint Use Task Force in 1998 (Joint Commission, 1999). In October 1998, the general public first became aware of major issues involving the use of restraints when the Hartford, Connecticut, US newspaper *Hartford Courant* published an investigative series that revealed 142 restraint-related deaths had occurred in the United States over the previous ten years (Weiss et al., 1998). However, the true nationwide impact occurred in April 1999, when the popular American television news show *60 Minutes II* did a major exposé on the widespread problems, adverse outcomes, and deaths related to the use of restraints at psychiatric hospitals in the Charter Behavioral Hospital chain (Kohn, 1999).

The television program led to national outrage and caught the attention of politicians in Washington, DC. In 1999, three separate resulting bills about the use of psychiatric restraints were introduced in the US Congress (US General Accounting Office, 1999). Responding to the demand for change, the two primary organizations responsible for oversight of US hospitals, the Health Care Financing Administration (HCFA; later changed to the Centers for Medicare and Medicaid Systems, CMS) and JCAHO, promptly published new, very restrictive requirements and guidelines for restraint use ([No author listed], 2000).

The new regulations, recognizing the medical risks of restraint use and their detrimental psychologic effects on patients, endeavored to decrease the use of restraints and their duration of application dramatically. Restraints for psychiatric conditions could be used in emergency situations only when there was an imminent risk that a patient might physically harm himself or others. Restraints were to be driven by behavior rather than diagnosis. A patient in restraints would need to be under direct, in-person supervision of staff at all times. A physician would personally need to evaluate a patient in restraints within one hour of application. Moreover, substantial documentation would be required for each and every restraint episode, including clear reasons for the restraint application and itemization of all efforts to avoid their use ([No author listed], 2000).

These new requirements had a significant impact on health care systems nationwide. Also, as review of restraints policies and reduction efforts at hospitals now had become an integral component of JCAHO and HCFA surveys, hospitals under this unprecedented pressure made noticeable decreases in numbers and duration of restraint episodes (McBeth, 2004). Attempting alternatives before considering restraints became a standard protocol in not just psychiatric units, but in general medical emergency departments as well, although overall reliance on physical restraints and coercive medications remained persistently commonplace (Downey et al., 2007).

What did not change initially, with the new focus on physical restraints, was the medication approach to agitated patients. Medication used in such situations was typically described as "chemical restraint," and was used with the goal of heavily sedating patients, rather than as a treatment for the underlying condition causing agitation. However, that was

also about to change, with the introduction of new compounds specifically indicated and approved for the treatment of agitation.

Development of Second-Generation Injectable Antipsychotics

The haloperidol and lorazepam combination most frequently prescribed for agitated patients, while certainly effective, left a lot to be desired. It came with a high risk of severe dystonic reactions, extrapyramidal symptoms, akathisia, and dysphoria, and could lead to profound oversedation, in which a patient might be obtunded and unarousable for ten hours or longer (CADTH, 2015). Patient preference was generally against haloperidol (leading many individuals to claim they were "allergic to haloperidol"), and the agent was not even approved by the US Food and Drug Administration (FDA) as a treatment for agitation. There was clearly room for additional approaches to agitation treatment.

In 2001, the first parenteral formulation of a second-generation antipsychotic (also known as atypical antipsychotics), intramuscular ziprasidone, became available as an FDA-approved specific treatment for agitation in schizophrenia and bipolar disorder (Lesem, 2001). Intramuscular olanzapine was approved in 2004 (Wagstaff, 2005), followed soon afterward by intramuscular aripiprazole in 2006 (Sanford, 2008). All three of these agents were indicated for the treatment of agitation, and offered similar or better efficacy in comparison to haloperidol, but with a more tolerable adverse effect profile (CADTH, 2015). These new options could also be used individually to replace the entire haloperidol and lorazepam combination, meaning that only one injection was necessary rather than two or three. And there was significantly less risk of oversedation, and better patient acceptance. However, despite these advantages, the injectable atypical antipsychotics were slow to gain acceptance over traditional approaches (Wilson, 2014).

The Expert Consensus Guidelines Series

Despite the increasing attention on agitation medications and the use of physical restraints, there had not been much of an attempt to establish treatment recommendations for agitation. This changed in 2001 with the publication of The Expert Consensus Guidelines Series: Treatment of Behavioral Emergences (Allen et al., 2001). An updated version of these guidelines was published in 2005 (Allen et al., 2005).

With a limited literature base and the inherent difficulties in getting informed consent with an agitated patient, the Expert Consensus articles relied not just on published data, but also on surveyed recognized clinical and academic experts in agitation to determine best practices. Furthermore, the researchers also sought to define a previously undiscussed but critical target: What are the characteristics of the ideal treatment for agitation? (Allen et al., 2001; Allen et al., 2005).

The experts agreed on several aspects of what an ideal medication for acute agitation would be (Table 1.1). The agent should be easy to administer and non-traumatic in its administration; it should provide rapid tranquilization without excessive sedation; it should have a swift onset of action and a sufficient duration of action to prevent untimely recurrence of the agitation; and it should have a low risk for significant adverse events and drug interactions (Allen et al., 2001; Allen et al., 2005). These same criteria have since become something of a gold standard in describing the ideal treatment for agitation, and these principles have been echoed in more recent guidelines research (Holloman and Zeller, 2012; Garriga et al., 2016).

Table 1.1. Characteristics of an ideal agent for treatment of agitation (Allen et al., 2001; Allen et al., 2005)

Easy to administer
Non-traumatic administration
Provide rapid tranquilization without excessive sedation
Swift onset of action
Sufficient duration of action to prevent untimely recurrence of the agitation
Low risk for significant adverse events and drug interactions

The concept of an ideal medication was no doubt a revelation for many in the clinical arena, who long had been taught that the proper approach to agitation was to sedate to unconsciousness. However, for many reasons, including efficiency of throughput and dispositions, and in the best interests of the patients, avoiding oversedation made good sense. For example, oversedated patients cannot care for their own needs or communicate with providers about pain or other symptoms. Additionally, it is not possible to interview an obtunded individual to determine the course of treatment, diagnosis, or disposition, thus delaying care and unnecessarily prolonging bed occupation in emergency settings.

Changing the philosophical approach around agitation medication also fits in well with another mindset shift in the early part of this century, and that was that clinicians should be "treating" patients rather than "chemically restraining" them.

Chemical Restraints

A frequent criticism of contemporary health care's approach to mental illness has been the excessive degree of "stigma" created around patients and their symptoms. This may often be unintentional, but is detrimental to the patients nonetheless. There is no greater example of this than the concept of "chemical restraints."

Even the terminology itself is stigmatizing. In no other medical conditions are drugs referred to as "chemicals." One would never hear of "chemically treating the diabetic" or "chemically relieving the asthmatic," but it is still possible to hear about "chemically restraining the schizophrenic." Calling psychiatric medications "chemicals" implies that they are somehow different from other drugs, perhaps insinuating that psychiatric symptoms are not genuine, or that agitation deserves punishment rather than healing.

Beyond semantics, even the definition of "chemical restraints" implies something that clinicians should not want to enact. The Joint Commission defines chemical restraint as "a drug or medication, or a combination, when it is used as a restriction to manage the patient's behavior, restrict the patient's freedom of movement, or to impair the patient's ability to appropriately interact with their surroundings – and is not standard treatment or dosage for the patient's condition" (Longtin, 2010). Other definitions refer to concepts around chemical restraint such as "staff convenience" or "discipline" – neither of which sounds like part of proper medical care. In addition, if one refers to medication use as a chemical restraint, the Joint Commission requires the same level of scrutiny, medical evaluation, and documentation as physical restraints.

Consequently, many hospitals have included in their bylaws that they *never* utilize chemical restraints in their institutions; rather, they only prescribe appropriate medications

indicated for specific clinical conditions. Indeed, moving away from the historical concept of chemical restraints and toward the understanding that medications are used to treat the condition of agitation and its underlying causes, fits in well with the evolving approach to agitation over the past two decades. Still, most clinicians did not regard agitation as much more than restraint use and medications, at least until a new universal methodology debuted in 2012.

Project BETA

Though a new philosophy of medication treatment for agitation had emerged by 2010, all other facets of agitation were approached idiosyncratically, depending on one's work site, colleagues, or geographical region. Questions such as "what constitutes medical clearance in agitation?," "when are physical restraints appropriate?," "do different diagnoses require different interventions?," and "where does de-escalation fit in?" were all likely to result in various answers, depending on whom one asked. There were no real guidelines for agitation outside of medication recommendations and restraint regulations.

To address this, in 2010, the American Association for Emergency Psychiatry spearheaded a multidisciplinary, multicenter task force of more than forty experts, charged with creating guidelines on all aspects of agitation care (Holloman and Zeller, 2012). Titled Project **BETA** (**B**est Practices in the **E**valuation and **T**reatment of **A**gitation), the eighteen-month effort divided the team into five workgroups: Medical Evaluation and Triage; Psychiatric Evaluation; De-escalation; Psychopharmacology; and Use/Avoidance of Restraints. These groups were derived from the concepts of the "Six Goals of Emergency Psychiatric Care":

(1) Exclude medical etiologies for symptoms and ensure medical stability;
(2) Rapid stabilization of the acute crisis;
(3) Avoid coercion;
(4) Treat in the least restrictive setting;
(5) Form a therapeutic alliance; and
(6) Formulate an appropriate disposition and after-care plan (Zeller, 2010).

The results were published as a six-article special section of the *Western Journal of Emergency Medicine* in 2012, and quickly became the most downloaded and most-cited articles in the history of that journal, showing just how eager emergency professionals were for solid information on agitation (Holloman and Zeller, 2012; Knox and Holloman, 2012; Nordstrom et al., 2012; Richmond et al., 2012; Stowell et al., 2012; Wilson et al., 2012). To date, the guidelines have been translated into Spanish and French and presented at conferences on four different continents. Hundreds of hospitals worldwide have adopted the guidelines, reporting dramatic improvement in reducing restraint use, lowering assaults and injuries, and improving patient satisfaction scores (Balfour, 2014; Cole, 2014).

Several of the core recommendations in Project BETA were new to many clinicians (Zeller, 2012). These included:

1) New-onset agitation should be considered of medical origin rather than psychiatric, until proven otherwise;
2) De-escalation is the center of the approach to the agitated patient, and should be ongoing during the intervention, and considered part of diagnostic and medication procedures;

3) The working diagnosis should drive the treatment strategy;
4) Patients should be involved in medication choice when possible, and this is part of helping a patient to regain control; and
5) Oral medications are preferred over parenteral, and second-generation antipsychotics are preferred over first-generation agents.

A prevailing theme in Project BETA was that de-escalation and voluntary cooperation should almost always be attempted, and that better outcomes would result from avoiding restraints and forcible medications. This seemed counterintuitive at first to many, who felt that restraining all apparently dangerous patients would mean a safer treatment unit. However, Project BETA revealed that as many as two-thirds of patient-to-staff assaults and injuries occur during the "takedown" process of containing and tackling individuals to force them into physical restraints (Holloman and Zeller, 2012). If the majority of assaults and injuries occur during the restraint process, one could postulate that avoiding the restraint process more often would result in fewer assaults and injuries – and indeed, the results of facilities that decreased restraint use have shown such better outcomes (Forster, 1999).

New Pharmacologic Routes for Agitation Treatment

With Project BETA demonstrating that individuals with agitation can often be cooperative and participate in their care, there has been a willingness to consider novel, patient-friendly treatments for the condition. Perhaps the most intriguing of these is inhaled loxapine, an FDA-approved, aerosolized antipsychotic medication that is voluntarily breathed in by the patient and reaches its maximum blood concentration in just two minutes (Zeller and Citrome, 2016). Also interesting is the use of the rapidly absorbed sublingual antipsychotic asenapine. While asenapine is not presently indicated for agitation, the literature contains reports of its efficacy (Zeller and Citrome, 2016).

International Guidelines for Agitation

The first-ever international expert consensus guidelines on agitation were published in 2016 (Garriga, 2016). Featuring the input of agitation scholars from five different continents, including Europe, Asia, Australia, and North and South America, the guidelines used a Delphi method to find consensus on general principles divined from a meta-analysis of 2,175 agitation articles. Similar to Project BETA, the experts agreed that:

1) Verbal de-escalation and calming techniques should be the first choice in agitation approach, with physical restraints only as a last option;
2) Medication for agitation should be used to calm, not oversedate;
3) Ruling out medical causes of agitation is of utmost importance; and
4) Collaborative treatments are always preferable to compulsive measures.

The Future

The overarching, indeed gratifying, theme of the advancements in agitation care over the past twenty years has been one of compassion rather than coercion. While in the past, many might have seen unpleasant treatments and heavy sedation as "deserved" by malevolent patients who needed to be restrained and sedated for the safety of those around them, today

more clinicians view agitated patients not as bad people, but good people suffering from bad symptoms. Some authorities describe agitation as similar to the "worst headache ever" for the individuals experiencing it – and as most of us can understand pain more easily than psychiatric conditions, the analogy makes us more eager to help these patients rather than fear them. Finally, outcomes for agitation will only continue to get better and better as agitation becomes more understood, clinical staff become more compassionate, and pharmacologic options continue to improve.

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Chapter 2

The Biology of Agitation

Scott A. Simpson

Agitation is a clinical phenomenon with complex pathophysiology. This chapter reviews the biological processes relevant to producing agitation among the variety of illnesses described later in this textbook. A description of the subject literature is provided, followed by greater detail on the genetics, neuroanatomy, neurotransmitters, and other chemical systems implicated in producing agitation.

Overview

Our understanding of the biology of agitation is based on a variety of studies and methodologies, each with different insights and limitations. Different studies include:

1. Observational studies of agitated patients. These studies are most applicable to clinical practice, but often focus on extremes of behavior. Agitation's similarity to other clinical presentations – including aggression, akathisia, panic, and irritability – makes case identification difficult (de Almeida et al., 2005). Because obtaining laboratory samples from agitated patients is often not possible, clinical studies rely on biomarkers retrieved after the resolution of acute agitation.
2. Studies of disease pathology. Understanding the pathology of diseases associated with agitation aids in describing biology relevant to behavioral dyscontrol. This approach has proven especially helpful for describing the neuroanatomy of agitation.
3. Drug studies and trials. Identifying effective pharmacotherapy for agitation has allowed inferences into pertinent neurotransmitter systems based on medications' mechanism of action. However, medications act on complex systems with nonspecific effects, so these studies only inform our knowledge of agitation in a more general way (de Almeida et al., 2005).
4. Animal models. Laboratory studies allow standardized examination of behavior after extensive genetic and environmental manipulation. Animal behaviors that reflect agitation include tail-rattling in mice and aggressiveness in zebrafish (Ziv et al., 2013; Takahashi, Shiroishi, and Koide, 2014; Takahashi et al., 2015). These studies are more removed from clinical practice, but allow greater precision in understanding the mechanisms of behavior change.

One significant limitation in understanding the basic science of agitation is that agitation presents so heterogeneously. Agitation reflects an acute trigger acting on some underlying diathesis in a particular environment. The presentation of agitation ranges from the purposeless hyperactivity of a delirious patient to the instrumental, predatory aggression of an antisocial person (Miczek et al., 2002). Chronic and acute risks of agitation reflect cognition, temperament, psychosis, intoxication, anxiety, choice, and executive function.

Agitation has been described as a "transnosologic" syndrome, a clinical manifestation arising from any number of underlying diagnoses (Lindenmayer, 2000). As a consequence, investigators studying agitation must choose whether to focus on the clinical syndrome (regardless of disease process) versus a diagnosis that may not generalize to other causes of agitation.

Genetics

Some chronic risks of agitation are heritable and genetic. There is an evolutionary advantage to some agitation. Aggression is observed across all animal species and increases proportionally to the aggressiveness of an intruder (Takahashi et al., 2014; Takahashi et al., 2015). Greater motor activity levels enable animals to protect home environments and offspring, and to engage in proactive coping with novel stressors (de Boer, Van der Vegt, and Koolhaas, 2003). More active animals develop routines that are less susceptible to aversive threats – a beneficial habit in some environments (Benus et al., 1991).

Most directly, the genetic risk for agitation can be conferred through highly heritable illnesses like schizophrenia or borderline personality disorder. Some single gene mutations have been associated with agitation. For example, patients with antisocial personality have been found to have a point mutation in the monoamine oxidase A (MAOA) gene that infers deficient activity of that enzyme and thus abnormal serotonin metabolism (Brunner et al., 1993). Males' recognized higher risk for aggression may reflect the homozygosity of MAOA conferred by the Y chromosome (Eme, 2010). Genome-wide association studies have identified single polymorphisms correlated with risk-taking and excitement-seeking (Terracciano et al., 2011).

But most agitation is unlikely to be explained by point mutations and single disease models. One reason for this complexity is that phenotypes reflect the interaction of a genome with the environment. Consider that the aforementioned effect of MAOA mutations on antisocial personality may be augmented by childhood exposure to maltreatment (Miczek et al., 2002; Li and Lee, 2010; Buades-Rotger and Gallardo-Pujol, 2014). Changing the parenting conditions of lab animals alters their adrenal activity and susceptibility to agitation (Li and Lee, 2010; Takahashi et al., 2015). The expression of genes may also be changed by environmental conditions: in rats, lysergic acid diethylamide changes the expression of serotonin receptors and related transcription factors (Nichols and Sanders-Bush, 2004).

Genes may even more indirectly increase the risk of agitation by their complex contributions to temperament and character. Experimental adjustment of aggressiveness affects ostensibly distinct behaviors that are necessary for building resilience and coping, such as the exploration of novel stimuli (de Boer et al., 2003). Genetic expression may be further modified by epigenetic processes like methylation, which has been recognized in modifying behavior (Kumsta et al., 2013). Ultimately, the roles of epigenetics and gene–environment interactions on the risk of agitation are incompletely understood.

Neuroanatomy

Agitation involves conscious and unconscious behaviors as well as motor hyperactivity. These three aspects of agitation are roughly associated with activity in the cortex (conscious behaviors), subcortex and limbic system (unconscious behaviors), and basal ganglia–globus pallidus–substantia nigra circuit (motor hyperactivity) in the

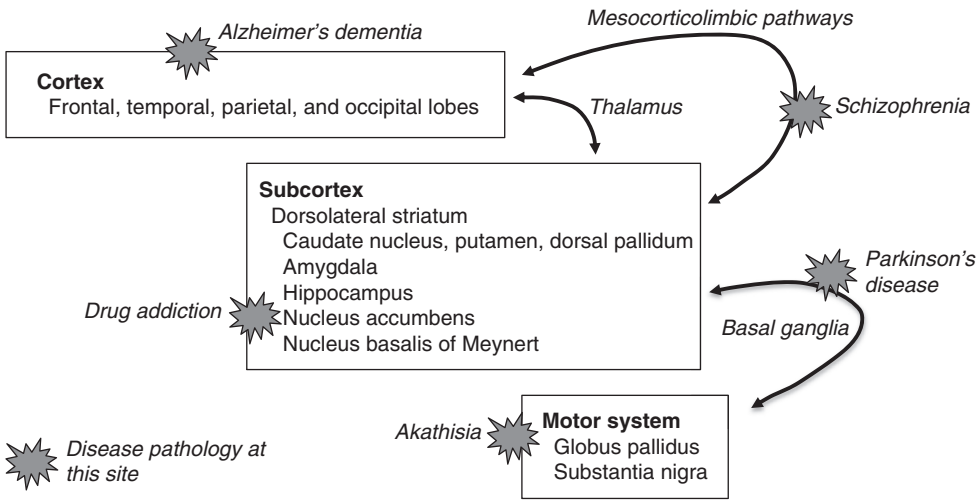

Figure 2.1. Neuroanatomical sites involved in agitation.

central nervous system (CNS). Figure 2.1 is a simplified diagram of anatomical structures relevant to agitation. Actually, these regions are structurally interconnected through numerous pathways and utilize multiple neurotransmitters that are described in greater detail later in this chapter.

The cortex is the seat of executive function, decision making, judgment, and abstraction. Aberrations in the cortex impair a person's capacity to act in a socially appropriate fashion and maintain behavioral control in otherwise benign circumstances. The famous case of Phineas Gage illustrates the behavioral changes wrought by damage to the cortex. Gage was a railroad worker whose frontal cortex was damaged by an iron rod in 1848. Subsequent to the accident, Gage suffered severe personality changes that made him "impatient of restraint or advice" (O'Driscoll and Leach, 1998). Organic processes also cause damage to the cortex, if in a less dramatic fashion. Disease severity in Alzheimer's dementia correlates with damage to the cortex (Kirby and Lawlor, 1995). As the site of more complex thought, the cortex is responsible for cognition distortions and misinterpretations. These cognitive distortions generate agitation among patients with posttraumatic stress or predatory aggression (Siegel and Victoroff, 2009; Taft, Creech, and Kachadourian, 2012). Frontal cortical serotonin transmission is a promising target for drug treatments of impulsivity (Miczek et al., 2002).

Subcortical structures, including the dorsolateral striatum, are considered the seat of mood and emotions. These structures also mediate the physical expression of purposeful movement initiated by the cortex and are associated with subconscious and automated behaviors. Subconscious impulses are those that are beyond the awareness of a person, such as the cravings a drug user experiences after exposure to certain triggers. The mesocorticolimbic system connects a variety of subcortical midbrain structures with the cortex. The hyperactivity of these pathways during agitation and periods of threat speak to the complex conscious and unconscious machinations involved in expressing agitation (Miczek et al., 2002).

Within the subcortical ventral striatum, the nucleus accumbens is associated with behavioral reinforcement, including dangerous behaviors such as substance abuse and aggression (Miczek et al., 2002). It may also be involved in more complicated emotional expressions such as grief (Bosch et al., 2016). That the nucleus accumbens is so closely integrated into pathways connecting the cortex and subcortex suggests that the nucleus may, in some instances, signal to the cortex that conscious action is necessary. In other instances, the nucleus "colors" the expression of behaviors dictated by the cortex. Substance use disorders exemplify the power of the nucleus accumbens: dopamine hyperactivity in the nucleus associates with the reinforcing effects of substance use and may overwhelm a person's better judgment. Impairment of more complex mentation in the cortex may increase susceptibility to dangerous urges prompted by the nucleus accumbens (Di Chiara et al., 2004).

Other subcortical structures have been implicated in agitation. In the medial temporal lobe, the amygdala and hippocampus are necessary for emotional recall and memory, respectively. Isolated degeneration of the amygdala has been found to cause agitation, cognitive impairment, and mood changes (Sachdev et al., 2007; Trzepacz et al., 2013). Among patients with Alzheimer's disease, damage to the amygdala and hippocampus is associated with increased aggression and agitation on standardized assessments (Shibuya-Tayoshi et al., 2005). Medications enhancing hippocampal nerve growth may be effective in the treatment of depression (Fava et al., 2015).

Agitation is defined by psychomotor hyperactivity. Hyperactivity requires action by areas of the brain necessary for producing movement. The basal ganglia, globus pallidus, and substantia nigra are structures with both direct and indirect connections to the cortex and subcortex. Being necessary for movement, these structures are implicated in the motor hyperactivity of agitation (Lindenmayer, 2000). This motor system can also contribute to agitation; Parkinson's and Huntington's diseases afflict the basal ganglia. Obsessive-compulsive disorder has been localized to the basal ganglia and its connections to the frontal lobe (DeLong and Wichmann, 2007). The effect of dopamine-blocking medications in this system cause dyskinesia and akathisia.

The close connections among these regions depend on the integrity of their constituent neurons and interneuron connections. Disease processes disrupt these connections and increase the risk of agitation. For example, the aggregation of tau protein in Alzheimer's disease impairs cortical neurotransmission, which generates behavioral disturbances (Van der Jeugd et al., 2013). In animal models, abnormal pruning of dendritic connections is associated with agitation (Kim et al., 2015). Conversely, cognitive enhancement may reflect healthy neuroplasticity, or the neuron's ability to change and generate new dendritic connections (Smith, Gibbs, and Farb, 2014). Neuroplasticity is degraded by chronic stress (Radley et al., 2011), whereas treatment trials of stroke patients suggest that serotonin reuptake inhibitors may enhance plasticity and restore motor function (Siepmann et al., 2015).

Neurotransmitters

In the body, a range of chemicals is important in the expression of agitation. Some of these agents act as neurotransmitters in communication between neurons (e.g., serotonin). Other agents alter neuronal anatomy and plasticity (e.g., pregnenolone) (Smith et al., 2014) or influence genetic expression (e.g., testosterone) (Ambar and Chiavegatto, 2009).

Table 2.1. Neurochemical system of agitation and associated diseases, medications, and drugs of abuse

Neurochemical system	Diseases causing agitation	Medications treating agitation	Drugs of abuse causing agitation
Serotonin	depression, anxiety, aggression	selective serotonin reuptake inhibitors, tricyclic antidepressants	hallucinogens
Dopamine	schizophrenia	antipsychotics	cocaine, amphetamines
GABA	alcohol intoxication	benzodiazepines, anticonvulsants	alcohol
Glutamate/ NMDA	dementia, paraneoplastic encephalitis	memantine	hallucinogens
Acetylcholine	dementia, delirium	acetylcholinesterase inhibitors	nicotine
Anandamide/ Endocannabinoid	unknown	tetrahydrocannabinol, dronabinol	marijuana
Steroid hormones	Cushing's disease, adrenal and ovarian tumors	pregnenolone	anabolic steroids

GABA-gamma-aminobutyric acid; NMDA-N-meth-D-aspartate

The activity of one agent may also affect the expression and activities of another (Liechti, 2015). Agitation may result from manipulating neurotransmission through medications or drugs of abuse. For example, amphetamines impair presynaptic dopamine reuptake and induce greater release of dopamine from the presynaptic neuron. The result – greater effective dopamine activity in the striatum – is responsible for the psychosis and agitation wrought by these drugs. Numerous pharmacologic agents have been identified that induce hyperactivity, either by direct effect or withdrawal (Sachdev and Kruk, 1996). Table 2.1 summarizes diseases, medications, and drugs of abuse by their neurotransmitter system of action.

Serotonin

Serotonin is a monoamine neurotransmitter derived from the amino acid tryptophan and produced in the raphe nuclei of the brain stem. More often associated with mood disorders, serotonin is also the foremost neurotransmitter implicated in agitation and aggression. There is a relative deficiency of CNS serotonin among aggressive animal phenotypes, violent criminals, and persons who complete suicide (Brunner et al., 1993; Maes et al., 1995; Bethea et al., 2015). Degeneration of serotonergic pathways also increases the risk of agitation among patients with Alzheimer's-type dementia (Porsteinsson, Keltz, and Smith, 2014).

In animal models, genetic manipulation of serotonin transmitters predictably modulates aggression (Miczek et al., 2002). Even ecological research correlates the seasonal variation in violent suicides with the availability of serotonin's precursor molecule (Maes et al., 1995). Perturbations in serotonin are implicated in the pathophysiology of depression, schizophrenia, dementia, Parkinson's disease, delirium, and alcohol withdrawal (Van der Mast and Fekkes, 2000). Serotonin is also necessary for more complex executive function, harm aversion, and perhaps the expression of ethical decision making in interpersonal interactions (Siegel and Crockett, 2013).

Serotonin has complex effects in the CNS. No neurotransmitter operates in isolation: serotonergic receptors also modulate dopamine transmission, and several studies suggest that serotonergic activity levels must be examined in the context of other neurotransmitters. For example, the ratio of dopamine to serotonin reuptake inhibition correlates with intoxication and addictiveness of abused drugs (Liechti, 2015). Alcohol consumption and steroid treatment affect CNS serotonergic activity (Takahashi et al., 2014). Although much agitation and aggression reflects a decrease in serotonergic activity, the opposite also occurs: excessive activity causes serotonin syndrome, hyperthermia, hyponatremia, and seizures. Whether provoked by conscious choice, unconscious impulse, or disease pathology, agitation is partly a disorder of serotonergic neurotransmission.

Dopamine

Like serotonin, dopamine is a monoamine neurotransmitter with a wide distribution in the central nervous system. Dopamine is synthesized by neurons of the central nervous system and utilized as an intercellular transmitter to G-coupled protein receptors. Dopaminergic activity in the nucleus accumbens is associated with reward salience. In connections between the cortex and subcortex, dopamine is implicated in the psychopathology of schizophrenia. Given its importance for both higher-order cognition in the cortex as well as more primitive emotional reactivity in the subcortex, dopamine is implicated in most episodes of agitation, regardless of etiology (Miczek et al., 2002). Increased dopaminergic transmission is the primary mechanism of action for many drugs of abuse, particularly cocaine and amphetamines. Medications that antagonize dopamine's G-couple receptors – especially antipsychotics – are used in the treatment of agitation.

Dopamine is present in the basal ganglia and substantia nigra and thus necessary for the production of voluntary movement. The depletion of dopamine in Parkinson's disease or the reduction of dopamine transmission by medication treatment induces muscle rigidity and dyskinesia. The resulting discomfort can contribute to agitation. Akathisia may result from dopamine antagonism in the substantia nigra (Sachdev and Kruk, 1996).

GABA

Through action on multiple receptor types, gamma-aminobutyric acid (GABA) opens chloride ion channels in the neuronal cell membrane. GABA decreases the excitability of the neuron and renders neurons less prone to "firing." GABA is found throughout the CNS, although it is particularly prominent in the subcortex. That alcohol, benzodiazepines, and barbiturates act on the GABA system speaks to the role of GABA in agitation (Miczek et al., 2002). Initially and at lower levels, increased GABA activity produces mild behavioral disinhibition and impairs higher cortical function. These lower levels may inhibit some aggression (Miczek et al., 2002), but greater levels of GABA activity cause significant

performance impairment and agitation, as exemplified by a person intoxicated on alcohol. This greater impairment reflects not only active GABA, but also GABA's effects on increasing dopamine and serotonin transmission (Miczek et al., 2002). Anticonvulsants' activation on GABA receptors may account for their benefits in decreasing agitation in dementia (Gallagher and Hermmann, 2014), although these findings have not reliably extended to other illnesses (Waters, Morrall, and Murdoch-Eaton, 2010; Hirota et al., 2014).

Glutamate

Glutamate is the primary excitatory neurotransmitter in the brain. Its role is often contrasted with that of inhibitory GABA. Although numerous glutamate transporters and receptor targets have been identified, most clinical attention focuses on the N-meth-D-aspartate (NMDA) receptor (Meldrum, 2000). Glutamate and NMDA receptors contribute to neuronal plasticity, concentration, and memory. Disturbance of the NMDA receptors by paraneoplastic autoantibodies causes anxiety, insomnia, cognitive impairment, and psychosis (Maneta and Garcia, 2014). Glutamatic innervation appears to be lost in the cortex of patients with Alzheimer's dementia (Hardy et al., 1987), and the NMDA antagonist memantine has been studied in the treatment of this disease (Herrmann et al., 2011). Activity at glutamate receptors is one mechanism of action of the novel drugs of abuse, cathinones and hallucinogens (Liechti, 2015).

Acetylcholine

In the peripheral nervous system, acetylcholine is the primary neurotransmitter at the neuromuscular junction and in the parasympathetic nervous system. Within the CNS, acetylcholine plays key roles in cognition, memory, and reward salience. The loss of cholinergic neurons in the nucleus basalis of Meynert underlies the cognitive degeneration of dementia (Bosboom, Stoffers, and Wolters, 2003). Cholinergic deficiency that results from medical conditions or medications also contributes to the development of delirium (Hshieh et al., 2008). Acetylcholine is necessary for maintaining cognition that allows patients to problem solve, tolerate distress, and consciously control agitated behaviors. Cognitive impairment may also render environmental stimuli more threatening. Preserving cholinergic tone through the use of acetylcholinesterase inhibitors is the primary pharmacotherapy for dementia.

Acetylcholine has other CNS actions that are pertinent to agitation. Subcortical stimulation of acetylcholine receptors improves anxiety and mood (Picciotto et al., 2015). Nicotine stimulates the acetylcholine system; in rats and cats, nicotine reduces aggression at low doses, but may increase it at higher doses (Picciotto et al., 2015). Intriguingly, the acetylcholinesterase inhibitor galantamine reduces methamphetamine-induced psychosis in monkeys (Andersen, Werge, and Fink-Jensen, 2007). This finding speaks to the overlap of acetylcholine with dopamine in signaling cognition, mood, reward, and movement.

Anandamide

The endocannabinoid system comprises two cannabinoid receptors and the brain's endogenous cannabinoid ligand, anandamide. This system is best known as the site of action of tetrahydrocannabinol, the active ingredient of cannabis. Cannabinoid receptors are located in the immune system and throughout the CNS with a concentration in

subcortical structures and the hypothalamus (Ramirez et al., 2005). The natural purpose of anandamide is to moderate appetite, thermal regulation, neuroinflammation, oxidative stress, and excitotoxicity (Waters et al., 2010; Liu et al., 2015). However, evidence for the therapeutic benefits of endocannabinoid agonists in ameliorating neuropsychiatric symptoms is only mixed, for example, in dementia (Van den Elsen et al., 2015). The implications of the cannabinoid system for agitation are best understood through clinical studies associating cannabis use with violence (Wilkinson, Stefanovics, and Rosenheck, 2015). This relationship may stem from greater impulsivity and cognitive impairment resulting from cannabis use. Withdrawal from cannabis may promote agitation by increasing irritability, anger, aggression, and restlessness (Haney, 2005).

Additional Neurochemical Systems

In addition to neurotransmitters, other chemical signaling systems are implicated in agitation. These systems include hormones and inflammatory markers.

Hormones

Hormones are signaling chemicals that regulate activities of other, distant cells. Some hormones are produced within the CNS (e.g., oxytocin), while others are produced outside the CNS (e.g., testosterone). Regardless of where they are produced, hormones affect the expression of mood, thoughts, and behaviors. By virtue of their complex interactions with neurotransmission, hormonal signaling systems may produce acute agitation or increase a persons' risk for developing agitation.

Steroid hormones are derived from cholesterol and produced by endocrine cells of the adrenal cortex, testes, ovaries, and placenta. Steroid hormones like testosterone, glucocorticoids, and pregnenolone affect agitation and aggression. Testosterone is commonly considered to drive aggression, although the evidence for this supposition is ambiguous. Administering testosterone to laboratory animals induces aggression and alters serotonin metabolism (Ambar and Chiavegatto, 2009), but observational studies of humans have not consistently associated higher levels of testosterone with aggression (de Boer et al., 2003). Glucocorticoids are produced in the adrenal cortex, but almost all cells contain glucocorticoid receptors. Steroid pharmacotherapy (e.g., prednisone) activates this system and may cause anxiety, mood disorders, and psychosis. Elevated glucocorticoid hormone levels also confer elevated aggressiveness in zebrafish – a perturbation correctable by administering the serotonin reuptake inhibitor fluoxetine (Ziv et al., 2013). The steroid hormone pregnenolone modulates synaptic plasticity and has been investigated as a pharmacotherapy in schizophrenia (Smith et al., 2014). Pregnenolone reverses schizophrenia-like behavior in mice with a knockout gene for the dopamine transporter (Wong et al., 2012). These experimental findings illustrate the diverse effects of hormones and their importance to neurotransmission.

Peptide hormones are built on a protein structure rather than cholesterol. Examples of peptide hormones are oxytocin and vasopressin. Oxytocin is produced in multiple endocrine organs as well as the hypothalamus. Oxytocin plays a role in helping mammals form attachments and complex social interactions (Kumsta and Heinrichs, 2013). Its expression is decreased among persons with greater stress, anxiety, or significant psychiatric morbidity (Myers et al., 2014). Mutations in the oxytocin receptor gene have been postulated to interact with environmental stressors to increase an individual's risk for mood disorders (Myers et al., 2014). Another peptide hormone, vasopressin, is critical for osmotic regulation as well as

social communication and interpersonal functioning (de Wied, Diamant, and Fodor, 1993). No clinical studies have studied the direct effect of peptide hormones on agitation.

Inflammatory Markers

Hyperinflammatory states exist in multiple psychiatric conditions, including schizophrenia and depression (Kiecolt-Glaser, Derry, and Fagundes, 2015; Volk et al., 2015). Similarly, agitation and aggression correlate with elevated levels of circulating cytokines and interleukins. These relationships may be more than correlative: in experimental models, the injection of interleukins into mammals' CNS can provoke and potentiate aggressive behavior (Zalcman and Siegal, 2006). In observational studies, infection with the parasite *Toxoplasma gondii* has been associated with suicidal behaviors (Zhang et al., 2012). Available evidence suggests that inflammation among patients with agitation is likely, but the significance of this connection remains unclear. Inflammatory states may drive psychiatric illness. Or it may be that inflammation results from glucocorticoid dysregulation, sleep changes, or alterations in the body's natural biome.

Agitation: More than a Sum of Parts

A range of anatomic pathways, genotypes, neurotransmitter systems, and inflammatory states is associated with agitation. How all these systems fit together remains somewhat mysterious. In practice, a patient who is agitated demands acute management, and underlying risk factors often remain elusive to the clinician. It is challenging to study, in vivo, neurotransmitters as they act in complex feedback loops across numerous anatomic pathways. Moreover, some factors that play a role in agitation, like interpersonal trust and social decision making, are difficult to describe biologically.

Agitation is not easily dissembled into a series of biological processes. Nonetheless, although every episode of agitation is unique, commonalities exist to form a basis for assessment and treatment.

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Chapter 3

Medical Evaluation of the Agitated Patient

Seth Thomas and Nathan Beckerman

Introduction

The presentation of agitated patients to a medical facility such as an emergency department (ED) can be a very frequent occurrence. The clinician's mental and physical preparation to evaluate the agitated patient is of the utmost importance, to ensure safe and rapid identification and stabilization of emergent medical conditions, as well as exclusion of any medical causes for the patient's presentation.

To complicate matters, the signs and symptoms of agitation in the emergency department setting may be the manifestation of a long list of complex etiologies, often with multiple contributing comorbid conditions. Some of these can lead to death or permanent disability if not identified and treated. This chapter will provide an organizational framework to assist in the medical evaluation of the agitated patient to accomplish the aforementioned goals in an expedited, efficient, and safe manner.

Initial Evaluation

During the initial evaluation of the acutely agitated patient, the clinician must balance and maintain three priorities: safety of the patient and staff, immediate identification or exclusion of life-threatening conditions, and consideration of a broad differential diagnosis to identify or exclude other common etiologies. Safety of the patient and staff is by far the most important consideration and should always be the first priority. Depending on the patient's level of agitation and the level of threat he or she poses, the clinician should tailor his or her approach to suit the patient's needs and circumstances. For instance, while a cooperative patient with minimal levels of agitation may be able to be interviewed and examined in a regular ED triage area, a severely agitated and imminently violent patient should be safely moved to a room devoid of other stimuli or potential weapons. Despite tailoring one's approach to the initial evaluation, it is important to remember that any patient, regardless of initial degree of agitation, is at risk for escalation and violence under the right circumstances. For this reason, we recommend that the clinician and all staff are familiar with signs of impending violence and initiate appropriate safeguards to reasonably prevent escalation. Signs of impending violence may include (Rice & Moore, 1991):

- Provocative behavior
- Angry demeanor
- Loud, aggressive speech
- Tense posturing (e.g., gripping arm rails tightly, clenching fists)
- Pacing or frequently changing body position
- Aggressive acts (e.g., pounding walls, throwing objects, hitting oneself)

Universal safeguard measures for the initial evaluation include:

- Routine, non-confrontational, and nondiscriminatory search and disarming of patients (ACEP, 1997)
- Interviewing in a calm, quiet, private, but non-isolated setting (Rice & Moore, 1991; Tardiff, 1992)
- Environment free of objects that could be used as weapons (Rice & Moore, 1991; Kuhn, 1999)

Once the appropriate accommodations have been made to provide the ideal assessment environment, and all safety measures have been implemented, the patient should undergo an initial evaluation common to all ED patients. The purpose of the medical evaluation is to exclude a medical etiology of the patient's symptoms or so-called medical mimics of psychiatric disease and to ensure medical stability by detecting and treating other significant illnesses or injuries (Lukens et al., 2006; Tolia & Wilson, 2013).

Long understood to be the cornerstone of a comprehensive medical evaluation, the history and physical examination (H&P) hold clues in the form of signs and symptoms that may either outright solve the medical mystery or at least direct the approach to advanced diagnostic testing. When presented with an acutely agitated patient, it may be easy for the clinician relying on pattern recognition or algorithmic thinking to prematurely attribute the agitation to psychiatric causes (anchoring bias) and potentially miss or ignore (confirmation bias) other significant findings that could indicate life-threatening illnesses or injuries (Sandu & Carpenter, 2006). Performing a comprehensive H&P on every patient forces the clinician to evaluate each patient as an individual, thereby helping to minimize the introduction of bias into clinical decision making.

Obtaining a thorough history is an exceptionally important component of the initial evaluation. Depending on the degree of the patient's agitation and his or her ability to cooperate, the history of present illness (HPI) often holds the greatest potential to provide meaningful clues to the clinician regarding the etiology of a patient's symptoms. Cooperative patients with mild levels of agitation often can provide detailed descriptions of the circumstances of their presentation, including triggers and necessary interventions. On the other hand, uncooperative or severely agitated patients may offer little to no useful information and will require reliance on other resources such as friends or family members, law enforcement officers, social workers, or emergency medical services (EMS) personnel. Regardless of the state of a patient's agitation or the circumstances of presentation, obtaining and documenting collateral information is very important and can reveal critical information such as the timing and nature of the patient's decompensation, concomitant substance abuse, medication changes, history of noncompliance, and contributing medical conditions.

While the HPI holds invaluable information, the initial evaluation is considered incomplete until the clinician has performed a thorough physical examination. At a minimum, each patient must have a complete set of vital signs obtained, including temperature, blood pressure, heart rate, respiratory rate, and blood oxygen saturation while breathing room air. The astute clinician should be able to identify vital sign abnormalities that hold clues to a medical etiology for their presentation. For instance, although one would expect a moderately agitated patient to have modest elevations in blood pressure or heart rate, patients with agitation who have fever (>38°C), hypoxia, or hypotension must be presumed to have a potentially life-threatening etiology of their agitation until proven otherwise.

Although not routinely obtained on every patient with a behavioral health complaint presenting to the ED, screenings for hypoglycemia with a quick and inexpensive point-of-care (POCT) blood glucose test, also referred to as fingerstick blood glucose (FSBG), are warranted for patients with agitation. Significant abnormalities in any of these vital signs or evidence of hypoglycemia (<70 mg/dL) should serve as an indicator of a potentially serious underlying cause of their agitation and merit further investigation.

In addition to the complete set of vital signs and screening FSBG, each patient must receive a complete head-to-toe physical examination from the clinician. Labored breathing with rales may indicate an underlying pneumonia or diabetic ketoacidosis (DKA) while ocular nystagmus may suggest alcohol or drug intoxication or a central nervous system lesion.

Differential Diagnosis of Acute Agitation

Patients exhibiting acute agitation may present anywhere along the behavioral spectrum from non-agitated (normal level of activity) to severe or extremely agitated posing an immediate danger to themselves or others. It is important to recognize that a patient's level of agitation is often dynamic, responding both to intervention (de-escalation or medications) and outside stimulation or perceived threats. Recognizing, predicting, and counteracting any rapid escalations in a patient's level of agitation is a necessary quality of the clinician.

The differential diagnosis of the undifferentiated patient with agitation is broad. Although in an emergency department setting, drug and alcohol intoxication or withdrawal are the most common causes of agitation in combative patients, one must be cautious not to fall victim to affective or cognitive bias and neglect to consider other significant causes (Lavoie, 1993; Dubin & Weiss, 1997). Mnemonics have been developed to assist in the generation of appropriate differentials but, like other mnemonics, their utility is of questionable value during active evaluation of patients. Before assuming that a patient's agitation is a manifestation of a psychiatric disorder, it is important that potentially life-threatening and common organic etiologies are excluded by some combination of thorough history, physical examination, and laboratory evaluation when indicated.

The following categories summarize many of the common and potentially life-threatening etiologies of the acutely agitated patient (Moore & Pfaff, 2015):

- Toxicological
  - Alcohol intoxication or withdrawal
  - Stimulant intoxication
  - Other drugs or drug reactions
- Metabolic
  - Hypoglycemia
  - Hyperglycemia/diabetic ketoacidosis
  - Hypoxia
  - Hyper/hyponatremia
- Neurologic
  - Stroke
  - Intracranial lesion (e.g., hemorrhage, tumor)
  - CNS infection

  - Seizure
  - Dementia
- Other medical conditions
  - Hyperthyroidism/thyroid storm
  - Shock
  - AIDS
  - Hypothermia or hyperthermia
- Psychiatric
  - Psychosis
  - Schizophrenia
  - Paranoid delusions
  - Personality disorder
- Antisocial behavior

Delirium

Due to the difficulty examining acutely agitated patients, even the most experienced clinician may not identify significant findings on history and physical (H&P) in patients with acute agitation. For this reason, the authors advocate selective diagnostic testing of patients with new onset psychiatric symptoms or agitation. The primary goal of further diagnostics in these patients is to exclude acute delirium, which often masquerades as psychiatric illness.

Delirium, defined as a transient, usually reversible cause of cerebral dysfunction resulting in a state of confusion or disturbance of consciousness, is not a specific diagnosis, but rather a constellation of symptoms common to patients suffering from potentially emergent medical conditions that require prompt diagnosis and intervention (Brown & Boyle, 2002; Alagiakrishnan, 2015). Characteristically, the delirious state includes disturbance in attention and memory impairment. The attention disturbance is evident on exam by easy distractibility or a reduced ability to focus and sustain or shift attention appropriately. This results in a difficulty following commands and/or maintaining conversations to the point of the patient's speech being incoherent. Memory impairment usually involves recent memory; patients are often disoriented to time or place but rarely to person. Excluding delirium as a primary cause of a patient's agitation may be as straightforward as identifying and correcting acute hypoglycemia or as complicated as excluding any number of acute medical problems outlined in the section on differential diagnosis of acute agitation.

Special mention should be made of the entity of "excited delirium" (EXD). First mentioned in the modern literature in 1985, excited delirium has been commonly associated with deaths of severely agitated individuals in the custody of law enforcement. However, one study found that this is the circumstance less often than initially believed. What is known about excited delirium is that it is a particularly dangerous condition for both patient and medical staff, presenting with bizarre, violent, and/or aggressive behavior; paranoia; panic; unexpected strength sometimes described as superhuman; and hyperthermia. The most commonly identified precipitant of EXD is stimulant drug use, with cocaine by far the most common agent, though methamphetamine, PCP, and LSD have also been

reported. Much less commonly, EXD may also be brought on by primary psychiatric or systemic illness (Takeuchi, Ahern, & Henderson, 2011), again reinforcing the need for appropriate medical evaluation to exclude underlying medical problems, either as causes or results of the patient's agitated state. When present, EXD requires prompt recognition and early intervention by the clinician to stabilize the condition.

Diagnostic Evaluation of Psychiatric Patients

The utility of diagnostic testing such as laboratory tests and radiologic imaging for the evaluation of psychiatric patients has been a topic of debate in the medical literature for several decades. Dating as far back as 1977, authors such as Willett and King documented their experience in instituting routine screening of psychiatric patients with a standard set of laboratory tests, only to conclude that "routine blood and urine screening tests add very little to the care of psychiatric inpatients" (Willett & King, 1977). Yet, to this day, depending on variables such as local styles of practice, standards of care, postgraduate training, patient populations, and inpatient psychiatric acceptance criteria, in many settings, routine testing of psychiatric patients to provide "medical clearance" still occurs with surprising frequency. In many facilities and regions, the prevailing practice is to obtain a standardized laboratory panel, including a CBC, comprehensive metabolic panel (CMP), and acetaminophen, salicylate, and ethanol levels, as well as a urine drug screen (UDS). Women of childbearing age are often screened for pregnancy with a qualitative beta-hCG. Not only is this non-selective method time-consuming and costly, the results rarely, if ever, provide clinically relevant information (Sheline & Kehr, 1990; Feldman & Chen, 2011).

In 2006, the American College of Emergency Physicians issued a clinical policy that addressed the ambiguity of the term "medical clearance" and answered critical questions with regard to the utility of routine laboratory testing on psychiatric patients. According to the writing committee, the term "focused medical assessment," defined as a process in which a medical etiology for the patient's symptoms is excluded and other illness and/or injury in need of acute care is detected and treated, is a more appropriate description (Lukens et al., 2006). Today significant support exists in both the emergency medicine and psychiatry literature that any diagnostic evaluation of the undifferentiated psychiatric patient should be driven by the findings obtained from a thorough history and physical examination and that routine diagnostic testing of patients is of relatively low yield (Gregory, Nihalani, & Rodriguez, 2004; Lukens et al., 2006). In other words, examine thoroughly and test selectively (Gregory et al., 2004; Tolia & Wilson, 2013). The same is true of the acutely agitated patient – any diagnostic evaluation of the acutely agitated patient should be driven by the findings obtained during the initial evaluation. That said, as the degree of agitation increases or as the age of the patient approaches extremes, the history and physical examination become more limited in their ability to provide robust, reliable information. Therefore, in these patients and in those presenting with a suspected new-onset psychiatric condition, the clinician should lower the threshold for ordering diagnostic tests. One should remember, however, that regardless of the level of agitation, a laboratory or other diagnostic evaluation cannot replace a thorough physical exam and without one, the patient's assessment is incomplete.

Standardized screening protocols to help guide the focused medical assessment have been developed and implemented in some settings and have great potential to safely

expedite the screening of patients while improving efficiency in a resource-conscious way. These protocols are designed to identify signs, symptoms, or high-risk features with a higher likelihood of clinical significance when evaluating patients presenting to an ED with agitation or other psychiatric symptoms. The protocols obligate clinicians to perform a thorough history and physical exam and allow them to identify low-risk patients who require little to no further diagnostic testing before being evaluated by a behavioral health specialist. Although local and regional differences may exist due to diversity in patient populations, diagnostic abilities of psychiatric facilities, and the level of trust between ED physicians and psychiatrists, many of these protocols share common foundational elements in the form of questions designed as an algorithm. One such algorithm Zun and colleagues developed in their work with the Illinois Mental Health Task Force used five fundamental binary questions (Zun & Downey, 2007):

- Does the patient have any new psychiatric condition?
- Does the patient have any history of active illness needing evaluation?
- Does the patient have any abnormal vital signs?
- Does the patient have an abnormal physical exam (unclothed)?
- Does the patient have any abnormal mental status?

Dr. Seth Thomas in collaboration with many emergency medicine and psychiatry colleagues developed a similar evaluation through their work with the Sierra-Sacramento Valley Medical Society in 2015. The algorithm, referred to as the SMART Medical Clearance Protocol (SMART), shares many similarities to other protocols yet is customized to address the local variation in practice and patient populations (Figure 3.1).

SMART adds specificity to some disease processes and includes a section to address the need to obtain therapeutic levels of certain medications prior to transfer. Sections such as these may vary considerably with respect to the needs, abilities, and comfort level of practice locations. Preliminary adaptation of SMART has revealed promising results, including a very low miss rate and the potential for substantial cost savings by avoiding unnecessary diagnostic testing.

Agitated Elderly Patients: Special Considerations

Acutely agitated elderly patients represent a special challenge to the clinician, and a rapidly growing problem. With the number of people in the United States expected to double between 2006 and 2036, the number of these individuals visiting the emergency department for complaints of acute agitation or other mental status change can only be expected to increase as well. While agitation in young patients is much more likely to be due to primary psychiatric illness or substance abuse, acute agitation in older adults must be presumed to be a manifestation of acute delirium until proven otherwise (Nassisi et al., 2006). In fact, in 2013, one study reported a prevalence of delirium in 1.5 million elderly ED patients annually (Han, Wilson, & Vasilevskis, 2013).

Recently, a two-step approach to screening for acute delirium in elderly patients has been proposed, and shows promise. This consists of the Delirium Triage Screen (DTS) (Figure 3.2), designed as a highly sensitive rule-out test, and the Brief Confusion Assessment Method (bCAM) (http://eddelirium.org/delirium-assessment/bcam/), designed as a highly specific rule-in test (Han et al., 2013). Performed first, if the DTS was negative, delirium was ruled out. If the DTS was positive, the bCAM then ruled in the presence of delirium. Both

SMART Medical Clearance Form	No*	Yes	Time Resolved
Suspect New Onset Psychiatric Condition?	1		
Medical Conditions that Require Screening?	2		
Diabetes (FSBS less than 60 or greater than 250)			
Possibility of pregnancy (age 12–50)			
Other complaints that require screening			
Abnormal:	3		
Vital Signs?			
Temp: greater than 38.0°C (100.4°F)			
HR: less than 50 or greater than 110			
BP: less than 100 systolic or greater than 180/110 (2 consecutive readings 15 min apart)			
RR: less than 8 or greater than 22			
O_2 Sat: less than 95% on room air			
Mental Status?			
Cannot answer name, month/year and location (minimum A/O x 3)			
If clinically intoxicated, HII score 4 or more? (next page)			
Physical Exam (unclothed)?			
Risky Presentation?	4		
Age less than 12 or greater than 55			
Possibility of ingestion (screen all suicidal patients)			
Eating disorders			
Potential for alcohol withdrawal (daily use equal to or greater than 2 weeks)			
Ill-appearing, significant injury, prolonged struggle or "found down"			
Therapeutic Levels Needed?	5		
Phenytoin			
Valproic acid			
Lithium			
Digoxin			
Warfarin (INR)			

*** If ALL five SMART categories are checked "NO" then the patient is considered medically cleared and no testing is indicated. If ANY category is checked "YES" then appropriate testing and/or documentation of rationale must be reflected in the medical record and time resolved must be documented above.**

Date: _____ **Time:** _____ **Completed by:** _____ _____, MD/DO
Signature Print

SSVMS
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Figure 3.1. SMART Medical Clearance Protocol.

use the Richmond Agitation-Sedation Scale (RASS), which ranges from −5 (coma) to +4 (combative), with 0 representing a normal level of consciousness (Table 3.1) (Sessler, Grap, & Broph, 2001; Sessler et al., 2002; Ely et al., 2003). Each then incorporates testing for inattention with various cognitive exercises. The bCAM goes on to assess for disorganized thinking to confirm the presence of delirium. Combined, this approach was moderately

Table 3.1. Richmond Agitation-Sedation Scale

Points	Criteria	Definition
+4	Combative	Overtly combative, violent, immediate danger to staff
+3	Very Agitated	Pulls or removes tube(s) or catheter(s); aggressive
+2	Agitated	Frequent non-purposeful movement, fights ventilator
+1	Restless	Anxious but movements not aggressive vigorous
0	Alert and Calm	
−1	Drowsy	Not fully alert, but has sustained awakening (eye-opening/eye contact) to voice (>10 seconds)
−2	Light Sedation	Briefly awakens with eye contact to voice (<10 seconds)
−3	Moderate Sedation	Movement or eye opening to voice (but no eye contact)
−4	Deep Sedation	No response to voice, but movement or eye opening to physical stimulation
−5	Unarousable	No response to voice or physical stimulation

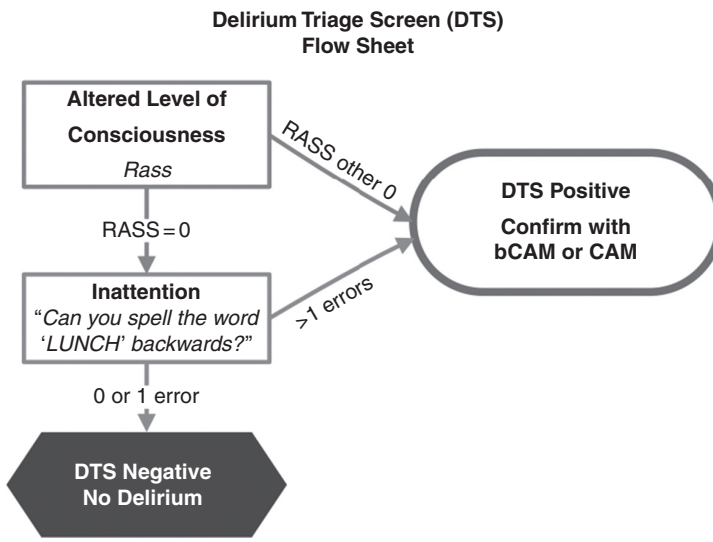

Figure 3.2. Delirium Triage Screen (DTS). Copyright © 2012 Vanderbilt University. Reproduced with permission.

sensitive (82%) and quite specific (96%) in diagnosing or excluding delirium using a psychiatrist's assessment as the reference (Han et al., 2013).

Agitation in elderly patients may be further complicated by the presence of dementia, particularly if not yet formally diagnosed. On initial evaluation, it may be unclear whether a patient's confused state is acute or chronic. Behavioral disturbances, including agitation, are common among patients with dementia and may include aggression, combativeness, hallucinations, or delusions. Acutely, it may be impossible to reliably distinguish between delirium and dementia. For this reason, an acute medical etiology, including pain or infection, must be sought in any agitated elderly patient.

Agitated elderly patients in many cases may constitute an exception to the doctrine of "examine thoroughly and test selectively." While the "examine thoroughly" maxim certainly still applies, the clinician must consider an expanded diagnostic evaluation. Occult infections, particularly urinary tract infections, are common. For this reason, complete blood count, urinalysis, and chest x-ray are all indicated. Chronic metabolic diseases, including renal and hepatic insufficiency, are also more prevalent, necessitating a search for any acute worsening via chemistry panel and liver function testing, including serum ammonia level. Older adults are also not immune from substance abuse, and toxicology studies should also be obtained, including alcohol, acetaminophen, and salicylate levels. UDS should be considered. If this expanded initial evaluation fails to reveal a cause for the patient's acute presentation, depending on the scenario, thyroid function studies, neuroimaging, and even lumbar puncture to rule out meningitis or encephalitis may need to be considered (Nassisi et al., 2006).

One final consideration in elderly patients actually falls under the "examine thoroughly" maxim. This is an examination of the patient's list of medications. Elderly patients may be prescribed any combination of several classes of medications that, even at therapeutic doses, can cause acute agitation or delirium, or may indicate the presence of underlying neurologic disease, including dementia. These include corticosteroids, anticholinergics, antihistamines, antidepressants, sedatives (i.e., zolpidem or benzodiazepines, which can cause paradoxical agitation), and acetylcholinesterase inhibitors (i.e., donepezil for Alzheimer's dementia), among others. If an acute medical cause is discovered, or a drug side effect is suspected, the patient may ultimately require acute medical admission for treatment or medication management. For further information on evaluation and treatment of agitation for the geriatric patient, please see Chapter 6 of this volume.

Pitfalls in the Medical Evaluation of Agitation

- Neglecting to perform a thorough history and physical examination
- Assuming a patient's agitation is a symptom of substance abuse or psychiatric disorder, especially in elderly patients
- Failing to diagnose and treat an underlying cause of delirium
- Indiscriminately ordering comprehensive diagnostic screening tests on every patient

Conclusions

The medical evaluation of agitated patients can be a challenging endeavor. Not only is the clinician faced with excluding a wide range of medical etiologies of the patient's symptoms, but also he or she must do so in a safe and methodical fashion so as to not

miss clues to a potentially life-threatening underlying condition. Performing a thorough H&P, including a neurologic examination and cognitive evaluation, is an absolute necessity and the cornerstone of the focused medical assessment. The differential diagnosis of agitation is also broad, and clinicians may be prone to affective and cognitive biases requiring dedication to maintaining a broad differential diagnosis. Characteristics of unique populations, particularly the elderly, must also be considered in the approach to evaluation. Clinicians adhering to practicing in this manner will be able to safely utilize selective diagnostic testing to supplement their evaluation, thereby reducing cost and improving efficiency.

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Chapter 4

Agitation Due to Substance Use, Abuse, and Withdrawal

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Agitation, excessive motor activity associated with a feeling of inner tension (American Psychiatric Association 2013), is a frequent behavioral pattern observed in substance users. It can be part of an intoxication and withdrawal scenario, and might persist in substance-related neurodegenerative conditions, such as Wernicke-Korsakoff syndrome. As treatment differs with the underlying condition, an accurate diagnosis is essential for a targeted pharmacological treatment.

The Extent of Addiction-Related Health Problems

The Frequency of Substance Use and Abuse

According to the World Health Organization (WHO), the extent of worldwide psychoactive substance use is estimated at 2 billion alcohol users, 1.3 billion smokers, and 185 million illicit drug users. In an initial estimate of factors responsible for the global burden of disease, tobacco, alcohol, and illicit drugs contributed together 12.4 percent of all deaths worldwide in the year 2000. Looking at the percentage of total years of life lost due to these substances, it has been estimated that they account for 8.9 percent (World Health Organization 2015). Abuse of drugs, including alcohol and tobacco, is the number one cause of preventable illness and death in the United States. Each year, more than 500,000 deaths in the United States are attributable to abuse of alcohol, tobacco, or other drugs (Health Science Centre 2014).

Adolescents and Young Adults

Persons between eighteen and twenty-five years of age are the most likely to use illicit drugs. The age at onset of alcohol and illicit drug use is a powerful predictor of lasting alcohol and drug problems, especially if use starts before age fifteen. According to the National Household Survey on Drug Abuse (U.S. Department of Health and Human Services 2013), teenagers most frequently use alcohol, tobacco, and marijuana. The incidence of binge drinking – defined as having five or more drinks on the same occasion on at least one day in the past thirty days – is 9 percent for persons twelve to seventeen and 42 percent for persons eighteen to twenty-five. The incidence of heavy alcohol use – defined as drinking five or more drinks on the same occasion on each of five or more days in the past thirty days – is 2.4 percent for persons twelve to seventeen and 15 percent for persons eighteen to twenty-five years of age. In 2005, 20 percent of fifteen-year-olds and 40 percent of eighteen-year-olds reported that they have used marijuana. Typically, adolescents whose drug involvement progresses to illicit substances start with commercially available drugs such as alcohol and tobacco, then progress to marijuana and finally other drugs or combinations

of drugs (polytoxicomania). For this reason, cigarettes, alcohol, and marijuana are sometimes called "gateway" drugs.

The Elderly

Aging often goes along with chronic, painful physical disorders that may be treated with painkillers that have the potential for abuse. Vulnerability to addiction may be increased by feelings of anger, depression, and anxiety, leading to tranquilizer use. Alcoholism in the elderly remains an underreported disorder. Besides over-the-counter medication, such as vitamins or food supplements, the elderly often take a fair amount of prescription drugs and commonly use several prescriptions and over-the-counter medications concomitantly that, in combination, may induce states of agitation, for example, a serotonergic syndrome or an anticholinergic delirium.

The Frequency of Admissions for Withdrawal Syndromes and Delirium

An estimated 50 percent of people who fulfill criteria for alcohol addiction will experience withdrawal symptoms if they stop drinking. Of those people, 3 percent to 5 percent will experience alcohol withdrawal delirium (delirium tremens) (Badi and Boskey 2012). Furthermore, up to one-third of people experiencing significant alcohol withdrawal may experience an withdrawal seizure (Hughes 2009).

The Frequency of Alcohol-Related Dementias (ARD)

The lifetime prevalence rate of Wernicke-Korsakoff syndrome (WKS) has been estimated between 0 percent and 2 percent in the general population, but appears on the rise over recent decades. Besides genetic vulnerability, thiamine deficiency may play a crucial role in developing WKS. Chances to develop WKS are fifteen-fold higher in subjects with alcohol use disorder compared to the general population. However, there is no linear relationship between alcohol consumption and manifestation of WKS. For example, in France, a country well known for its consumption and production of wine, prevalence of WKS was only 0.4 percent in 1994, while Australia had a prevalence rate of 2.8 percent. Specific sub-populations seem to have even higher prevalence rates, including people who are homeless, older individuals (especially those living alone or in isolation), and psychiatric inpatients (Harper et al. 1995).

Extent of Agitation as a Problematic Behavior

The Frequency of Agitated Behavior in Psychiatric and AE Settings

Agitation is a symptom of several psychiatric conditions, including schizophrenia, bipolar disorder, personality disorders, general anxiety disorder, panic disorder, and major depression (Nordstrom and Allen 2007). For example, 14 percent of hospitalized patients with schizophrenia show agitation and violent behavior on admission (Soyka 2002). As many as 1.7 million emergency department visits in the United States per year may involve agitated psychiatric patients (Allen and Currier 2004).

Agitation may also occur in several somatic conditions, for example, neurological disorders such as Parkinson's disease, Alzheimer's disease, and other types of dementia (Lesser and Hughes 2006), in a wide range of general medical conditions (e.g., thyrotoxicosis, hypoglycemia, encephalitis, meningitis), and in those with brain traumas (Battaglia 2005; Singh et al. 2014).

A prospective study in a medical-surgical intensive care unit (ICU) setting showed that agitation developed in 52 percent of patients. Both psychoactive substance use and medical conditions contributed. Stepwise logistic regression revealed as significant independent risks factors for development of agitation psychoactive drug use at the time of ICU admission (odds ratio, 5.63) history of alcohol abuse (odds ratio, 3.32), dysnatremia (odds ratio, 4.95), fever (odds ratio, 4.52), use of sedatives in the ICU (odds ratio, 4.03), and sepsis (odds ratio, 2.61) (Jaber et al. 2005).

The Frequency of Agitated Behavior in Substance User/Abuser

Agitation represents a quite common feature of substance use and/or intoxication (Citrome 2004; Battaglia 2005). Estimates for the overall prevalence of agitation in individuals with alcoholism are 25 percent, and 35 percent for illicit substance use (Swanson et al. 1990). For comparison, the same study reported figures for agitation in schizophrenia or mood disorders of 11–13 percent. Of note, impulsive and aggressive behavior is not only an issue with respect to harm to others, but is also a predictor of suicide attempts in alcohol abuse patients (Koller et al. 2002).

The Frequency of Agitated Behavior during Substance Withdrawal

Withdrawal is a substance-specific, substance-induced disorder that follows the cessation of use or reduction in intake of a psychoactive substance that had been regularly used to induce an altered level of consciousness or mental state. Agitation is a leading symptom of withdrawal for almost all psychoactive substances with the capability of addiction, and there is hardly any patient not showing some signs of increased excitability. However, milder forms of agitation may also frequently occur as part of a discontinuation syndrome with the cessation of commonly prescribed psychiatric medication, especially some antidepressants, or some analgesics.

The Frequency of Agitated Behavior in Delirium and ARD

Similar to withdrawal, psychomotor agitation, hyperarousal, and hyper-excitability are almost compulsory in delirious subjects, together with confusion and impairment of consciousness. Agitated, aggressive behavior in the context of an Excited Delirium Syndrome (ExDS) often also has severe legal implications. In a Canadian prospective study, more than 80 percent of subjects where use of force was inevitable showed effects of emotional disturbance, drugs, alcohol, or a combination of these at the scene at the time of the police operation, and two-thirds were violent. Of these subjects, 16.5 percent were classified as having at least three predefined signs of ExDS (Hall et al. 2013). If the cognitive features of delirium persist and evolve into substance-related dementia, such as Korsakoff's syndrome, the rate of agitation may decrease, but remains frequent (25% to 40% of subjects).

Signs and Symptoms of Intoxication, Withdrawal, Delirium, and ARD

Intoxication

Intoxication is a reversible, substance-specific syndrome following the acute exposure to a substance of abuse. The significant changes associated with intoxication are due to the

direct physiological effects of the substance on the brain, and commonly include disturbances of perception, thinking, judgment, and psychomotor and social behavior. Symptoms of intoxication can be physical, such as slurred speech when intoxicated with alcohol, or psychological, such as feeling relaxed when intoxicated with cannabis. Being intoxicated does not regularly imply that a person has a substance use disorder. Nor does it regularly imply that the subject presents with agitation; there is a wide individual variance of the effects of a psychotropic substance ranging from excitement to somnolence.

Alcohol Intoxication

Symptoms of alcohol intoxication may include euphoria, flushed skin, and decreased social inhibition at lower doses, with larger doses producing progressively severe impairments of balance, muscle coordination (ataxia), and decision-making ability (potentially leading to violent or erratic behavior), as well as nausea or vomiting. Excessive blood levels of alcohol (more than 300 mg/dL) are likely to cause coma and death from the depressant effects of alcohol on vital structures of the brain; however, tolerance might be higher in subjects regularly consuming large amounts of alcohol (Adinoff, Bone, and Linnoila 1988). Thus, ethanol's acute effects are dependent on blood alcohol concentrations and tolerance; in lower concentrations it may lead to excitation (and agitation), with higher concentrations, however, CNS-depressant effects prevail.

Pathological Alcohol Intoxication

Pathological alcohol intoxication refers to a syndrome characterized by agitation and aggressiveness that already occurs with low alcohol blood concentrations that do not lead to signs of intoxication in an average person. It may go along with other symptoms such as confusion, delusions, and hallucinatory phenomena, and is more likely to occur in the presence of additional somatic stressors or disorders (fatigue, infectious diseases, atherosclerosis, etc.). After recovery, subjects often report amnesia for the episode.

Opioid Intoxication

Opiate overdose symptoms and signs can be referred to as the "Opioid Overdose Triad": decreased level of consciousness, pinpoint pupils, and respiratory depression that might lead to death (Debono, Hoeksema, and Hobbs 2013). Other symptoms include seizures and muscle spasms. Agitation is not a frequent feature of opioid intoxication.

Cannabinoid Intoxication

Tetrahydrocannabinol (THC), is the main psychotropic compound among approximately 400 different cannabinoids in the natural plant. Acute effects while under the influence include euphoria and anxiety (Osborne and Fogel 2008), restlessness, enhanced alertness, confusion, paranoia, and hallucinations that may cause agitation and violent episodes.

Stimulants

Stimulants may also cause a variety of adverse symptoms. Stimulants are psychoactive drugs that induce transient improvements in either mental or physical functions or both. The most common examples of stimulants are cocaine and methamphetamine.

Abuse of central nervous system (CNS) stimulants is common. Addiction to some CNS stimulants can quickly lead to medical, psychiatric, and psychosocial decline. Common effects of stimulants may include increased alertness, awareness, wakefulness, endurance, productivity, motivation, arousal, locomotion, heart rate, blood pressure, and a diminished desire for food and sleep. Use of stimulants may cause a decline of hormones and/or neurotransmitters that physiologically fulfill similar functions.

Once the effect of the stimulant has worn off, the user may feel depressed, lethargic, confused, and miserable. Users describe it as a "crash," resulting in continuous use of the stimulant. This pattern appears especially pronounced with cocaine. Cocaine increases alertness, feelings of well-being and euphoria, energy and motor activity, feelings of competence, and sexual desire. Common side effects include anxiety, increased temperature, paranoia, restlessness, and teeth grinding. With prolonged use, often accompanied by lack of sleep, the drug can cause itching, tachycardia, hallucinations, and paranoid delusions. Possible lethal side effects include rapid heartbeat, tremors, convulsions, markedly increased core temperature, heart attack, stroke, and heart failure.

Other Drugs of Abuse

Signs and symptoms of a drug overdose may vary depending on the drug or toxin used. The symptoms can often be divided into differing toxidromes. A toxidrome is a syndrome caused by a dangerous level of toxins in the body (Mofenson and Greensher 1970). It is often the consequence of a drug overdose. Common symptoms include dizziness, disorientation, nausea, vomiting, and oscillopsia. A toxidrome may constitute a medical emergency requiring treatment with support of a poison control center. Aside from poisoning, a systemic infection or sepsis may also lead to a toxidrome. "Classic" toxidromes are presented in Table 4.1, but symptoms are often variable (Goldfrank et al. 1998) or obscured by the co-ingestion of multiple drugs (Stead, Stead, and Kaufman 2006).

The symptoms of an anticholinergic toxidrome include blurred vision, coma, decreased bowel sounds, delirium, dry skin, fever, flushing, hallucinations, ileus, memory loss, mydriasis (dilated pupils), myoclonus, psychosis, seizures, and urinary retention. Complications include hypertension, hyperthermia, and tachycardia. Substances that may cause this toxidrome include antihistamines, antipsychotics, antidepressants, and antiparkinsonian drugs (Stead et al. 2006), as well as atropine, benztropine, datura, and scopolamine.

The symptoms of a cholinergic toxidrome include bronchorrhea, confusion, defecation, diaphoresis, diarrhea, emesis, lacrimation, miosis, muscle fasciculations, salivation, seizures, urination, and weakness. Complications include bradycardia, hypothermia, and

Table 4.1. Toxidrome (modified from Goldfrank et al. 1998)

Symptoms	BP	HR	RR	Temp	Pupil size	Bowel sounds	Diaphoresis
anticholinergic	~	Up	~	up	up	down	down
cholinergic	~	~	~	~	down	up	up
hallucinogenic	up	up	up	~	up	up	~
sympathomimetic	up	up	up	up	up	up	up
sedative-hypnotic	down	down	down	down	~	down	down

tachypnea. Substances that may cause this toxidrome include carbamates, mushrooms, and organophosphates (Stead et al. 2006; Holstege and Borek 2012).

The symptoms of a hallucinogenic toxidrome include disorientation, hallucinations, hyperactive bowel sounds, panic, and seizures. Complications include hypertension, tachycardia, and tachypnea. Substances that may cause this toxidrome include substituted amphetamines, cocaine, and phencyclidine.

The symptoms of a sympathomimetic toxidrome include anxiety, delusions, diaphoresis, hyperreflexia, mydriasis, paranoia, piloerection, and seizures. Complications include hypertension, and tachycardia. Substances that may cause this toxidrome include salbutamol, amphetamines, cocaine, ephedrine, methamphetamine, phenylpropanolamine (PPAs), and pseudoephedrine. It may appear very similar to the anticholinergic toxidrome, but is distinguished by hyperactive bowel sounds and sweating (Stead et al. 2006).

The symptoms of sedative/hypnotic toxidrome include ataxia, blurred vision, coma, confusion, delirium, deterioration of central nervous system functions, diplopia, dysesthesias, hallucinations, nystagmus, paresthesias, sedation, slurred speech, and stupor. Apnea is a potential complication. Substances that may cause this toxidrome include anticonvulsants, barbiturates, benzodiazepines, gamma-Hydroxybutyric acid, Methaqualone, and ethanol.

In principle, agitation may occur with every toxidrome – in some with a greater likelihood (e.g., a sympathomimetic or hallucinogenic toxidrome) – whereas in others agitation appears less likely but may still occur and complicate treatment.

Withdrawal

The probability of withdrawal symptoms upon discontinuation is different for every drug. Some drugs are associated with significant physical withdrawal symptoms (alcohol, opiates, tranquilizers). Other drugs induce little physical impairment upon discontinuation, but cause marked emotional withdrawal symptoms (cocaine, marijuana, ecstasy). The way withdrawal expresses itself is also highly individual. Typical behavioral withdrawal symptoms include

- Anxiety
- Restlessness
- Irritability
- Insomnia
- Poor concentration
- Depression and social isolation

and are usually accompanied by physical withdrawal symptoms such as

- Sweating
- Tachycardia
- Headache
- Palpitations
- Muscle tension
- Tightness in the chest
- Difficulty breathing
- Tremor
- Nausea, vomiting, or diarrhea

Psychological and behavioral symptoms of withdrawal may outlast physical symptoms for weeks and months (post-acute withdrawal symptoms). They may mimic a depressive or bipolar mixed mood disorder showing

- Mood swings
- Anxiety
- Irritability
- Tiredness
- Variable energy
- Low enthusiasm
- Variable concentration
- Disturbed sleep

During the acute phase of withdrawal, potentially life-threatening medical complications may occur, for example:

- Grand mal seizure
- Heart attack
- Stroke
- Traumatic brain injury following a fall
- Delirium tremens

Agitation is almost an obligatory symptom in the acute withdrawal scenario, and may persist as an expression of mood disturbance into the post-acute phase.

Delirium

Delirium is a serious alteration of brain and body function that, as far as cognition is concerned, results in confused thinking and reduced awareness of the environment. The start of delirium is usually rapid – within hours or a few days. Delirium can often be traced to one or more contributing factors, such as a severe or chronic medical illness, changes in metabolism or electrolytes (such as low sodium), medication, infection, surgery, or alcohol or drug withdrawal (delirium tremens). In emergency settings, it is not uncommon for a patient to go through an initial screening and have a diagnosis of delirium overlooked. The patient may be mistakenly diagnosed as psychotic, based on the fact that physical signs and symptoms of delirium may be subtle and easily go undetected (Stowell et al. 2012).

Symptoms

The symptoms of delirium usually built up over a few hours or a few days. They often fluctuate, usually being more prominent at night time, but may also be absent for short intervals. Key signs and symptoms include

- Reduced awareness of the environment
- Cognitive impairment, especially poor memory, particularly of recent events
- Directing, focusing, sustaining, or shifting attention
- Disorientation
- Distorted speech, along with difficulties reading or writing
- Psychotic symptoms and behavioral peculiarities, including

  - Hallucinations
  - Restlessness, agitation, or combative behavior
  - Crying, moaning, or making other sounds
  - Social withdrawal – especially in older adults – and reduced motor activity or lethargy
  - Disturbed sleep pattern with reversal of night-day sleep-wake cycle
- Emotional turmoil, manifesting itself as
  - Anxiety, fear, or paranoia
  - Depression
  - Irritability or anger
  - A sense of feeling elated (euphoria)
  - Apathy
  - Rapid and unpredictable mood shifts
  - Personality changes

Delirium may manifest itself with a varying mix of symptoms and different degrees of agitation:

- Hyperactive delirium. Probably the most easily recognized type, this may include restlessness (e.g., pacing), agitation, rapid mood changes, or hallucinations.
- Hypoactive delirium. This may include inactivity or reduced motor activity, sluggishness, abnormal drowsiness, or dizziness.
- Mixed delirium. This includes both hyperactive and hypoactive symptoms. The person may quickly switch back and forth from hyperactive to hypoactive states.

Alcohol-Related Dementia

Alcohol-related dementia (ARD) presents as a global deterioration in intellectual function. ADR can produce a variety of psychiatric problems, including psychosis, depression, anxiety, and personality changes. Patients with ADR often develop apathy, related to frontal lobe damage that may mimic depression.

Memory is not always affected, but as ARD may coincide with other forms of dementia, it often manifests itself with a wide range of symptoms. Individuals with ARD often present with frontal lobe pathology leading to disinhibition, loss of planning and executive functions, and a disregard for the consequences of their behavior. Other types of ARD such as Korsakoff's syndrome (see later in this chapter) present with changes in memory, primarily a loss of short-term memory, as a main symptom. Accordingly, the degree of agitated behaviors differs within the ARD spectrum.

Heavy alcohol abuse may result in peripheral neuropathy, as well as cerebellar ataxia. Due to unpleasant sensation in their extremities and unsteadiness on their feet, these patients may appear physically agitated.

Wernicke-Korsakoff Syndrome (WKS)

WKS is the co-occurrence of a primarily neurological disorder, Wernicke's encephalopathy (WE), and Korsakoff's syndrome (KS). Due to the close relationship between these two disorders, patients are usually diagnosed with WKS as a single entity.

WKS has been linked to thiamine (vitamin B_1) deficiency, which can cause a range of disorders, including beriberi and WKS. These disorders may manifest together or separately.

WE, KS, and WKS are most commonly seen in people who abuse alcohol. Failure to diagnose WE early and lack of treatment leads to death in approximately 20 percent of cases, while 75 percent are left with permanent brain damage associated with WKS. Of those affected, 25 percent require long-term, institutionalized care (Thomson and Marshall 2006).

WE is characterized by a triad of the following symptoms:

- Ocular disturbances (ophthalmoplegia)
- Changes in mental state (dementia)
- Unsteady stance and gait (ataxia)

Other symptoms described in WE include stupor, hypotension, and tachycardia as well as hypothermia, epileptic seizures, and a progressive loss of hearing (Sechi and Serra 2007).

KS is characterized by an acute onset of severe memory impairment without any dysfunction in intellectual abilities. The DSM-IV lists the following criteria for the diagnosis of Korsakoff's syndrome:

- Anterograde amnesia
- Variable degree of retrograde amnesia

and, in addition, at least one of the following: aphasia, apraxia, agnosia, or a deficit in executive functions. Although KS is usually a consequence of long-standing alcohol use, in rare instances, it may develop due to thiamine deficiency as a consequence of stomach cancer, anorexia nervosa, or gastrectomy.

Confusion, confabulation, and hallucinations are cognitive key symptoms of KS (Thomson and Marshall 2006). These may lead to states of increased anxiety and agitation; most patients with KS, however, present as perplexed rather than agitated or aggressive.

Scales Useful in Assessing Agitation in Intoxicated Patients

Several psychometric tools have been used in the measurement of the severity of agitation, the risk of escalation to aggressive behavior, and the assessment of treatment response (Zeller and Rhoades 2010). By the nature of things, agitation is usually brief and self-limiting in acutely intoxicated patients or rapidly fluctuating in patients with delirium. Thus, comprehensive and brief rating scales that can be frequently repeated are most useful, such as the Agitation Severity Scale (ASS) (6), the Behavioural Activity Rating Scale (BARS) (Strout 2014), the Overt Aggression Scale (OAS) (Swift et al. 2002), or the Staff Observation Aggression Scale (SOAS) (Silver and Yudofsky 1991).

For a full risk assessment, they should be complemented with a specific scale predicting violent behavior and a suitable scale for monitoring other intoxication and withdrawal symptoms.

A predictive tool of aggressive/violent behavior is the Broset Violence Checklist (BVC) (Linaker and Busch-Iversen 1995). The BVC has been developed as a predictive tool of a violent episode in the next twenty-four hours in psychiatric inpatients (Woods and Almvik 2002; Abderhalden et al. 2004). The BVC measures six items: confusion, irritability, boisterousness, physical threats, verbal threats, and attacks on objects. It is hypothesized that an individual displaying two or more of these behaviors is more likely to be violent in the next twenty-four-hour period.

The Clinical Institute Withdrawal Assessment for Alcohol (Sullivan et al. 1989), commonly abbreviated as CIWA or CIWA-Ar (revised version), is a ten-item scale used in the assessment and management of alcohol withdrawal. Each item on the scale is scored independently, and the summation of the scores yields an aggregate value that correlates to the severity of alcohol withdrawal, with ranges of scores designed to prompt specific management decisions such as the administration of benzodiazepines. The maximum score is 67. Mild alcohol withdrawal is defined with a score less than or equal to 15, moderate with scores of 16 to 20, and severe with any score greater than 20. The ten items evaluated on the scale are common physical and cognitive symptoms and signs of alcohol withdrawal.

The goal of the CIWA scale is to provide an efficient and objective means of assessing alcohol withdrawal. Studies have shown that using the scale in alcohol withdrawal helps to prevent over-sedation with benzodiazepines in patients with milder alcohol withdrawal, and yields a lower risk of under-treatment in patients with greater severity of withdrawal (Mayo-Smith 1997). The CIWA-Ar is a shortened, yet improved version of the CIWA (Mayo-Smith 1997).

Treatment of Substance-Related Psychomotor Agitation

In the first expert consensus of Allen and colleagues (Allen et al. 2001), three general possible etiologies of agitation were described: a general medical condition, substance intoxication/withdrawal, and a primary psychiatric disorder. The Project BETA workgroup (Nordstrom et al. 2012) added in its 2012 Consensus Statement of the American Association for Emergency Psychiatry a fourth category named "undifferentiated agitation."

A prompt and goal-directed evaluation of the etiology of agitation and immediate management steps are essential to gain control over a potentially dangerous behavior that could progress to violence. Besides posing a danger to others, psychomotor agitation has been also described as a possible predictor of suicide behavior (Sani et al. 2011; McClure et al. 2015). Delayed and insufficient management of agitation can result in an unnecessary use of coercive measures (involuntary medication, physical/mechanical restraint, seclusion), escalation to physical violence, adverse outcomes for staff and patients, and substantial economic costs to the health care system (Hankin, Bronstone, and Koran 2011).

Similar general principles apply when treating agitation due to substance abuse as if it were due to other mental disorders. The first step is to obtain vital signs, gather as much as possible of a medical and psychiatric history, and perform a visual examination of the patient assessing his or her appearance, behavior, level of awareness, attentional deficits, and cognitive skills. Additional information from collateral sources and medical records are important to evaluate preexisting conditions, disorders, and medications (Stowell et al. 2012).

Parallel to diagnosis, an appropriate intervention to control agitation needs to be initiated. Nonpharmacological methods of behavioral control, such as placing the patient in a safe and tranquil environment and verbal de-escalation, are the initial step in the management of the agitated patient (Hill and Petit 2000; Marder 2006). If a pharmacological intervention is needed, medication should ideally be easy and non-traumatic to administer, provide rapid tranquilization without excessive sedation, have a fast onset of action and a sufficient duration of action, and have a low risk for significant adverse events and drug interactions (Allen and Currier 2004). The pharmacological management of acute agitation has traditionally employed three classes of medications: first-generation antipsychotics (FGA), second-generation antipsychotics (SGA), and benzodiazepines (BZD) (Marder 2006).

More recently, additional pharmacological strategies have evolved with the introduction of better-tolerated non-oral pharmacological options and a wider choice of formulations for oral use and inhalation (Baker et al. 2003; Popovic et al. 2015). Seclusion and restraint should be used only as a last resort if the safety of the patients or others cannot be ensured otherwise. Once the critical situation is under control, debriefing of the patient and staff is essential to reestablish therapeutic relationships.

The proper management of an agitated patient is essential to keep staff safe and ensure appropriate treatment for the patient (Wilson et al. 2012b). Every staff member should be familiar with accepted guidelines and internal risk management policies. This guidance needs constant review and development. Regular de-escalation training sessions should be performed.

Alcohol and illicit drugs are not only frequent reasons behind agitated behavior, but also readily treatable causes if recognized. The Project BETA workgroup (Nordstrom et al. 2012; Stowell et al. 2012) suggests that psychiatrists should exclude delirium, cognitive impairment, intoxication, withdrawal, or a medical condition first before considering a mental disorder other than substance use as a cause of agitation.

Intoxicated Patients

The use of stimulating illicit substances such as cocaine, ecstasy, ketamine, bath salts, inhalants, and methamphetamines should be verified or ruled out by physical examination, urine toxicology, and careful questioning of patient and potential witnesses. In most cases of CNS stimulant use, agitation is transient, and calming the patient by verbal de-escalation and providing a tranquil setting is sufficient. In more severe cases, vital signs need to be monitored until recovery. If pharmacological treatment is needed to control agitation and/or aggressive behavior, short-acting benzodiazepines are the treatment of choice (Wilson et al. 2012b). Use of the benzodiazepine will allow for the patient to calm, possibly sleep, and detoxify; typically this alone will be sufficient to relieve agitation symptoms. In a small number of patients who chronically abuse stimulants, particularly amphetamines, psychotic symptoms may develop. In these patients, a first- or second-generation antipsychotic may be useful in addition to a benzodiazepine (Ricaurte and McCann 2005), but in most cases it is worth attempting a benzodiazepine alone first, and only adding the antipsychotic at a later point if the psychotic symptoms have not ameliorated.

The most common cause of substance-induced agitation is alcohol. In agitation secondary to alcohol intoxication, non-pharmacological interventions, such as reduced environmental stimulation, are the primary and preferred method of treatment (Allen et al. 2005). If medication is required, previous expert consensus documents have recommended benzodiazepines, given the possibility that a component of withdrawal may be contributing to the agitation (Allen et al. 2005). However, alcohol intoxication and withdrawal should be seen as distinct, non-overlapping presentations, which clinicians can generally differentiate. In addition, although there is no clear scientific evidence of respiratory depression with benzodiazepine use in monotherapy, there is a potential for clinically significant respiratory depression when benzodiazepines are administered to alcohol-intoxicated patients, as both agents are central nervous system (CNS) depressants (Wilson et al. 2012b). Thus, antipsychotics rather than benzodiazepines should be used to treat agitation in the context of alcohol intoxication (whereas the opposite is true in alcohol withdrawal). Both clinical experience and published literature suggest that the use of the first-generation antipsychotic

haloperidol in intoxicated patients is safe and effective. Second-generation antipsychotics, however, have not been well studied in this context. Thus, haloperidol remains the preferred choice in this clinical scenario, as it has minimal effects on vital signs, negligible anticholinergic activity, and minimal interactions with other non-psychiatric medications. However, it has the propensity to lengthen QTc intervals. As a consequence, lowest effective dosages should be used, intravenous administration should be avoided, and, ideally, the ECG should be checked prior to medication – which may be not always an easy task in a real-world scenario. If haloperidol needs to be administered intravenously, the dose should be limited to 5 to 10 mg/day and administered in conjunction with continuous ECG monitoring.

Although there is good evidence for second-generation antipsychotics (SGA) in agitated patients with psychotic or severe affective disorders, their use in alcohol-intoxicated patients has rarely been investigated. Case studies suggest that the use of the more sedative antipsychotic olanzapine together with benzodiazepines was safe in agitated psychiatric patients. However, in some patients who had ingested alcohol, intramuscular olanzapine + benzodiazepines was associated with decreased oxygen saturations (Wilson et al. 2012a).

State of Withdrawal

Patients going through alcohol withdrawal present with a range of physical symptoms, most causing discomfort, but some may become life-threatening, especially in patients who already have a condition such as cardiovascular disease, hypertension, diabetes, or an electrolyte dysbalance. Signs and symptoms of discomfort such as sweating, tachycardia, muscular weakness, headaches, or nausea may cause agitation, and symptomatic treatment of the underlying complaint should be offered. In addition, vital signs should be monitored and sufficient fluid intake must be ensured. Finally, appropriate environmental modifications should be made such as: assuring that the patient is physically comfortable, decreasing external stimuli through the use of relative isolation (a quiet room or an individual examination room), minimizing waiting time, and communicating with a safe, respectful, and caring attitude.

Figure 4.1 illustrates the pharmacological choices for the different alcohol- or toxin-related scenarios. As an unspecific approach to treat agitation and physical symptoms of withdrawal, benzodiazepines such as diazepam, lorazepam, and oxazepam should be tried. Chlordiazepoxide has a very long half-life, which might make it difficult to manage. Similar to flunitrazepam and alprazolam, chlordiazepoxide may also have a higher addiction potential than the other benzodiazepines. These agents all have a long record of efficacy for agitation, and are often preferred by clinicians when the patient is known to be suffering from alcohol withdrawal, or when the etiology of agitation is undetermined. However, in patients who are still massively intoxicated with alcohol, the use of benzodiazepines should be avoided (see previous paragraph). Benzodiazepines may cause excessive sedation and have the potential for respiratory depression (especially midazolam) or hypotension when used parenterally in patients with underlying respiratory conditions or in combination with other CNS depressants such as alcohol.

For agitated delirium not due to alcohol, second-generation antipsychotics are usually recommended as a first choice (Wilson et al. 2012b). If a patient develops delirium when stopping or reducing alcohol intake (delirium tremens), the addition of an antipsychotic to ongoing benzodiazepines might be indicated, especially if agitation is severe and due to

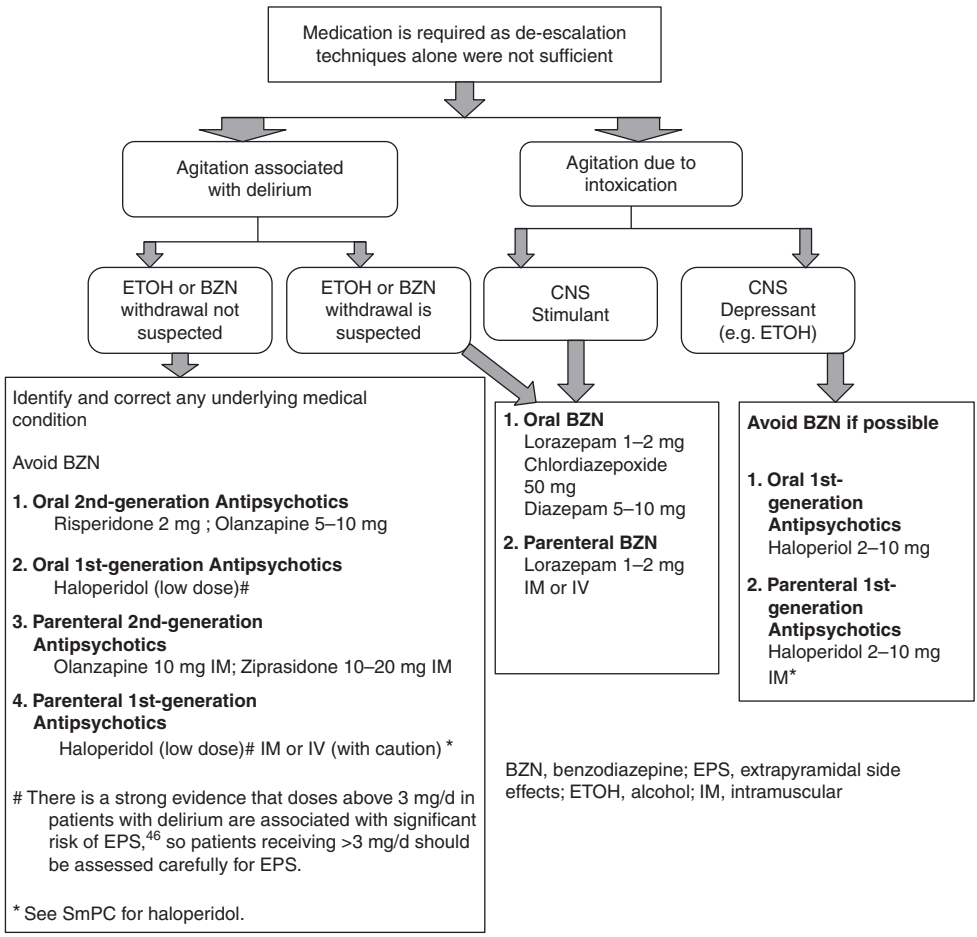

Figure 4.1. Suggested treatment algorithm for medication treatment in agitation related to current or previous alcohol or stimulant abuse. Modified from (Wilson et al. 2012b).

psychotic symptoms. Low-dosage haloperidol might be the safest and most effective choice, although this recommendation is based on clinical experience rather than on a convincing study record. Patients with delirium appear more sensitive to extrapyramidal symptoms, another reason doses should be kept as low as possible (Lonergan et al. 2007). More recently, dexmedetomidine, an alpha 2 agonist, has been recommended in more severe alcohol withdrawal (Dabrow, Giometti, and Weeks 2015). In a randomized controlled study, dexmedetomidine significantly reduced diazepam requirements in intensive care unit patients with alcohol withdrawal syndrome and decreased the number of patients who required haloperidol for severe agitation and hallucinations (Bielka et al. 2015).

Alcohol-Related Dementia

Most patients with ARD, including Korsakoff's syndrome, fall into the group of the elderly, and often suffer from comorbid physical conditions. Thus, similar principles for

the treatment of agitation apply as in other forms of dementia. According to the expert consensus of Allen and colleagues (Allen et al. 2005), the first-line treatment should consist of non-pharmacological strategies. A safe and familiar environment and reestablishment of a normal sleep-wake cycle may help to diminish frequency and severity of agitation. If pharmacological treatment of agitation in the elderly is needed, a cautious use of medication has been recommended, starting with low doses and small increments of dose. Appropriate observation of the medication effects and close meshed monitoring of the clinical situation, the risks of falls, signs of confusion, and over-sedation is mandatory (Marder 2006). Especially the risk of over-sedation and consecutive falls makes the use of benzodiazepines or sedative antipsychotics problematic. In 1998, the Expert Consensus Guidelines for the Treatment of Agitation in Older Persons with Dementia recommended the high-potency, first-generation antipsychotics for the management of delirium with agitation in elderly patients with dementia, with risperidone as recommended second-line treatment (Alexopoulos et al. 2005). This order of medication has changed since then: The more recent Expert Consensus Guidelines on Using Antipsychotics in Older Patients recommended using an atypical antipsychotic for agitation associated with delirium, psychosis, aggression, or anger (Alexopoulos et al. 2005), despite the FDA and EMA Black Box warnings of an increased risk of cerebrovascular incidents in older patients with long-term SGA exposure (Gill et al. 2005). They also considered the off-label use of valproate to manage anger with a risk of physical aggression (Alexopoulos et al. 2005). It appears that despite the clinical need, the appropriate treatment of agitation and aggression in dementia, especially ARD, remains under-researched, and opinion prevails over evidence.

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Chapter 5

Medical Causes of Patients with Agitation: Systemic Illness

Sandra Schneider and Adam Jennings

Case

An eighty-two-year-old female presented to an emergency department with a two-day history of increasing confusion and agitation. On the morning of her presentation, she was found wandering around her apartment building, combative and disoriented. Her daughter relates that in retrospect she was slightly confused two days prior during a phone conversation. Prior to this incident, she had been alert, oriented, and living on her own. She had no prior history of mental illness or similar events. Her only medical history was mild hypothyroidism. There was no history of hypertension. On exam, she was restless and very agitated to tactile or verbal stimulation. Her pulse was 120, BP 160/110, temperature 38°C, and respirations 28. Besides the tachycardia, her physical exam was normal. She was not oriented to person, place, or time.

Medical Causes of Agitation

While agitation is often a presentation of mental illness, it is important to detect a patient whose cause is medical and potentially treatable. One of the most common causes of agitation is a toxic ingestion, which is covered in another chapter. While intentional ingestions of drugs of abuse are most common in young adults and teenagers, elderly patients do abuse recreational drugs as well.

It is widely taught that the key to diagnosis is in the history. However, the patient who is agitated, particularly one whose sensorium is altered by medical or psychiatric disease, may not give a coherent, accurate history. In some cases, there may be very little or no history available. Once the agitation is controlled, a very thorough physical examination will often suggest the appropriate differential diagnosis. All patients should have vital signs recorded when possible, as well as point of care glucose levels. Routine testing, particularly beyond a simple blood count and electrolytes, is of very low yield (Nordstrom, Zun, & Wilson 2012; Tolia & Wilson 2013), and is not advised. Laboratory testing and imaging is best directed by specific concerns raised by the history and physical exam.

In order to have a normal mental status, a person must have a functional cortex and brainstem. In addition, he or she must have CNS substrates, including glucose and oxygen. Molecules that inhibit or overly stimulate neurotransmitters include common toxins (alcohol, drugs of abuse), urea, and ammonia. The presence of these molecules most often leads to somnolence, but can cause confusion and agitation.

High-Risk Presentations

Elderly: Elderly patients, particularly those who have a baseline dementia, can easily become agitated, particularly when there are new surroundings, their perception is altered (by drugs, fever, or dehydration), or they become frightened. Rapid or new-onset agitation, or a change in baseline agitation, suggests a possible medical cause. One of the most common causes in the frail elderly is infection. This can be a severe sepsis episode or a simple urinary tract infection. Infection appears to increase inflammatory cytokines, which interfere with synaptic transmission, and increase cortisol. The most common infections in the elderly are pneumonia and urinary tract infection. Symptoms and signs such as fever, rales, and dysuria are often absent in the frail elderly.

Older patients can also become agitated and disoriented from medication, particularly anticholinergics, sedative/hypnotics, and steroids. Although allergy and cold medications are obvious anticholinergic medications, many other medicines have anticholinergic side effects. Older patients have a baseline decrease in CNS acetylcholine, so anticholinergic medications, even in small and "normal" quantities, can result in confusion and agitation. Confusion and psychosis is also associated with corticosteroids and antiparkinsonian drugs.

Abnormal vital signs: While agitation and excitement can cause tachycardia (pulse >90 in an otherwise normal patient), when vital signs are abnormal, medical causes of agitation should be considered. This is particularly true of temperature, new-onset severe hypertension, hypoxia, and severe tachycardia. Patients with a history of hypertension who display a normal level of consciousness and do not have acute chest pain do not need to have their blood pressure acutely lowered, regardless of the reading. Fever creates a hypermetabolic state but, more important, is a hallmark of infection. Hypothermia is a sign of sepsis/infection. Severe hypothermia (<85°F) can cause an abnormal mental status and "paradoxical undressing." Individuals with severe environmental hypothermia have been found wandering outside naked and disoriented on cold, wintery days.

Table 5.1. High-risk presentations

Elderly
New-onset agitation/psychosis especially if age >45 years
Abnormal vital signs – particularly hypotension, fever, respiratory distress
Trauma – particularly head but any trauma
Loss of orientation
Suspicion of drug or alcohol intoxication or withdrawal (see prior chapter)
Severe, new-onset headache
Focal neurologic signs (abnormal extraocular movements, unilateral weakness, aphasia or slurred speech, new aniscoria)
Seizures, myotonic jerking
Loss of consciousness
Sudden onset of symptoms

Sudden loss of consciousness during an agitated presentation: Loss of consciousness is always a serious sign. "Excited delirium" describes a patient who is very agitated and combative, who suddenly loses consciousness and goes into cardiac arrest. While there is debate over whether this is a true medical condition, the American College of Emergency Physicians supports the concept of this disorder (Excited Delirium 2016). In addition, patients with other medical conditions such as thyroid storm, sepsis, and hypoxia may progress rapidly, losing consciousness.

New-onset mental illness: While mental illness is unfortunately common, a patient without a history of mental illness should have a medical examination, including laboratory testing, during the first presentation of agitation, particularly if the onset is sudden, or the age of the patient is unusual (e.g., elderly).

Atypical presentation of a patient with known mental illness: Most patients tend to have a similar presentation with each acute exacerbation of disease. Agitation in a patient who is normally depressed and hypoactive should warrant a medical evaluation. Patients with mental illness can also have serious and life-threatening medical diseases. Some staff may display a poor attitude toward individuals with mental illness, or may dismiss all of their symptoms to their underlying psychiatric disease (Zun 2012). Any atypical presentation for a patient with underlying mental illness should be worrisome.

Overt signs of drug or alcohol intoxication or exposure to toxins: This is covered in another chapter.

Head injury or trauma: Patients are often found wandering on the street, agitated, and confused and brought to the emergency department. Unfortunately, homeless and intoxicated people are frequently assaulted or they may fall. Head-injured patients and those with severe trauma that interferes with circulation or oxygenation will often be acutely agitated and require sedation prior to a diagnosis. Patients who take anticoagulants, have a bleeding disorder, or have an elevated INR due to liver disease may be at higher risk for CNS bleeding.

New neurologic findings: The presence of a new neurologic finding such as a cranial nerve palsy or unilateral weakness suggests a structural lesion in the brain and, depending on its location, may cause agitation.

Sudden onset of confusion/agitation: Most patients with mental illness decompensate over a period of hours to days. Signs of agitation start slowly, and may escalate quickly depending on the social setting. A sudden onset of agitation and/or confusion, particularly when accompanied by lip smacking or tics, suggest non-convulsive seizures. An EEG is diagnostic. A dose of benzodiazepines leads to prompt return to normal.

History of cancer or prior neurologic disease: Cancer may metastasize and cause structural abnormalities or bleeding in the brain. Patients with a remote history of cancer may still develop metastatic disease and are also at risk for a second tumor. Several cancers, particularly lung, breast, and prostate, may cause hypercalcemia, which presents with alter sensorium (generally somnolence, but confusion with agitation is possible). Other symptoms include dehydration, polyuria, and constipation.

Patients with a history of stroke and those who have suffered a traumatic brain injury are at risk for seizures, including non-convulsive seizures, which may present as confusion and unfocused agitation. The exact incidence of non-convulsive seizures after brain injury is not known. In one study of patients with severe traumatic brain injury, EEG monitoring detected seizures in 22 percent of patients, 52 percent of which were non-convulsive (Vespa 2003). In a separate study of patients with intracranial hemorrhage, EEG monitoring detected seizures in 28 percent, the majority of which were non-convulsive. Seizures after ischemic stroke occur in about 10 percent of patients and can be non-convulsive (Silverman 2002).

Delirium versus Dementia

There is often confusion between delirium and dementia. Dementia is a permanent change to the structure of the brain. It is generally slow in onset and progresses over months to years. While fluctuation is possible, return to an entirely normal baseline is unusual, and in general, dementia is irreversible. There are many causes of dementia (Alzheimer's, normal pressure hydrocephalus, Lewy body, etc.), but most patients present with a similar change in mentation. Although memory is affected, loss of orientation is not seen until late in the disease. Agitation is seen late in dementia or with a sudden change in environment, and is likely due to confusion and disorientation.

Delirium is generally sudden onset and often reversible. Delirium in young adults and children is most often caused by ingestions. In the elderly and those with debilitating disease, infection and medications are the most common causes. The most common infections are pneumonia and urinary tract infection. Fever may be absent; hypothermia is seen. An elevated white blood count is often seen. Many medications can cause delirium in the elderly, but the most common are anticholinergics and corticosteroids.

Delirium is often difficult to detect, particularly in a busy emergency department, and especially in patients whose mental baseline is unknown. Several tools such as the Confusion Assessment Method (CAM) and the Delirium Symptom Interview (DSI) are helpful (Inouye et al. 1990; Albert et al. 1992). Although delirium is common in the emergency department, it is rarely diagnosed, in part because other medical issues may have greater priority, and in part because emergency physicians often miss the diagnosis. It is estimated that 14–56 percent of hospitalized elderly patients have delirium (Fong, Tulebaev, & Inouye 2009).

While delirium has many causes, seven are associated with potentially fatal conditions, often referred to as WHHHIMP (Cassem et al. 2004). WHHHIMP stands for Wernicke's encephalopathy, hypoxemia, hypoglycemia, hypertensive crisis, intracranial bleeding, meningitis/encephalitis, and poisoning.

Delirium is associated with high morbidity and mortality. Patients admitted with delirium have a mortality rate of 10–26 percent (McCusker et al. 2002). Those who develop delirium in the hospital have a much higher rate (Pauley et al. 2015).

Patients with underlying dementia are particularly vulnerable to delirium. Both disorders are associated with decrease in brain metabolism and/or blood flow, cholinergic deficiency, and inflammation (Fong et al. 2009). Patients with dementia who display a sudden change in behavior, either hyper- or hypo-kinetic, should be medically assessed for infection, have their medications reviewed, and possibly have a head CT.

Medical Causes of Agitation

Many conditions make a patient irritable, uncomfortable, and tense (hyperthyroidism, hunger, anger, etc.). Fewer make a person so agitated that they are brought to the emergency department and require acute treatment. This section will deal with primarily those disorders that cause significant agitation. Medical agitation is generally caused by loss of CNS substrate (oxygen, glucose), electrolyte abnormalities that affect neurotransmission, metabolic abnormalities, toxins that interfere with normal synaptic transmission (infection, medications/toxins (see the previous chapter), uremia, ammonia), or CNS disease (trauma, seizures, infection).

Hypoxia: Oxygen is a required substrate for the brain, and acute hypoxemia can cause severe agitation, confusion, and aggressive, often non-directed behavior. As with many medical causes of agitation, slow reduction in oxygen levels over time, such as seen with smoking or chronic obstructive pulmonary disease, do not cause symptoms. Patients with severe chronic obstructive pulmonary disease tolerate significantly low oxygen levels and even marked elevation in carbon dioxide. However, acute lowering of oxygen, as is seen with large pulmonary emboli, tension pneumothorax, or airway obstruction (café coronary), can lead to rapid hypoxia and rapid onset of agitation. Oxygen saturation levels can be measured non-invasively, though there are many causes for falsely low readings such as poor perfusion, calloused skin, poor application, cyanide and methemoglobinemia, and anemia will cause a falsely elevated reading. When abnormal results are not explainable, a blood gas may provide additional information. If not treated, agitation due to hypoxia is often followed by sudden loss of consciousness and cardiac arrest.

Treatment involves first assuring the airway is open and air is entering the chest. Sedation may be necessary, though rapid deterioration with loss of consciousness is common. Visualization of the airway with removal of any visible foreign body may be necessary if good air flow does not occur. A surgical airway may be necessary. High-flow oxygen through a bag-valve-mask, ventilator, or with non-rebreather mask may raise the oxygen level while definitive treatment is started. Intubation is indicated when airway maneuvers are not successful. Tension pneumothorax should be considered in patients without breath sounds and hyper-resonance over one side of the chest, with distended neck veins, especially if there is a history of trauma or pulmonary disease.

Reversal of hypoxia should lead to rapid return of level of consciousness, unless the hypoxia has led to anoxic brain damage. Most patients with anoxic damage have had severe hypoxia for more than five to ten minutes and generally have a period of loss of consciousness.

Hypotension: Severe, sudden hypotension disrupts the delivery of oxygen to the brain. Most patients present with a decrease in consciousness and movement, though agitation can be seen. Like hypoxia, patients with agitation due to hypotension will rapidly deteriorate to a decrease in consciousness and potentially cardiac arrest within a few minutes. Treatment is dependent on the cause of the hypotension, which should be rapidly identified and reversed. Hypovolemic shock is due to acute fluid/blood loss and is treated with aggressive fluid and, when indicated, blood replacement. In patients with trauma, blood transfusion should be considered, even when the blood count is normal. Distributive shock seen in conditions such as septic and anaphylactic shock requires aggressive treatment with

intravenous fluids (30 cc/kg) for sepsis and epinephrine for anaphylactic shock regardless of prior cardiac history. In patients unresponsive to fluids, pressor agents such as norepinephrine or dopamine are often indicated. Cardiogenic shock presents with hypotension and often pulmonary edema. Treatment is direct at improving cardiac contractility and may require vasopressors. Rarely obstructive shock, due to massive pulmonary embolism or pericardial tamponade, will be the cause of shock.

Metabolic

Hypoglycemia: Since the brain relies on glucose as its main source of energy, hypoglycemia is a frequent cause of acute confusion and agitation. Aggressive behavior without specific motivation can be seen with acutely lowered blood glucose levels. The agitation and aggressive behavior seen with hypoglycemia can be dramatic and destructive to the proximal environment. Severe hypoglycemia is most common in insulin-dependent diabetics, particularly those with long-standing disease. In this population, hypoglycemia can occur suddenly without the warning of hunger, diaphoresis, or tremulousness. The scenario is most often insulin administration without sufficient caloric intake. As exercise consumes glucose, hypoglycemia is also common in athletes. Those on shift work may also find it hard to regulate their exogenous insulin administration and food intake. Insulin overdose, either intentional or accidental, can cause hypoglycemia, as can overdose of oral hypoglycemic agents.

Treatment of acute hypoglycemia is straightforward, and EMS, caretakers, or coaches treat most patients before the patient is brought to the hospital. Glucose levels can be rapidly measured with a small drop of blood and glucometer, which is both standard equipment for EMS and present in the homes of many diabetics. In general, symptoms of hypoglycemia such as agitation are not seen with glucose levels greater than 50–60 mg/dL. Glucose administration orally, if the patient is conscious and cooperative, glucose paste smeared onto the oral mucosa, or D50 intravenously should reverse the hypoglycemia and the symptoms within a few minutes. An ampule of D50 contains 100 calories, so it should raise the glucose to 244 ± 44 mg/dL (Balentine, Gaeta, & Kessler 1998). Consequently, it is very rare for symptoms to continue after glucose administration. In these rare cases, a second dose of glucose can be administered, but a secondary source for the agitation should be considered. When glucose administration is not available, intramuscular or sublingual glucagon (1 mg) will reverse hypoglycemia. As glucagon causes the release of glucose from the liver, patients with advanced liver disease or long-standing Type 1 diabetes may not respond to glucagon. However, it is important to note that glucose levels reduce to baseline within thirty minutes; therefore, patients who have recovered require a continuing source of glucose, either a high-carbohydrate meal or sustained intravenous glucose. With the exception of patients who have taken a significant insulin overdose, or those on oral hypoglycemic such as a sulfonylurea, patients who recover a normal mental status can be discharged after receiving a meal and medication adjustment. Admit patients who have hypoglycemia without cause, those who do not fully return to baseline after glucose normalization, and those with an overdose of insulin or oral hypoglycemic medications.

Thyroid: Hyperthyroidism is the result of an increase in circulating thyroid hormone. Thyroid hormone levels are regulated by the hypothalamus, anterior pituitary, and thyroid gland. Iodine is oxidized by the thyroid to thyroxine (T4) and triiodothyronine (T3) which

Table 5.2. Signs of Graves' disease

Signs seen with all types of hyperthyroidism
Warm skin
Heat intolerance
Hair changes – fine, alopecia
Increased bowel movements
Fine tremor, tongue tremor
Easy bruising
Weight loss
Irregular menses
Palpitations, tachycardia
Proximal muscle weakness (unable to rise from squat without assistance)
Increased deep tendon reflexes
Signs seen primarily with Graves' disease
Proptosis
Infrequent blinking
Failure to wrinkle the forehead when looking upward
Decreased ability to converge eyes
Lid lag
Goiter
Thickening of the skin (pretibial myxedema, acropachy)

is the active compound. About 90 percent of circulating thyroid hormone is T4, with the rest as T3. T4 is then converted peripherally to T3.

The two most common causes of hyperthyroidism are Hashimoto's thyroiditis and Graves' disease. Hashimoto's thyroiditis is an autoimmune disease, and occurs most commonly in adults between thirty and fifty years of age. Thyroid storm from Hashimoto's thyroiditis is rare. The thyroid is enlarged and nearly always tender. Patients frequently progress to a hypothyroid state, which commonly leads to symptoms of cold intolerance and fatigue. Graves' disease is also an autoimmune disorder where the body creates an antibody to thyroid cells, which mimics thyroid-stimulating hormone and causes the release of thyroid hormones. Graves' disease is most common in patients under the age of forty and is far more common in women. Patients with Graves' disease very often have characteristic proptosis, lid lag, and a goiter (see Table 5.2). Typical symptoms of hyperthyroidism, regardless of cause, include weight loss (occasionally weight gain), heat intolerance, irritability, proximal muscle weakness. In the elderly, hyperthyroidism may present with hypokinesis and dulled sensorium. This syndrome, known as apathetic hyperthyroidism, clinically resembles hypothyroidism. The etiology is not established; however, it is thought that it is linked to lower levels of brain catecholamines (noradrenalin and dopamine).

Elevation of free T3 or T4 is diagnostic of hyperthyroidism. Thyroid-stimulating hormone (TSH) levels are most often low or undetectable, though they may be normal or

Table 5.3. Conditions associated with thyroid storm

Infection
Trauma
Surgery
MI
DKA
Pregnancy and postpartum
Thyroid surgery
Ingestion of iodine
Abrupt cessation of anti-thyroid medication

elevated in hyperthyroidism that is of pituitary origin. Other laboratory abnormalities include hypokalemia (at times with periodic paralysis), hyperglycemia, hypercalcemia, elevation in liver transaminases, low serum cortisol, and leukocytosis.

Hyperthyroidism can cause nervousness and irritability. Psychosis and agitated depression have been reported (Sprall et al. 1982). Simple hyperthyroidism rarely causes significant agitation or confusion, though patients may be irritable and hyperactive. Thyroid storm is a severe, life-threatening form of hyperthyroidism associated with fever, tachycardia, and altered mental status. Thyroid storm may develop in patients with underlying hyperthyroidism (most commonly Graves' disease), as a stress response to infection, after a surgical procedure, following an intentional or accidental overdose of thyroid medications, or trauma. Please see Table 5.3. Patients most often appear agitated with tachycardia, tachypnea, and hypertension. Fever is universal. In late stages or in the elderly, patients may be somnolent or even comatose.

Thyroid storm is a life-threatening condition with a mortality rate of about 20 percent. Immediate treatment is indicated without waiting for laboratory confirmation. No value of T4, T3, or TSH predicts or diagnoses storm. Treatment begins with supportive care, including intravenous hydration and fever reduction. Aspirin should be avoided as it displaces thyroid hormone from its binding globulin. Haloperidol or benzodiazepines may be necessary for control of the agitation. Glucose levels should be monitored. Specific treatment of thyroid storm starts with beta-blockers (either propranolol or esmolol) titrated to effect. Beta-blockers should be avoided in patients with severe asthma or chronic pulmonary disease, in which case calcium channel blockers can be tried. Anti-thyroid medications (PTU or methimazole) should be given orally, rectally, or through an NG tube. Methimazole is the currently preferred drug, except in pregnancy. After waiting for one to six hours, iodine is administered (SSKI; five drops orally every six to eight hours). This massive dose of iodine actually suppresses thyroid hormone release, but this suppression tends to wear off after several weeks. Cortisol is often given as well, as it reduces the peripheral conversion of T4 to T3. Improvement should be seen within twenty-four to seventy-two hours.

Sodium: Hyponatremia may cause confusion and agitation; particularly it is of rapid onset. Symptoms of hyponatremia are determined by the rapidity in fall and the actual level. Most patients are not symptomatic until the level falls below 125 mmol/L (1 mmol/L=1 mEq/L).

Table 5.4. Drugs associated with hyponatremia

Antidepressants – tricyclics, monoamine oxidase inhibitors, SSRIs (esp. in elderly)
Antipsychotics – phenothiazines, butyrophenones
Antiepileptics – carbamazipines, valproic acid
Drug of abuse – MMDA, ecstasy, Molly
Non-steroidal anti-inflammatory drugs

Hyponatremia occurs when more water is ingested than can be secreted by the kidneys, or if there is renal disease, diuretics, or abnormal amounts of antidiuretic hormone (ADH) which prevents the secretion of dilute urine. Mild hyponatremia is most often caused by medications (diuretics) or the Syndrome of Inappropriate Antidiuretic Hormone secretion (SIADH). Significant hyponatremia (levels <125 mEq/L) is generally well tolerated if it develops over days to weeks, but severe hyponatremia that occurs rapidly does not allow for cellular equilibration and may lead to cerebral edema (Adrogue & Madias 2000). Rapid-onset severe hyponatremia is seen with acute water ingestion (such as overhydrating for a marathon or psychiatric polydipsia), and after head injury. It can be seen with MDMA and other drugs. Please see Table 5.4. Patients may present with seizures, cognitive impairment, unsteady gait, or coma, and the condition may progress to death. In these patients, cerebral edema and herniation may be seen. Slower onset of hyponatremia is commonly seen in patients who take diuretics and in those with congestive heart failure or liver disease. It can also be seen in patients with Syndrome of Inappropriate ADH (SIADH), which can complicate certain tumors. Urine sodium levels are essential to determining the correct treatment. Low urine sodium suggests that the kidneys are functioning and there has been an increase in water ingestion. Elevated urine sodium suggests there is excess ADH and fluid restriction may be indicated.

Falsely low sodium levels are seen with large elevations of triglycerides or proteins (such as with multiple myeloma). A falsely low sodium is also seen with elevations in glucose (a decrease of 0.8 mmol/l sodium for every 100 mg/dL increase in glucose over 100). Correction of these disorders will return the sodium to normal.

Treatment of mild or asymptomatic hyponatremia is dependent on the cause. If the patient has a normal mental status and no signs of acute agitation or seizures, a urine sample of sodium and osmolality should be collected. A slow infusion of normal saline (0.9%) should be started. Many of these patients will require fluid restriction to definitively treat their underlying disorder, so only small amounts of saline should be administered prior to the results of the urine sodium level. As the patient is asymptomatic, slow correction is appropriate.

Regardless of etiology, patients with acute, severe agitation, mental status changes, or seizure activity presumed due to severe hyponatremia require aggressive treatment with hypertonic saline, typically administered as a 100–150 mL bolus of 3 percent hypertonic saline over ten to twenty minutes (Henry 2015). Additional boluses can be administered until symptoms improve. When possible, a single urine sample for sodium level and osmolality should be obtained (often by urine catheter) before initiating saline, but in the acute patient, saline infusion should not wait for a urine collection. Patients should respond to a modest increase in serum sodium of 4–6 mmol/L. In patients with acute hyponatremia

(rapid onset), there is little concern for the rate of correction, though hypertonic saline infusion should be changed to normal (0.9%) saline as soon as symptoms abate or the 4–6 mmol/L rise is attained. Patients with chronic hyponatremia require very slow correction of 6–8 mmol/L per day. Rapid correction can lead to cerebral edema because of osmotic shifts in the brain. Overcorrection is to be avoided, as it is associated with osmotic demyelination syndrome (Henry 2016).

Hypernatremia (defined as a sodium level >145 mEq/L) most often causes confusion and depressed level of consciousness and rarely agitation, even in the elderly. Hypernatremia is most often due to dehydration, osmotic diuresis from elevated glucose, diuretics, and tube feedings. Severe, rapid onset of hypernatremia can cause seizures, cognitive dysfunction including confusion and irritability, myoclonic jerking, and lethargy. Treatment involves fluid replacement. Normal saline with a sodium concentration of 154 mEq/L is hypertonic in normal patients, but the solution is hypotonic in a hypernatremic patient. Half normal saline or 4.5 percent contains 77 mEq/L and will more rapidly reduce the sodium. Slow correction of the sodium is advised and calculators are available on many Internet sites (e.g., http://reference.medscape.com/calculator/hyponatremia-correction-infusate-rate).

Calcium/phosphorus: Mild or gradual onset of hypocalcemia is generally asymptomatic. Rapid-onset, severe hypocalcemia can cause confusion and agitation and often seizures (focal or generalized). Characteristically there are very brisk reflexes and a positive Chovstek's and Trousseau's sign. The hallmark of the disease is tetany, or spontaneous tonic muscular contractions. Severe hypocalcemia is most often seen after a parathyroidectomy or thyroidectomy that causes damage to the parathyroid gland, or with advanced cancers. Milder forms occur with vitamin D deficiency, pancreatitis, sepsis, and other critical illness. Like sodium abnormalities, the rate of fall of calcium rather than the absolute level determines the severity of symptoms. Chronic renal failure is often associated with low calcium, but rarely is it significantly symptomatic. Patients with severely lowered calcium should receive intravenous calcium gluconate.

Gradual onset hypercalcemia is generally asymptomatic, though renal stones may form. Agitation is rarely seen and only with rapid increases of serum calcium. Constipation and nausea are common. The vast majority (90%) are caused by either malignancy or hyperparathyroidism. An unusual cause is with milk-alkali syndrome, where increased calcium ingestion along with metabolic alkalosis can cause an acute increase in calcium and decrease in phosphate. Milk-alkali syndrome can be caused by the ingestion of large amounts of antacids containing calcium carbonate. Patients present with agitation, altered mental status, and myoclonus. Treatment is directed at the cause. Most patients are dehydrated, so early intravenous hydration is important. Furosemide is often added to increase calcium excretion once hydration is accomplished.

Hypophosphatemia is often seen with hypercalcemia, but can be associated with malnutrition and refeeding. It is frequent present in diabetic ketoacidosis. No specific treatment is needed in most patients who are asymptomatic, as treatment of the underlying illness will reverse the deficit. Symptomatic hypophosphatemia can be seen with hyperparathyroidism (also with hypercalcemia), and ingestion of aluminum containing antacids. Patients are often fatigued, but can be agitated and confused. Symptomatic patients can be treated with infusion of potassium phosphate until the symptoms are relieved.

Hepatic encephalopathy: Severe liver failure can present with altered mental status, most often somnolence, but agitation can also be seen. Liver failure is associated with elevated levels of ammonia, mercaptans, and free fatty acids. In addition, there appears to be alteration in the metabolism and function of neurotransmitters (including dopamine, noradrenaline, serotonin, GABA) and accumulation of substances such as phenylethanolamine, octopamine, synephrine, and histamine, which act as false neurotransmitters, leading to an altered mental function (Fogel, Andrzejewski, & Maslinsik 1990). While ammonia itself may or may not interfere with cognitive abilities, elevation of ammonia is a marker for liver-failure-associated encephalopathy. Patients are most often somnolent and disoriented. Asterixis is common, though it can also be seen in patients with other disorders such as uremia and respiratory failure. Fetor hepaticus is a characteristic sweet, musty smell to the breath. Lethargy is more common than agitation, particularly in more advanced settings. Sedation can be difficult, as most sedating agents will increase the encephalopathy. Nonetheless, sedation is necessary in severe cases. The treatment should be directed at the cause of the decompensation. Several conditions may lead to hepatic encephalopathy in patients with advanced liver disease, including renal failure; infection; constipation; medications such as sedatives, opioids, antidepressants, and antipsychotics; diuretics; and GI bleeding. Blood in the gut is metabolized to ammonia and nitrogen and clearing the gut with lactulose as well as addressing the bleeding site is important. Other treatment includes neomycin or other antibiotics to decrease the concentration of gut bacteria and rifaximin (used more commonly in Europe) (Bass et al. 2010).

Renal failure: High levels of urea and other renal-excreted molecules interfere with neurotransmission. Activation of N-methyl-D-aspartate (NMDA) and inhibition of GABA is seen. Patients in end-stage renal failure with signs of uremia (pericarditis, elevation in BUN and creatinine) may present with agitation, myoclonus, and seizures, although somnolence is far more common. Most patients with end-stage renal disease are under medical care long before uremic symptoms begin, and dialysis prevents these symptoms even though the serum creatinine may continue to be elevated. Uremic encephalopathy can be seen with acute renal failure, though it is far less likely. Secondary hyperparathyroidism can increase calcium levels systemically and in the CNS, which can lead to agitation. Treatment is emergent dialysis.

Infection: Sudden mental status changes, either agitation or somnolence, with fever should strongly suggest infection. Systemic infection or sepsis can present with or without overt fever (particularly in the elderly), and hypothermia can sometimes be seen. Sepsis is defined as a confirmed or suspected infection with two of the following: fever or hypothermia, tachycardia, tachypnea or low $PaCO_2$, and elevated white blood count or bands. The presence of hypotension, an elevated lactate and/or end organ damage suggests severe sepsis, which carries a higher mortality. The cause of sepsis is usually an infection in the pulmonary or urinary tract, but may be seen with cellulitis, biliary tract infection, abdominal abscess, or dental abscesses (including Ludwig's angina). Meningitis is always a consideration, but is rarely the causes of sepsis. Lumbar puncture should generally be reserved for high-risk patients (such as those with an indwelling CNS apparatus, recent CNS/spinal surgery or injection, immunocompromised individuals, and intravenous drug users).

Any patient (especially the elderly) with a new change in mental status – either agitation or somnolence – and an infection should be evaluated for sepsis. Sepsis can be rapidly fatal,

and despite recent advances in therapy, mortality rates are high (Rivers et al. 2001; ProCESS 2014). Treatment begins with aggressive fluid resuscitation as 30 cc/kg bolus even in patients with a history of cardiac disease, blood cultures, and rapid administration of antibiotics. Where the cause is obvious (such as cellulitis or pneumonia), antibiotic coverage for the suspected organism is initiated. Where the cause is unclear, broad-spectrum coverage should be started after blood cultures are obtained.

Meningitis/encephalitis: With the advent of immunizations against pneumococcus and Neisseria, meningitis is less common in both the pediatric and adult populations. More important, the etiology has changed. Strep pneumonia is now the most common etiology in adults. Neisseria still occurs in college dormitories and military barracks, but is less common because of immunizations. Most impressive is the 94 percent reduction in H. influenza in children (Schuchat, Robinson, & Wenger 1997). Meningitis is seen sporadically in all populations, but is most common in patients with a history of head/facial trauma where there is communication between the nasopharynx and the subarachnoid space, and in those patients who have no functional spleen. Most meningitis seen in otherwise normal patients is viral. Chronic alcoholics are most likely to have pneumococcal meningitis. Immunosuppressed patients can have meningitis due to a many different organisms, including bacteria, viruses, protozoa, and fungi.

Patients present with severe headache and fever. A stiff neck is often present, but adults rarely have a positive Brudzinski's or Kernig's sign. Rash is present in about 60 percent of adults with meningococcemia (Brouwer 2010). Most patients with meningitis present with a normal mental status or with somnolence. Aggressive behavior is unusual, but seizures may be more common.

The diagnosis of meningitis depends on culturing the organism from CSF. Lumbar puncture is generally safe except in high-risk cases, which include patients who are immunosuppressed, and those who have focal neurologic findings, a history of cancer or CNS tumor, known or suspected mass lesions (including hemorrhage), infection or abscess in the puncture area, and those who have a bleeding disorder or are anticoagulated. Although studies have suggested that a CT scan prior to a lumbar puncture is not necessary in low-risk patients, many physicians will obtain a CT scan before the lumbar puncture if the patient is stable and Neisseria infection is not likely (Hasbun et al. 2001). Blood cultures are recommended.

Treatment is determined by the result of the gram stain or suspected cause, and admission to the hospital is recommended. Antibiotics should be started as soon as possible as there appears to be an association between delay in antibiotics and outcome (Proulx et al. 2005). Empiric treatment most commonly suggested is ceftriaxone two gram every twelve hours intravenous and in most cases vancomycin 15–20 mg/kg every eight to twelve hours intravenous with or without ampicillin. Recommendations change for patients with abnormal cellular immunity, those with hospital-acquired infection, and those with beta lactam allergies. It is recommended that a current reference such as http://www.uptodate.com/contents/initial-therapy-and-prognosis-of-bacterial-meningitis-in-adults be consulted before selection of a therapy. Many patients with suspected viral meningitis are started initially on empiric treatment until bacterial cultures are negative. Steroids are often added, as they appear to decrease the inflammatory response in the meninges and brain and have few negative effects (Van de Beek et al. 2004).

Encephalitis: Sudden onset of agitation with fever is more often due to encephalitis than meningitis. Patients are nearly always febrile, but neck stiffness is less common. Typically, patients have a viral prodrome and/or a herpetic outbreak prior to developing fever and agitation. Patients present with behavior and personality changes, photophobia, lethargy, seizures (focal or generalized), and confusion. Patients with West Nile Virus may develop flaccid paralysis (10%). Movement disorders are seen with St. Louis, Eastern equine, and Western equine encephalitis. Luckily, encephalitis is rare. Viral etiologies are most common; in the United States, these are Herpes 1 and 2, Varicella zoster, Eastern and Western equine, St. Louis, La Crosse, West Nile, and Powassam viruses.

Herpes encephalitis outside the neonatal period is generally associated with a local herpetic infection (cold sore). Fever is present in more than 90 percent (Whitley et al. 1982). While changes can be seen on CT, the definitive test is MRI where typical lesions are seen in the temporal lobe of 90 percent of patients (Tyler 2006). Lumbar puncture produces a CSF that typically shows pleocytosis, and PCR testing confirms the infection.

Varicella zoster encephalitis is rare, occurring in only 0.01–0.02 percent of cases of zoster (Gilden 2004). As expected, it is more common in immunosuppressed patients. Patients present with fever, behavioral changes generally during an attack of zoster, or within a month of infection (Gilden 2002). The CSF typically shows lymphocytosis. MRI may show multiple infarcts and demyelination (Espiritu 2007). PCR testing is positive in 94 percent of patients with confirmed disease (Elliot 1994).

Untreated herpetic encephalitis is often fatal. Even with treatment, deficits occur in about 50 percent of patients. Patients are treated with intravenous acyclovir. It is not clear whether steroids improve survival.

Epidemics of West Nile encephalitis have occurred sporadically over the past decade. West Nile is an arbovirus (like the Eastern and Western equine, St. Louis, and La Crosse viruses), and is transmitted by mosquito. West Nile has also been transmitted by organ transplantation. Most patients infected by West Nile are asymptomatic and appear to acquire immunity against future infection. Only 20 percent of those infected develop symptoms, typically rash, fever, and headache. Of those infected, only 1 percent or less will develop neurologic symptoms (Mostashari et al. 2001). Fever is nearly always present when patients have neurologic disease. Agitation, disorientation, headache, and stupor are described. A flaccid paralysis occurs in 10 percent. Other arboviruses cause similar symptoms, but flaccid paralysis is not seen. MRI findings suggest the presence of encephalitis in one-third and the true cause requires PCR testing of the CSF or brain biopsy. Treatment is supportive in an intensive care setting.

Rabies is a viral encephalitis, classically transmitted through the bite of a rabid animal. With widespread canine vaccination, dog bites are rarely the cause in the United States. Bites from rabid wild animals such as raccoons, skunks, or bats are more common. Bites from bats are often not felt. Rabies is also transmitted through organ transplantation. Patients present with fever, agitation, or lethargy and other typical signs of encephalitis. Supportive intensive care is indicated, but survival is unlikely.

CNS tumors: Mass lesions in the brain can cause changes in behavior, though sudden severe agitation is rare. Frontal lobe tumors can grow to significant size without being noticed, though personality changes are often present. Tumors elsewhere in the brain can cause focal findings, including extremity weakness or cranial nerve abnormalities. Diagnosis is made with a CT scan. Because CNS lesions rarely cause agitation, it is not necessary to obtain a CT

scan as part of medical clearance unless there are focal neurologic findings or the patient is at higher risk for a mass (such as cancer with metastatic disease, new-onset daily headache, HIV positive, transplant recipient).

Non-convulsive seizures: Non-convulsive seizures (NCS) may be a more frequent cause of agitation than currently appreciated. Depending on the population studied, they account for up to 25 percent of all seizures (Privetera et al. 1994). Patients with NCS present with sudden onset of confusion, agitation, decreased level of consciousness, fluctuations in behavior, and automatisms (tics, smacking lips, repetitive behavior). In one study of adult emergency patients with altered mental status, mini EEGs showed 5 percent had NCS (Zehtabchi et al. 2013). Of these 75 percent were in status. Of the patients with NCS or status, 69 percent were awake, 50 percent confused and/or agitated, and only 38 percent displayed twitching (Spindler et al. 2013). Hallucinations have been reported in patients with frontal-lobe NCS status (Takaya et al. 2005).

The etiology of NCS is similar to that of convulsive seizures. They are reported in patients with hepatic failure (Prabhakar & Bhatia 2003), are more common in the elderly (Telma et al. 2012), and are seen as an adverse reaction to antibiotics, particularly third- and fourth-generation cephalosporins (Sutter, Suegg, & Tschudin-Sutter 2015). As expected, they are common after traumatic brain injuries, stroke, and hemorrhage (Hirsch 2008).

The diagnosis of NCS and non-convulsive status epilepticus requires an EEG, a test not often available in the emergency department. Therefore, it is not unexpected that most cases are missed in the emergency setting (Kaplan 1996). Patients suspected of having a NCS or status should be treated with intravenous benzodiazepines. Rapid return to a completely normal mental status is highly suggestive of NCS, though the diagnosis requires EEG confirmation. NSC should be considered in patients with a sudden onset of agitation (or stupor), particularly if they have a history of rapid fluctuation in the past.

Environmental Causes

In addition to the many causes of acute agitation or aggression by organic medical illness, substances abuse, or psychiatric disease, many causes may occur from external sources. These include toxic exposures, physical injuries, and large variations in body temperature. At the root of the majority of these causes are inhibition or destruction of basic neuronal synapses and subsequent alteration in release of catecholamines. This is caused by direct injury, cellular destruction, hypoxia, or molecular decoupling. The key to diagnosing these entities is a careful physical exam observing for subtle signs of trauma, and noting odors such as smoke, suggesting carbon monoxide or cyanide, or pesticides. Vital signs are essential and may require a rectal temperature. EMS and family/friends/witnesses often disclose potential exposure or trauma.

Trauma: head injury: Perhaps one of the most common medical causes of acute agitation is head injury. Generally, there is a history of trauma, often with a period of loss of consciousness. Patients may be irritable, agitated, and aggressive. Head trauma often occurs in combination with ingestions of recreational drugs and/or alcohol, complicating the picture.

Trauma patients, even those with apparent isolated trauma, should be thoroughly examined and evaluated for injury to any part of the body. Though the majority of patients with a history of trauma and altered mental status (AMS) will have a traumatic brain injury, the AMS/agitation associated may be due to hypoperfusion, and may resolve with aggressive

resuscitation. An arterial blood gas can provide important information on oxygenation (PO_2), ventilation (PCO_2), and perfusion (base excess or lactate). Patients who are agitated and combative may need to be sedated or even paralyzed to prevent secondary injury. Patients with a suspected head injury should have their cervical spine immobilized, as many traumatic intracranial hemorrhages have an associated cervical spine fracture.

Physical signs of a head injury include hemotympanum, Battle's sign (ecchymosis behind the ear), and raccoon eyes, which are seen with a basilar skull fracture. It is also important to remember that the Cushing's triad of hypertension/bradycardia/irregular respirations may be absent in early intracranial hemorrhage and typically only manifests later. Vital signs are not always a reliable indicator of severity of disease. Heart rate and blood pressure may be very labile in early ICH. Hypotension and hypoxia worsen any injury to the brain. Fluid resuscitation is often necessary for other injuries, but should be less aggressive in patients with isolated brain injury. Sedation is often required as these patients may be very agitated.

Patients with altered mental status and a history of trauma, who are hemodynamically stable, should have a CT scan of the head, and in most cases, cervical spine imaging as well. Bleeding in the brain, subdural, epidural, subarachnoid, or contusion, may be seen, and most of these patients will require inpatient observation. Patients on anticoagulants may have delayed bleeding into the brain, and a repeat CT scan is often obtained in these patients six hours after the traumatic event (Menditto et al. 2012). Many patients with head trauma and agitation will not have a structural bleed, but instead have diffuse edema, suggesting a more generalized traumatic or hypoxic injury. Patients with an abnormal mental status and positive findings on a CT scan require admission and observation. Neurosurgical consultation may be advisable.

Inhalation of Toxic Gases

Cyanide: Cyanide exposures can occur from topical absorption, ingestion of liquid cyanide, or inhalation. Cyanide is surprisingly available to the general population. The primary forms of exposure are colorless gases, hydrogen cyanide (HCN) or cyanogen chloride (CNCl), or a crystal form such as sodium cyanide (NaCN) or potassium cyanide (KCN). Though traditionally thought of as a war agent, cyanide is found in natural substances/foods such as apricot, apple, peach pits, almonds, lima beans, and cassava. Cyanide is used extensively in industry, including paper manufacturing, photographic chemicals, plastics, metallurgy, metal cleaning, and gold ore removal. However, the most common exposure is during a fire, particularly where synthetic materials are burned (Jones, McMullen, & Doughterty 1987). Unfortunately, these chemicals are potential terrorist agents. Death ensues rapidly from large ingestions or exposure to cyanide, but if quantities are small enough, patients will survive to evaluation. Symptoms with smaller doses include dizziness, headache, nausea, vomiting, tachycardia, restlessness, weakness. There is often progression to seizures, syncope, hypotension, bradycardia, and complete cardiovascular collapse. Many times people will speak of the "bitter almond" smell of cyanide; however, the ability to detect this is reported to be only 40 percent of humans. A serum lactate of >10 may indicate cyanide poisoning in the setting of house fire exposure (Baud et al. 1991). Cyanide binds the Fe^{3+} ion of cytochrome oxidase, causing severe hypoxia at the cellular level and subsequent lactic acidosis. In addition, it releases biogenic amine, leading to vasoconstriction and release of NMDA that results in neurotoxicity and seizures.

Rapid administration of hydroxycobalamin, when cyanide toxicity is suspected, is typically safe and effective. It has been described as the ideal antidote for cyanide as it is fast, does not interfere with cellular oxygen use, and is more hemodynamically neutral and safe when there is concern for co-inhalation of carbon monoxide. Indications for this antidote are altered mental status, metabolic acidosis, seizures, or cardiovascular collapse for any suspected cyanide exposure. In a retrospective study of patients given empiric hydroxycobalamin, 67 percent of those with confirmed cyanide toxicity survived and tolerated the medication well (Borron et al. 2007).

Older treatments for cyanide sodium nitrite and sodium thiosulfate are now second-line therapy to hydroxycobalamin. They are more cumbersome to administer and have more side effects. Sodium nitrate induces methemoglobin, which then binds to cyanide, freeing the cytochrome oxidase and restoring cellular oxidation. However, methemoglobinemia causes decreased oxygen utilization and can be extremely dangerous if there is a carboxyhemoglobin level over 10 percent. In addition, sodium nitrate is a potent vasodilator, can cause significant hypotension, and should be used with caution if the systolic blood pressure is less than 100 systolic (Borron et al. 2007). Thiosulfate is then given, which donates a sulfur atom to cyanide creating thiocyanate, which can subsequently be renal cleared.

Carbon monoxide: Carbon monoxide (CO) is a colorless, odorless gas, which displaces oxygen from hemoglobin, causing cellular hypoxia. Patients develop agitation and confusion and progress to seizures and coma. Recent data support that approximately 15,000 ED visits and more than 400 deaths occur each year from non-fire-related CO poisonings (CDC 2005). Also, suicide attempts by CO poisoning are common. Most cars today, however, make limited amounts of CO. Patients without known exposure may be difficult to detect because pulse oximetry will not register any abnormalities. However, the patient will be hypoxic at the cellular level, leading to altered mentation and agitation. CO intoxication occurs by inhalation from sources of burning carbonaceous material. This includes most types of gas-powered heaters or grills and home fires. Symptoms of CO toxicity typically begin at around 10 percent CO blood level with headaches. Once levels reach 50–70 percent, the patient may experience coma, cardiovascular collapse, and death. Symptoms depend on length of exposure as well.

CO causes agitation by inhibiting the ability of the cell to utilize oxygen. CO causes reversible but very strong binding of CO to hemoglobin, displacing oxygen. This strong affinity causes a "functional anemia" and global hypoxia, which can manifest as agitation or altered mental status. Secondary damage from CO is lipid peroxidation and immune mediated inflammation that lends itself to downstream cognitive dysfunction and possibly cardiac dysfunction (Thom 1990; Suner & Jay 2008).

CO-poisoned patients are often agitated or somnolent. Patients may have a multitude of seemingly disjointed complaints, including chest pain, abdominal pain, nausea, vomiting, headaches, and myalgias. Vital signs may be abnormal with the most common finding being tachycardia. Tachypnea may or may not be present and is not reliable. Hyperthermia may occur due to increased metabolic demand. Physical exam can vary from completely benign to focal neurological deficits, rales in the lungs, and/or papilledema.

The primary aim of treatment is to deliver as much oxygen as possible to overcome the binding of CO to hemoglobin. Contacting a poison control service is advised. The presence of very high concentrations of oxygen assists with displacement of the CO. Breathing room air, the half-life of CO is three to four hours. Utilizing 100 percent oxygen (not a

non-re-breather mask) reduces the half-life to thirty to ninety minutes. Hyperbaric 100 percent oxygen at two and a half atmospheres will decrease the half-life even further to fifteen to twenty-five minutes. Patients who survive CO poisoning are at risk for later neurologic deterioration (Lee & Marsden 1994).

Hyperthermia: Exposure to heat is generally compensated by the body with vasodilation and sweating. Sweat leads to evaporation, one of the most effective systems of heat loss. When sweating fails, generally due to dehydration, and vasodilation has been maximized, heat gain often outstrips heat loss, raising the core body temperature. Heat gain may be increased by medical conditions that increase heat generation (hyperthyroidism or use of cocaine) or impede heat loss such as some skin conditions. Symptoms depend on the rate of rise of temperature as well as the temperature reached. Patients present flushed and hot to the touch, and the skin is generally dry. Agitation or somnolence may be present. Seizures and coma may occur. Treatment is rapid cooling using fans and mist or cooling blankets. Antipyretics such as aspirin or acetaminophen are not effective. Hyperthermia can cause rhabdomyolysis, liver failure, cardiac failure, and brain injury.

Hypothermia: Hypothermia below 34°C can cause altered mental status and agitation. Environmental hypothermia is caused by exposure to cold temperature. Exposure and falling body temperature causes shivering, which increases heat generation. However, at temperatures lower than 32°C, shivering ceases. Patients become confused, disoriented, and can be agitated. A peculiar phenomena of paradoxical undressing has been described. Patients may be found naked or discarding clothing in extremely cold conditions (Wedin, Vanggaard, & Hirvonen 1979). Rewarming is complicated and dependent on the core body temperature. In patients with mild to moderate hypothermia (>88°C), passive rewarming can be initiated with simple measures such as warm blankets. Warm saline should be used if fluid resuscitation is needed, as well as warming oxygen to prevent heat loss. Aggressive or active warming such as warming catheters, peritoneal lavage, and bladder lavage should be used if the patient has severe hypothermia with impending cardiovascular collapse or arrhythmia due to an irritated cold myocardium. In rare instances, initiation of antipsychotics can induce hypothermia early after initiation, especially in colder climates.

Diagnostic Keys

While an abnormal finding can suggest a medical cause for agitation, not all abnormal findings require an extensive evaluation. The list that follows is not meant to be all-inclusive, but to serve as a guide.

Vital Signs

Temperature: The presence of fever (>38°C) can reflect an underlying medical condition. Diseases associated with elevated temperature are listed in Table 5.5, and include neuroleptic malignant syndrome, thyroid storm and thyrotoxicosis, and sepsis. Temperature should always be recorded on every patient evaluated for agitation or mental health disturbance.

Hypothermia, typically defined as <36°C, when not due to exposure can indicate a life-threatening illness. A patient with this degree of hypothermia may be at high risk due to lack

Table 5.5. Differential diagnosis of hyperthermia syndromes

• Anticholinergic toxicity syndrome
• Aspirin toxicity
• Delirium tremens
• Heat stroke
• Malignant catatonia
• Neuroleptic malignant syndrome
• Parkinsonism-hyperpyrexia syndrome
• Sepsis-meningo-encephalitis
• Serotonin syndrome
• Sympathomimetic overdose
• Thyrotoxicosis
• Neuroleptic malignant syndrome

Table 5.6. Differential diagnosis for hypothermic medical conditions

• Adrenal insufficiency
• Diabetic ketoacidosis
• Hepatic or renal failure
• Hypoglycemia
• Hypopituitarism
• Hypothyroidism/myxedema coma
• Malnutrition
• Parkinson's disease
• Sepsis
• Stroke

of corrective mechanisms from the hypothalamus or lack of immune response, if this is due to underlying sepsis. Please see Table 5.6.

Blood pressure: Extreme blood pressure changes cause alterations in mentation and agitation. Hypoperfusion and subsequent alteration in cerebral blood flow can easily cause acute agitation in normal individuals. Hypotension can be caused by many occult causes that need immediate evaluation and emergent care. Please see Table 5.7. A thorough evaluation will need to be undertaken to determine the cause of the hypotension, which will guide evaluation and treatment.

High blood pressure without mental status changes and without end organ damage (renal or cardiac) does not need emergent treatment. Diastolic blood pressures <130 mmHg are generally not associated with end organ damage and hypertensive crises (Varon & Marik

Table 5.7. Differential diagnosis for patients exhibiting hypotension

• Sepsis
• Adrenal insufficiency
• Hypovolemia
• Hemorrhage-traumatic, GI losses, vaginal bleeding, etc.
• Ingestion of antihypertensive
• Cardiogenic shock
• Tamponade-tension pneumothorax or pericardial
• Pulmonary embolism
• Arrhythmia

2000). Hypertensive encephalopathy is defined as severe hypertension with altered mental status and end organ damage. Papilledema is nearly always present. Hypertensive encephalopathy is thought to be due to increased cerebral arteriolar pressures. CNS pressure thresholds are overcome and the arterioles begin dilating, causing micro edema and then altered mentation due to more global cerebral edema. This occurs when a patient's auto regulatory limits are bypassed, and that blood pressure is different for every patient. The difficulty for physicians is determining who has bypassed this threshold, as many individuals become accustomed to higher set points and will not have encephalopathy until they reach extremely high blood pressures. Untreated hypertensive encephalopathy has high mortality. However, reducing the blood pressure in patients with or without end organ damage can cause harm. With time, there is a resetting of the patient's CNS arteriolar baseline and if lowered too aggressively patients may experience an ischemic stroke. Current recommendations are to lower by no more than 10–15 percent unless the patient has underlying aortic dissection or eclampsia (Varon & Marik 2003). Management of hypertensive crisis is done by titration of IV antihypertensive medication to achieve BP reduction. Medications should be selected that target the underlying disease entity and this is beyond the scope of this chapter. Such medications include nitroglycerin for pre-load reduction in the volume-overloaded patient with pulmonary edema, IV esmolol, and nitroprusside for aortic dissection to decrease shear stress on the vessel wall, or hydralazine and/or labetalol for a patient with pre-eclampsia needing emergent delivery. Hypertension may have many causes, most of which do not cause agitation. Please see Table 5.8.

Heart rate: Heart rate is highly variable in all humans, but extremes of heart rate may indicate disease. Bradycardia is defined as a pulse less than sixty and is often benign if asymptomatic and the ECG show sinus rhythm. The ECG may show other causes such as second- or third-degree heart block, a junctional rhythm, or ventricular escape rhythms, but unless there is hypotension, bradycardia does not lead to agitation. It can be a clue to an ingestion (e.g., beta-blocker, calcium channel blockers, digitalis) or a serious underlying medical condition like acute myocardial infarction, sarcoidosis, tuberculosis, or hypothyroidism. Bradycardia with hypotension requires treatment. Atropine 0.5 mg, and repeated every three to five minutes with a max of 3 mg often raises the heart rate. Cardiac pacing with a transcutaneous or trans-venous pacer may be indicated.

Table 5.8. Differential diagnosis for patients exhibiting hypertension

• Benign essential hypertension
• Malignant hypertension
• Hypo- or hyperthyroidism
• Renal failure
• Acute cardiac volume overload/CHF exacerbation
• Pheochromocytoma
• Sympathomimetic ingestion
• MAOI use
• Oral contraceptives
• Etoh abuse
• Coarctation of the aorta
• Antihypertensive w/d primarily clonidine
• Pre-eclampsia
• Ischemic CVA
• Hemorrhagic CVA – Intraparenchymal/Subarachnoid
• Aortic dissection

Normal sinus rhythm is defined as a heart rate between 60 and 100 beats per minute. A delicate balance between the sympathetic and parasympathetic systems maintains this normal rate. The etiology of sinus tachycardia in the altered or agitated patient is almost always multifactorial, resulting from innate catecholamine response to stressful stimuli, and often compounded by ingestion of synergistic drugs. If the remainder of a patient's vital signs are normal but a patient remains tachycardic despite being calm and ingestion is not suspected, further evaluation may be needed. Please see Table 5.9. Acute treatment of isolated, asymptomatic sinus tachycardia is not generally indicated.

Respiratory rate and pulse oximetry: Respiratory rate is rarely accurately quantified, but can be an excellent indicator of underlying pathology. Many emergent medical conditions have tachypnea as part of their presentation. However, it also can be a component of many primary psychiatric complaints. This must be a diagnosis of exclusion, and all tachypnea must be critically analyzed (Lewis & Howell 1982). Presence of tachypnea should always prompt immediate evaluation with pulse oximetry and physicians should have a low threshold to administer supplemental oxygen. Generally, a reading less than 94 percent on pulse oximetry should be treated with oxygen via nasal cannula and monitored for improvement. Please see Table 5.10.

Physical exam: A complete physical exam may uncover subtle signs of underlying disease, and the highest yield often is the neurologic exam of the agitated and altered patient. Signs of trauma, thyroid goiters, and focal extremity weakness are clues to underlying pathology. Ophthalmoplegia may suggest Wernicke encephalopathy, which does not always present with

Table 5.9. Differential diagnosis for patients exhibiting tachycardia

• Acute MI
• Anemia
• Antihypertensive withdrawal, beta-blockers
• Anxiety
• Acute decompensated heart failure
• Hyperthyroidism
• Hypovolemia
• Shock – septic/cardiogenic/obstructive
• Hypoxia
• Pain
• Pheochromocytoma
• Pulmonary embolus
• Inappropriate tachycardia (diagnosis of exclusion)

Table 5.10. Differential diagnosis for patients exhibiting tachypnea

• Acidosis-diabetic ketoacidosis, aspirin toxicity
• Electrolytes hypoglycemia, hypocalcaemia
• Arrhythmia
• Heart failure
• Pulmonary embolism
• Pulmonary parenchymal disease – asthma, COPD, pneumothorax
• Hyperthyroidism

the complete triad (Harper, Giles, & Finlay-Jones 1982) or an mass lesion. Pronator drift (or Barre sign) is sensitive for detecting upper extremity weakness (Darcy & Moughty 2013).

Lab/imaging: Patients described earlier as high risk should have a screening laboratory evaluation consisting of electrolytes, CBC, EKG, and, if indicated, thyroid function tests (TSH, Free T3/T4). Additional tests may be indicated when specific disorders are suspected. These tests are not indicated for all patients presenting with agitation. Elevated white blood count or abnormalities in electrolytes may suggest the cause of the agitation. A serum lactate >4 indicates severe tissue injury and anaerobic metabolism, and suggests hypoperfusion in a patient with tachycardia or hypotension. Severe sepsis and septic shock cause elevation in lactate. In a study of infected patients presenting to the ED, those with a lactate of 4 or greater had a 28.4 percent mortality within three days (Shapiro et al. 2005).

Complete blood count: The CBC has little utility in the routine screening of the psychiatric patient. Elevation in white blood count can be seen in infection, due to medications and

also to cytokine release from the agitation (Anfinson & Kathol 1992). An elevation in bands or juvenile neutrophils or neutrophil predominance may suggest infection. The presence of macrocytosis suggests chronic and significant alcohol intake. Low platelets can be another indicator of alcohol abuse or liver disease. Severe leukocytosis (WBC >100,000) occurs in leukemic and myeloproliferative disorders and can result in vascular occlusion and subsequent altered mental status or focal neurologic deficits. These patients should be aggressively volume resuscitated starting with two liters of IV crystalloid to help create a dilution effect and improve perfusion.

ECG/monitor: Routine ECGs are indicated on any psychiatric patient over the age of fifty admitted to the psychiatric unit. In the younger age group, the general consensus is that screening should be done if they are on psychotropic drugs that alter cardiac conduction or there is concern of cardiac ischemia or other cardiac pathology (Hollister 1995).

Approach to the Agitated Patient

Many patients, with and without underlying mental health disorders, present with agitation. The first consideration should always be for the safety of the staff, other bystanders, and the patient. Verbal de-escalation or restraints may be necessary before an evaluation can begin. Full vital signs should always be taken. The patient should be screened for the high-risk criteria listed earlier in this chapter. Patients with normal vital signs and no high-risk criteria, particularly those with a history of psychiatric disease, require no further evaluation. Patients in the high-risk category should have a medical evaluation and when indicated should undergo laboratory testing and imaging. Those suspected of non-convulsive seizures should receive an EEG if immediately available, or have a trial of benzodiazepines. Because patients with severe agitation can be unstable, medical resuscitation equipment should be available.

Resolution of the Case

The patient's pill bottles were examined in search of a possible overdose. It was discovered that her prescription for levothyroxine had been written for 3.0 mg/day instead of 0.3 mg/day and the pharmacist had instructed the patient to take that excessive dose. The patient was immediately treated with beta-blockers and returned to her normal baseline mental status in the next forty-eight hours. This case of thyroid storm was caused by an unintentional overdose of thyroid medications.

Additional Illustrative Cases

Case 1: A thirty-two-year-old male presents with auditory, command-type hallucinations, which started one week ago and have been getting gradually worse. He has a history of paranoid schizophrenia with several episodes of acute psychosis. He reports compliance with his risperidone. He has no suicidal or homicidal ideations. He has no other past surgical or medical history. He denies any chest pain, abdominal pain, and urinary symptoms. He has no neurological complaints and notes that he actually feels quite well. He has a normal neurological, cardiac, respiratory, and skin exam.

HR – 89, BP – 156/94, RR – 12, Temp – 98.6

Assessment: This is a well-appearing male with acute psychosis from his baseline paranoid schizophrenia. He has mild alteration in his BP, but no indication of end organ damage. He can be evaluated without laboratory or radiologic evaluation.

Case 2: A twenty-two-year-old male with no past medical history presents to the ED with his family. He had returned from college and began acting strangely. His mother states he has been speaking to himself and is very withdrawn. He admits to hearing voices, and denies homicidal or suicidal ideation. He denies any other complaints at this time, and admits to occasionally smoking marijuana. There is a family history of schizophrenia. He is alert and oriented, he has no focal weakness, sensory deficits, ocular movement problems, or speech difficulties and is ambulatory in the room. His oral mucosa is moist/pink, and his thyroid is without goiter or bruit. He demonstrates a normal work of breathing with clear lungs and his cardiac exam is benign.

Temp – 98.6, HR – 87, BP – 110/65, RR – 12, pulse oximetry – 100 percent on room air

Plan: This is the first presentation of a patient that seems to be demonstrating signs of schizophrenia. He has a history of recreational drug use, but his vitals and physical exam are normal. Because this is a first presentation CBC, basic chemistry including glucose, renal function, and sodium are indicated. Urine drug screens can be ordered in this situation, but are not mandated. This patient had a normal workup and was evaluated by our psychiatrists, treated, and sent to outpatient follow-up.

Case 3: A fifty-five-year-old female is brought to you for evaluation due to acting strangely. She was found close to your facility darting in and out of traffic on foot and had been noted earlier in the day throwing rocks at children at a local neighborhood park. She is restrained, speaking unintelligibly, but occasionally will say things such as "let me go" or "get away from me." No other history is available. She has multiple abrasions to her hands and forehead and several contusions over her arms at various stages of healing. Her oropharynx is dry, with poor dentition, pupils are 7 mm and equal/reactive, thyroid is not enlarged. She is restrained, but she has intact strength in all four extremities. She has a regular tachycardia without murmur. Lungs are clear.

Temp – 100.4, HR – 139 sinus, BP – 156/95, RR – 22, pulse oximetry 99 percent on room air

Plan: This is an acutely agitated female with psychotic features, but with multiple vital sign abnormalities. First priority should be resuscitation, and then evaluation. First choice for sedation should be benzodiazepines, as her vitals indicate possible sympathomimetic or possible anticholinergic toxidrome. She is hyperthermic, tachycardic, tachypneic, and hypertensive, so she has many entities discussed earlier in this chapter that should be on her differential, including thyroid storm, sepsis, encephalitis, and drug ingestion, including ASA and sympathomimetic, or occult head injury. Evaluation should include CBC, chemistry, creatine phosphokinase, lactic acid, urinalysis with drug screen, TSH with free T4, syphilis screen, CT head, and EKG. This patient may need a lumbar puncture if her mentation does not clear rapidly or another source is not identified.

The patient was found to have normal head CT, CBC, thyroid function tests, and syphilis screen. Her EKG showed regular sinus tachycardia with normal intervals, her serum lactic acid returned at 2.7, and her CK was elevated at 19,000 with a creatinine of 2.1. She had no other abnormalities on her chemistry studies. She received multiple doses of lorazepam with eventual resolution of her agitation. She was at that point able to inform us that she had been using methamphetamines continuously for three days prior to presentation. Her mental status eventually returned to normal, and after three days of IV hydration, her serum creatinine improved to 1.3 and her rhabdomyolysis resolved.

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Chapter 6

Special Populations: Agitation in Elderly Patients

Eric L. Anderson

Case Reports

Case Report #1: Ms. M., a sixty-seven-year-old widow, presented to her outpatient psychiatrist for evaluation of agitation and mood swings ongoing for several weeks. She had a known history of bipolar disorder, which was stable on a regimen of lithium. When she presented, she and her family had noticed changes in her mental status, to include instability of her mood and unprovoked agitation, uncharacteristic for her. Initial testing of her lithium levels revealed therapeutic, nontoxic levels. After several weeks of medication adjustments, including the addition of atypical antipsychotic agents, it was felt admission for inpatient treatment was warranted. During the course of her admission workup, a head CT was completed. The results of that CT indicated multiple intraparenchymal lesions, consistent with glioblastoma multiforme. Two weeks after her psychiatric admission, Ms. M. succumbed to her malignancy.

Case Report #2: Mr. J., a seventy-year-old married male, presented to a local emergency department (ED) for complaints of suicidal ideations in the context of alcohol withdrawal. He endorsed a lifelong struggle with excessive alcohol use and desired treatment. He denied any history of medical or psychiatric illness; nonetheless, given concerns for his safety, he was admitted to a psychiatric treatment facility. To treat his detoxification from alcohol, benzodiazepines were used on an as-needed basis, based on a standard alcohol withdrawal protocol. During his course of treatment, Mr. J. demonstrated agitation and extreme suspiciousness toward the staff and other patients. He accused various staff members and patients of spying on him, and he was convinced cameras were placed in his room to record his every action. He also complained of auditory perceptual disturbances of people talking, even when no one was near him. During this time, no significant evidence for alcohol withdrawal manifested. Upon obtaining collateral information from his family members, they reported Mr. J. had experienced such symptoms sporadically during his life, but they seemed diminished whenever he drank alcohol. Ultimately, Mr. J. was diagnosed with schizophrenia in addition to his alcohol misuse syndrome, and discharged on a low-dose antipsychotic.

Introduction

Agitation in elderly patients presents a unique problem to health care providers. Many elements of the differential diagnosis and treatment algorithms remain the same as with younger patients, but elder patients with agitation present an additional set of unique diagnostic and treatment challenges. The purpose of this chapter is to present

guidance in evaluating and treating agitated elderly patients, defined as patients over the age of sixty-five.

Background

In 2012, there were 43.1 million people in the United States over the age of sixty-five, comprising about 14 percent of the total U.S. population (Sikka, Kalra, and Galwankar, 2015). More than 15 percent of all ED visits are by patients over the age of sixty-five (Nassisi et al., 2006; Goveas and Harsch, 2008). While the majority of elderly patients visit the ED for medical reasons, 5 percent of all visits by the elderly are for psychiatric reasons (Ettinger et al., 1987). In elderly patients presenting for psychiatric reasons, 20–50 percent may be at risk for agitation, and 10 percent may become agitated or violent during their assessment (Zeller and Rhoades, 2010). Elderly patients are more likely to have emergent issues than their non-elderly counterparts, and they are also less likely to use the ED for primary care or pure social problems (Ettinger et al., 1987). Elderly patients have higher acute visit rates, longer ED stays, and, if admitted, have longer hospital stays than younger adults (Walsh et al., 2008).

Elderly patients differ from non-elderly patients in numerous ways that are important to consider in their evaluation. Elderly patients tend to have multiple chronic physical disorders, and therefore typically take numerous daily medications (Tueth, 1994). The average elderly patient presenting to the ED has more than four routine medications per day; 91 percent have at least one daily medication and 13 percent have eight or more daily medications (Sikka et al., 2015).

Patients over the age of sixty-five also have different physiological considerations. Age-related changes to metabolism affect both pharmacokinetics and pharmacodynamics in the elderly, resulting in a higher risk of side effects (Zayas and Grossberg, 1998; Rossi, Swan, and Isaacs, 2010). Elderly patients experience a decrease in their body's responsiveness to hormones, decreased renal blood flow, and decreased hepatic blood flow. Renal blood flow loss is on the order of 1 percent per year, leading to a progressive decline in total renal clearance. Both the renal and hepatic blood flow decreases are important because they translate to increased half-lives for medications cleared by these routes. As humans age, a systemic decrease occurs in tissue elasticity. Rigidity of cardiac muscle leads to decreased cardiac output. Lung diffusion capacity also decreases, so arterial pO2 declines. The effectiveness of the immune systems declines, so elderly patients are more susceptible to infections. While gastrointestinal absorption does not vary significantly, decreased blood flow to the skin and decreased tissue elasticity mean medications administered by the transdermal route may have reduced action. Finally, with advancing age, both skeletal muscle mass and total body fat decrease (Turnheim, 2003).

Presentation

Agitation, regardless of age, is generally defined as restlessness, excessive or semi-purposeful motor activity, irritability, hyper-responsiveness to both external and internal stimuli, nonspecific and relatively unrelated behaviors, and a fluctuating and unpredictable or unstable course (Lindenmayer, 2000; Zeller and Rhoades, 2010). While no single underlying etiologically based pathophysiology has been clearly identified, the neurocircuitry of agitation may be common across a variety of diseases, which explains why a reduction in dopaminergic or noradrenergic responses and/or an increase in GABAergic responses

Table 6.1. Predictors of agitation in the elderly (Bross and Tatum, 1994; Tueth and Zuberi, 1999; Kennedy, 2003; Piechniczek-Buczek, 2006; Han et al., 2009)

Delirium
Intoxication
Assaultive behavior prior to the ED (recent more so than remote)
Past episodes of agitation
Active psychiatric conditions: psychosis, mania, paranoia
Pain
Verbal threats
Aggressive physical behavior: hyperactive, clenched fists/jaw, combat stance
Substance abuse, such as alcohol
Personality disorder, such as antisocial
Cognitive deficits, such as dementia
Sensory deficits, such as vision or hearing
Noncompliance with treatment
Uncontrolled anxiety, such as panic
Poor insight
Seizure disorder
Head injury
Social isolation
Concomitant use of multiple meds
Functional dependence

will usually decrease agitation (Bellnier, 2002). Agitation can be verbal, physical, or both. Verbal agitation manifests as screaming, name calling, cursing, derision of others, or repetition of words, sounds, or questions. Physical agitation presents as belligerence, kicking, punching, hitting, scratching, biting, pushing, sexual disinhibition, or undressing or voiding where not appropriate. No matter the age of the patient, it is imperative to discover the intention and motivation for the behavior (Goveas and Harsch, 2008).

Agitation in younger patients is more likely to be secondary to substance abuse or psychiatric illness, which is not the case with elderly patients (Nassisi et al., 2006). In the elderly, the most common causes of agitation are non-psychiatric, such as altered mental status due to dementia, delirium, environmental changes, or medical illnesses (Tueth, 1994; Goveas and Harsch, 2008). In younger patients with agitation, there is often a prodromal period of restlessness, loud speech, and pacing. This prodromal period is frequently absent in elderly patients. However, warning signs for agitation do exist (Table 6.1). For example, when family or caregivers are at the bedside, but the patient remains anxious, suspicious, evasive, or confused, anticipate possible behavioral disturbances such as agitation.

Elderly patients who are agitated present with confusion, aggression, psychosis, and behavioral disturbances. Hospitals lack familiar cues and are active and stimulating.

Agitated elders may unwittingly fall from bed, pull out lines, lash out, or grip at staff or objects, unlike younger patients. Thus, expedited assessment and targeted treatment are two primary goals in agitated elderly patients.

Assessment

Elderly patients are complex, so a "sort out" rather than "rule out" approach to the assessment may be more helpful in this population. Assessment of elderly patients tends to be more time-intensive because they rarely present with a single, well-defined issue. To the contrary, they often have multiple medical or neurological comorbidities (Goveas and Harsch, 2008). Assessment begins with safety of the patient, caregivers, other patients, and staff. Older adults are vulnerable to the disorienting effects of the ED, so efforts to place them at ease may aid both in obtaining necessary information and preventing agitation (Kennedy and Lowinger, 1993).

While the assessment of elderly agitated patients is similar in many ways to the assessment of their younger counterparts, important differences do exist. A brief summary of the assessment, provided in more detail elsewhere, is provided in Table 6.2. Evidence indicates that in agitated elderly patients, the history of present illness, past medical history, physical examination, and evaluation of current medications has the highest utility for determining the cause of agitation (Odiari et al., 2015).

First, a detailed history of present illness must involve caregivers, family, providers, or witnesses. This should include their observations of the patient's baseline mental status and

Table 6.2. Assessment of the agitated elderly patient (Goveas and Harsch, 2008; Xiao et al., 2012)

> Initial stabilization: airway, breathing, LoC
> Chief complaint, identification
> Reliability of information provided by the patient
> Informants
> History of present illness
> Past psychiatric history: diagnoses, treatment (outpatient and inpatient), and compliance
> Past medical history: chronic and acute illnesses, head injuries, falls, seizures, diabetes, recurrent infections, etc.
> Medications: prescribed and over-the-counter, herbals; compliance; recent additions, changes, or deletions; who manages; confirm with pharmacy prescription
> Substance use history: illicit, alcohol, abuse of legitimate prescriptions
> Physical examination: especially vital signs, oxygen saturation, neurological examination, and evidence for abuse/neglect
> Mental Status Examination: including a cognitive function assessment such as the MMSE, CAM, or MoCA
> Home functioning: ability to perform activities of daily living
> Labs: glucose, complete blood count, urinalysis, metabolic panel, TSH, and other labs as deemed necessary by the examination
> Imaging: head CT

behavior (Nassisi et al., 2006). Another function of obtaining collateral is to assess the stress level of caregivers and their ability to continue to provide care for the patient (Goveas and Harsch, 2008). In many cases, due to agitation or poor cognitive function, external collateral information may be the only way to piece together the patient's pre-hospital course. Important to this process is determining the timing of and factors associated with the agitation: When did it begin? Does it change throughout the day? Was there a recent sleep pattern or medication change? (Bross and Tatum, 1994).

The medical and psychiatric histories should include any history of psychiatric conditions, such as bipolar disorder, depression, and psychotic disorders, or medical conditions, such as dementia or recurrent delirium. However, note that 60 percent of hospital patients over the age of sixty-five have or will have a mental or cognitive health problem, such as delirium, dementia, or depression (Goldberg et al., 2012). Most conditions presenting as psychiatric emergencies stem from a non-psychiatric, organic cause (Borja et al., 2007). It is often difficult to separate out these etiologies one from the other; therefore, the patient's past history, especially a past psychiatric history, should not lead clinicians to prematurely limit or close their differential and conclude that the patient's presentation is merely an exacerbation of an underlying mental illness (Borja et al., 2007; Peisah et al., 2011).

The medication and substance use history should include medications in use, their administration history, and any history of noncompliance or overuse (Nassisi et al., 2006; Odiari et al., 2015). There should be a careful assessment for alcohol use or misuse, illicit drug use, and overuse or abuse of over-the-counter, non-prescription medications, and herbal supplements (Goveas and Harsch, 2008).

Physical examinations in agitated elderly patients should always include vital signs measurement and oxygen saturation. Point-of-care glucose testing is considered a vital sign in elderly patients and should be measured (Nassisi et al., 2006; Odiari et al., 2015). A complete neurological examination should evaluate for focal deficits and sensory deficits, such as hearing and vision impairment.

The Mental Status Examination is detailed elsewhere, but every agitated elderly patient should have a thorough Mental Status Examination completed. As part of this evaluation, a cognitive evaluation is necessary (Goveas and Harsch, 2008). The most frequently used cognitive tests used in the acute setting include the Folstein, Folstein, and McHugh Mini Mental Status Examination (MMSE), the Montreal Cognitive Examination (MoCA), the Confusion Assessment Method (CAM) (Inouye et al., 1990), and the Memorial Delirium Assessment (MDA) (Bross and Tatum, 1994; Breitbart et al., 1997; Goveas and Harsch, 2008). The MMSE has 87 percent sensitivity and specificity of 82 percent to detect organic brain syndromes, such as delirium, in hospitalized patients (Nassisi et al., 2006). The CAM has sensitivity of 93–100 percent and specificity of 90–95 percent for delirium (Nassisi et al., 2006). As part of the cognitive evaluation, the patient's functional status should be assessed. This includes the patient's ability to perform both basic and instrumental activities of daily living.

A number and variety of agitation scales exist, such as the Aggressive Behavior Scale, Brief Agitation Rating Scale, and Positive and Negative Syndrome Scale – Excited Component. Scales may serve a useful function for staff more so than patients, as they can prevent defensive behaviors such as ignoring or avoiding the patient (Richmond et al., 2012). None has been tested exclusively in the elderly population, and few have been used to assess the efficacy of medications used to treat agitation (Zeller and Rhoades, 2010). Another drawback of agitation scales is they only provide a snapshot of the patient at a specific point

in time. Therefore, these scales have limited utility in the acute assessment and management of agitation in the elderly.

Laboratory testing is a matter of debate, but many authors agree that in elderly patients with agitation, a complete blood count, metabolic panel to include liver and renal functions, thyroid function, Vitamin B12 and folate levels, urinalysis, EKG, and chest radiograph are appropriate baseline tests to help rule out common causes, such as delirium (Tueth, 1994; Nassisi et al., 2006; Odiari et al., 2015). Other studies should be guided based on findings from the physical examination and include a head CT, lumbar puncture, blood culture, toxicology screens, and blood gases (Tueth, 1994; Nassisi et al., 2006). The purpose of laboratory testing is to rule out underlying medical etiologies such as infection, electrolyte disturbances, and medications (Tueth and Zuberi, 1999).

Differential Diagnosis

As noted earlier in this chapter, elderly patients with agitation differ from younger patents in the likely etiology leading to the behavioral disturbance. The most common causes of agitation in the elderly are delirium, dementia, and psychoses, either primary or secondary (Tueth and Zuberi, 1999). The purpose of the evaluation detailed previously is to sort through the patient's symptoms in order to determine the likely cause in order to guide treatment. Table 6.3 lists some of the more common causes of agitation in the elderly.

Delirium: Delirium is present in 10 percent of all elderly ED patients (Hustey, 2005; Han et al., 2009). Patients who are delirious present with problems with attention, disorganized thinking, or behavior, a fluctuating clinical course, changes in level of consciousness, and/or perceptual disturbances that are typically relatively recent or rapid in onset (Tueth, 1994; Sikka et al., 2015). A global disturbance in cognition and consciousness presents with global cognitive impairment. This disturbance is due to a medical condition (Nassisi et al., 2006), but in half of all cases, the inciting etiology is not readily identified. Two subtypes exist, the hypoactive type, which is the most common, and the hyperactive type (Hustey, 2005; Han et al., 2009). In the hyperactive type, patients present with increased activity, agitation, anxiety, and aggression (Hustey, 2005; Han et al., 2009). Patients discharged from the ED with unrecognized delirium have higher death rates compared to those with recognized delirium or without delirium (Kakuma et al., 2003).

Risk factors for delirium include dementia, functional dependence, and hearing impairment, with dementia the strongest risk factor (Han et al., 2009). Common causes include medications such as anticholinergic or sedating agents, physical illness, metabolic disease, and substance withdrawal (especially alcohol). Many of the causes of agitation listed in Table 6.3 are also causes of delirium.

In elderly patients with agitation, one should presume the altered mental and behavioral status is secondary to delirium until proven otherwise (Nassisi et al., 2006; Peisah et al., 2011). In one review it was noted that delirium occurs in 22–38 percent of hospitalized elderly patients (Bross and Tatum, 1994). However, it was only correctly diagnosed in fewer than 20 percent of cases. Another study showed that 76 percent of cases of delirium were missed by ED physicians (Han et al., 2009). In another recent study, emergency physicians who used routine clinical observations without cognitive evaluations missed diagnosing delirium in up to two out of three patients (Suffoletto et al., 2013).

Table 6.3. Causes of agitation (Kennedy and Lowinger, 1993; Tueth and Zuberi, 1999; Nassisi et al., 2006; Piechniczek-Buczek, 2006; Borja et al., 2007; Conwell and Thompson, 2008; Goveas and Harsch, 2008; Odiari et al., 2015; Sikka et al., 2015)

Delirium
Dementia
Medications (interactions, toxicity, side effects, overdose), such as anticholinergics, antihistamines, steroids
Pain
Infection or sepsis
Hypoglycemia or hyperglycemia
Substance intoxication (especially alcohol) or withdrawal
Hypotension
Dehydration
Hepatic failure
Renal failure
Cardiac disease (CHF, MI, arrhythmias)
Electrolyte disturbances (especially sodium, magnesium, phosphorous, and calcium)
Hypoxemia or hypercarbia
CNS injury, infection, lesions such as CVA, SDH, encephalitis, meningitis
Endocrine disease (especially thyroid, diabetes, or adrenal)
Acute abdominal pathology (ischemia, volvulus, appendicitis, diverticulitis)
NMS
Trauma
Functional impairment or frustration
Physical needs: hunger, thirst, need for toileting, constipation
Home life (rigid or inattentive caregiving, abuse, neglect, family discord, living alone/low social support, changes in support network, relocation)
Environmental factors (overstimulation/understimulation, noise, crowding)

Therefore, in elderly patients with agitation, standardized cognitive testing such as the CAM, MoCA, MMSE, or MDA is recommended.

Dementia: Dementia impacts 8–10 percent of those older than sixty-five, nearly 50 percent of those over eighty-five (Sikka et al., 2015). In addition to being a strong risk factor for delirium (Nassisi et al., 2006), there is a high rate of psychosis (50%) in patients with dementia (Tueth, 1994). In patients with dementia, aggression, agitation, and irritability are common, with at least one out of two outpatients with certain types of dementia having agitation (Amann et al., 2009). Regardless of cause, patients with dementia have a predisposition to agitation in the ED due to neurobiological dysregulation, cognitive

impairment, and the unfamiliar environment of the ED (Raskind, 1999). Precipitants for agitation in dementia are listed in Table 6.3.

Psychosis: Psychosis is a disturbance in thought processes or the loss of contact with reality (Piechniczek-Buczek, 2006). Perceptual disturbances such as hallucinations are the most familiar type of psychosis, but delusions and disorganized thought or behavior are also psychotic symptoms. The presence of psychosis does not automatically equate to a psychiatric illness, as these symptoms are not specific to psychiatric disorders. Late-onset psychotic symptoms are typically related to brain changes instead of new, primary psychiatric conditions (Goveas and Harsch, 2008). The incidence increases with age, possibly secondary to frontal and temporal lobe age-related deterioration (Piechniczek-Buczek, 2006).

Depression: Depression is common in older patients; 30 percent of elderly patients visiting the ED may suffer from it. Depressed elder patients tend to be more somatic and cognitively impaired than younger patients, placing them at greater risk for agitation. Depressed elderly patients are at a high risk for suicide, especially in the presence of agitation; their rate is almost twice that of the general population (Alexopoulos et al., 2002; Waern et al., 2002; Conwell and Thompson, 2008).

Management

The basic principles of management of agitation in elderly patients are similar to non-elderly patients: creation of a safe environment for the patient, caregivers, staff, and others, and to facilitate assessment and treatment of the patient (Piechniczek-Buczek, 2006). Common pitfalls to avoid in this population include treating the agitation without seeking or understanding the etiology of the agitation, ordering automatic and unreviewed as needed medications, especially antipsychotics, and oversedation. As with younger patients, management should seek to gain control of the behavior utilizing the least restrictive means possible (Tueth and Zuberi, 1999). Management can be broadly divided into two categories: medication and non-medication. Given the complexity of elderly patients medically and socially, a team approach is best in managing agitation.

Non-medication management: For patients who present not in an agitated state, timely recognition of the potential for agitated behavior and efforts to prevent agitation are best (Nassisi et al., 2006). Predictors of agitation are listed in Table 6.1 and can be used as a guide to help prevent agitation. Other non-medication ways to try and prevent agitation include the management of sleep deprivation, assessing for and treating dehydration, and addressing immobility, vision impairment, and hearing impairment (Nassisi et al., 2006). Finally, given it is an independent risk factor for agitation, pain complaints should be identified and managed as expeditiously as possible.

For patients who are already agitated but not imminently dangerous to themselves or others, an individual treatment plan with cognitive behavioral therapeutic approaches using verbal de-escalation is recommended (Amann et al., 2009) (Table 6.4). Staff should be both appropriate and trained in behavioral management of agitation (Richmond et al., 2012). This plan should include environmental cues, family/loved ones' involvement to reorient the patient, and avoiding excessive noise or stimulation (Nassisi et al., 2006). Patients should be moved to an area where they can best be closely observed. Remove or control for any

Table 6.4. Behavioral management strategies for agitation in elderly patients (Nassisi et al., 2006; Piechniczek-Buczek, 2006; Goveas and Harsch, 2008; Amann et al., 2009; Peisah et al., 2011; Richmond et al., 2012)

Involvement of family, caregivers, or other loved ones
Quiet environment
Move to area easily observed
Remove means of self-harm: cords, hangars, tubes, etc.
Restrict access to harmful environment: stairs, windows, balconies, etc.
Methods of distraction
Early, calm, simple verbal reassurance
Polite and brief interactions
Gentle but firm redirection
Manage or control for sensory deficits, such as hearing and vision
One-to-one nursing

potential means for self-harm, be it intentional or accidental (Richmond et al., 2012). This includes open windows, balconies, hand hoists, stairs, cords, and coat hangers. Distraction devices, such as having something tactile the patient can manipulate (stacks of towels, magazines, cards) and placement of tubes out of reach are part of this treatment plan. Screen for falls and implement fall prevention measures. Consider one-to-one nursing in patients who are unpredictable or difficult to redirect, even with family/caregiver support (Peisah et al., 2011). Other behavioral management strategies include gentle redirection of distressed patients, calm interaction, and the promotion of appropriate social activities and interactions (Piechniczek-Buczek, 2006). Verbal interactions should include repeated reassurance, speaking slowly and calmly, using simple sentences and questions, and being polite (Goveas and Harsch, 2008; Richmond et al., 2012). The show of force, where multiple staff members present themselves before the patient in an effort to control behavior by the suggestion of strength in numbers, does not typically work in agitated elderly patients, and thus should be avoided (Goveas and Harsch, 2008).

Medications: The primary goal of medication management of agitation in the elderly is rapid calming without excessive sedation in order to identify the cause of the agitation and to target management toward specific behaviors (Goveas and Harsch, 2008; Peisah et al., 2011). There is little evidence in the literature to guide medication management of elderly patients. Avoid unnecessary use, over use, and medication combinations when possible (Nassisi et al., 2006). This approach in turn will aid in determining the diagnosis more accurately because then the patient can more willingly participate in the evaluation (Cremens, 2004). In the elderly patient, start at a low dose, 50 percent of the usual starting dose, and increase slowly, bearing in mind the altered absorption, metabolism, and clearance described earlier in this chapter (Turnheim, 2003). Whenever safe and possible, the patient or their caregiver's preference in medication should be honored.

The preferred route of medication remains the same as for younger patients with agitation: oral (PO), then intramuscular (IM), then intravenously (IV) (Zeller and

Rhoades, 2010). One rationale for avoiding IM and IV administration in the elderly is that these forms can be seen as punishment, enslaving, or a violation of a person's integrity rather than therapeutic (Yildiz et al., 2003). When administering medications, bear in mind that the elderly are highly susceptible to adverse drug reactions.

For patients with altered mental status or agitation where the inciting cause is unknown, the American College of Emergency Physicians recommends the use of either a benzodiazepine, such as lorazepam or midazolam, or a first-generation antipsychotic (FGA), such as haloperidol or droperidol, as monotherapy. In patients with a known psychiatric illness, either an FGA or an atypical, second-generation antipsychotic (SGA) is recommended, with no specific agent recommended (Lukens et al., 2006). But, as noted previously, these recommendations were not specific to elderly patients. While the American Association for Emergency Psychiatry (AAEP) stated a preference to avoid using antipsychotics or benzodiazepines in the frail elderly as first-line treatment, suggested second-line agents include risperidone, haloperidol, and olanzapine (Allen et al., 2005). No first-line agents were provided in their recommendations. Other agents listed as treatment options include ziprasidone, quetiapine, droperidol, and chlorpromazine (Allen et al., 2005).

In its recommendations published in 2012, the AAEP's "BETA project" (Best practices in the Evaluation and Treatment of Agitation) recommended treatment based on the likely etiology. For agitation associated with delirium not due to benzodiazepine or alcohol withdrawal, risperidone, olanzapine, and haloperidol were recommended orally, followed by IM olanzapine, ziprasidone, or haloperidol, the latter which could be used IV (Wilson et al., 2012). For agitation associated with psychosis in a patient known to have an underlying psychiatric disorder, similar recommendations were made, but with the exception of adding a benzodiazepine concurrently with haloperidol (Wilson et al., 2012). Again, these recommendations did not specifically consider the elderly patient.

Antipsychotics

Antipsychotics have the potential for metabolic, cardiovascular, and extrapyramidal (EPS) side effects (Amann et al., 2009). Low-potency FGAs such as chlorpromazine have high anticholinergic side effects and may worsen cognitive function. They are also sedating, so their use is not recommended in elderly patients (Goveas and Harsch, 2008). High-potency FGAs, such as haloperidol, have a lower risk for respiratory depression, hypotension, and anticholinergic side effects than low-potency agents (Nassisi et al., 2006). Droperidol is more potent and sedating, with a more rapid onset of action and shorter half-life than haloperidol. In a recent study of its use in elderly patients with agitation, it was found effective for sedation with no QT prolongation noted (Calver and Isbister, 2013). In addition to the usual concerns of FGA use, extra caution should be taken in patients with dementia with Lewy bodies, as high-potency FGAs can dramatically lower the threshold for EPS.

CATIE trials have demonstrated no statistically significant difference in efficacy or incidence of EPS when comparing FGAs and SGAs (Lieberman et al., 2005). However, SGAs have been recommended by consensus guidelines (Alexopoulos et al., 2005). In moderate doses, SGAs, specifically risperidone, ziprasidone, and olanzapine, are effective treatment alternatives for agitation in emergency settings (Yildiz et al., 2003). Olanzapine

and ziprasidone have evidence for utility in agitated younger patients, but evidence in the elderly is limited. Risperidone has been studied in detail for agitation, especially in patients with dementia. It has been shown to possess efficacy equal to haloperidol in controlling agitation in delirium (Peisah et al., 2011). These studies have been over time, however, and do not directly address efficacy to immediately control acute agitation (Nassisi et al., 2006). If an IM agent is necessary, olanzapine is preferred (Allen et al., 2005), but patients should be observed for hypotension or bradycardia (Peisah et al., 2011). Evidence also exists for the use of ziprasidone, with some studies finding it as effective as haloperidol (Kohen et al., 2005; Piechniczek-Buczek, 2006). It has a lower risk for EPS than haloperidol, but it has an elevated relative risk of prolonging the QTc interval (Bellnier, 2002). There are limited studies for the use of aripiprazole in acute agitation, but it has been noted to be well tolerated and effective in treating psychosis associated with certain kinds of dementia (Goveas and Harsch, 2008). Loxapine has recently been made available in an inhaled form. Although its efficacy has not been tested specifically in elderly patients, it has been shown to decrease agitation as early as ten minutes after administration. The risk of post-administration bronchospasm requires it be offered in a facility enrolled in a risk evaluation and mitigation strategies program (Citrome, 2015).

There is no role for long-acting or depot antipsychotic agents in the ED setting due to the length of time it takes for them to become effective (Goveas and Harsch, 2008).

Benzodiazepines

Benzodiazepines potentiate the effect of gamma amino butyric acid. Few studies for their use in acute agitation in elderly exist. Due to alterations in metabolism and elimination in the elderly, there is increased sensitivity to this class of medication (Rossi et al., 2010). Benzodiazepines carry with them the risk for falls, excessive sedation, and cognitive impairment, especially in long-term use (Nassisi et al., 2006). In general, avoid benzodiazepines with long half-lives (Goveas and Harsch, 2008). For example, diazepam has a long half-life for the parent compound (30–60 hours), and its active metabolites have a half-life of 30–100 hours (ePocrates, 2015). Lorazepam is widely used in younger patients, and while there is limited data in elderly patients, it has proven more effective than placebo. Additional advantages of this medication are its shorter half-life (14 hours), lack of active metabolites, and flexibility in routes of administration (PO tablet, PO liquid, IM, IV). Other shorter half-life benzodiazepines with no active metabolites include triazolam, oxazepam, and temazepam (Cremens, 2004).

Other Agents

There is limited evidence for antidepressants and anticonvulsants. The strongest evidence to date is for carbamazepine, but its time to action, pharmacokinetic interactions, and side effects limit its application in the acute setting (Amann et al., 2009). There may be a role for valproic acid, but evidence for its use in the acutely agitated elderly patient is lacking (Alexopoulos et al., 2005). A summary of these recommendations is provided in Table 6.5.

Restraints: Restraints have a limited role in the agitated elderly patient. While they may be used in severe agitation (Downes et al., 2009), restraint use can worsen agitation and aggression, and lead to other problems such as pressure wounds, abrasions, and compressive neuropathies. Restraints are never to be used as a replacement for nursing care or

Table 6.5. Medications for agitation in the elderly (Tueth and Zuberi, 1999; Kohen et al., 2005; Goveas and Harsch, 2008; Peisah et al., 2011; Calver and Isbister, 2013; Citrome, 2015)

Drug Class	Medication	Route	Initial Dose (mg)	Max Dose in 24 hours (mg)
Benzodiazepine	Lorazepam	PO	0.5–1.25	5
		IM		
Antipsychotics	Olanzapine	ODT	2.5–5	10
		IM	2.5	10
	Haldol	IM	0.25–0.5	2
		PO	0.5	5
	Droperidol	IM	2.5	10
	Ziprasidone	IM	20	
	Loxapine	INH	10	10
	Risperidone	ODT	0.5	2

patient supervision (Peisah et al., 2011). The use of restraints does not decrease the risk for falls (Goveas and Harsch, 2008). Restraints should only be considered after both behavioral and medication measures have failed and the patient becomes dangerous to themselves or others (Ward and Ahn, 2013). Restraints should only be applied by personnel trained in their application.

Conclusion

Agitated elderly patients are not an uncommon patient presenting to the ED. Their assessment is challenging because of the presence of multiple medical comorbidities and polypharmacy. Due to altered metabolism and elimination, their management with medication is different than in their younger counterparts. Enlistment of caregivers, a team approach, gentle verbal interactions, and environmental adjustments are non-medication methods to management. Evidence-based research to guide medication interventions is limited, but guidelines do exist. In general, start low, and go slow when it comes to medications in the elderly, keeping in mind the goal is to target specific behaviors in order to facilitate diagnosis and management rather than lead to sedation.

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Chapter 7

The Psychiatric Evaluation of Patients with Agitation

Joachim Scharfetter

Introduction

The entire process of a psychiatric evaluation is a dynamic progression, starting with the presentation of the patient, and possibly continuing even after the patient is discharged (Carlat, 2011; Shea, 1998; Shea, 2016; Silverman et al., 2015; Sommers-Flanagan and Sommers-Flanagan, 2015; Stowell et al., 2012). The examiner should consider differential diagnoses, refinements, and even complete diagnostic turns if he or she is willing to challenge a diagnosis in the light of new information and of increasing acquaintance with the patient.

The basis of psychiatric evaluation is information. At the beginning of the assessment process, this information is often scarce and chaotic: information has to be obtained, sampled, extracted, and evaluated in the best manner possible. Sound information can be achieved by getting answers to key questions: "What is going on? Why are you here? What has happened today that made you decide to come to this facility? Did things change for you? Was there anything like drugs or alcohol involved? Has this ever happened to you before? Were you given a diagnosis? Did you obtain treatment then? Did your treatment help? Do you recall the names of any medications you took at that time? What medications do you take now? Do you have any medical conditions that might be involved with the issues that brought you here?"

And, perhaps most useful, "How can we help you?"

Further complicating psychiatric evaluation of the agitated patient is the fact that it is typically conducted in tumultuous situations and buzzing surroundings, concomitantly with first treatment decisions, management of agitation and sometimes even imminent hostility, and in the midst of de-escalating efforts and decisions about the need for coercive measures.

It is perhaps best to see psychiatric evaluation as a multistep approach. Fortunately, all the various steps do not necessarily have to be conducted for each case – or at least not all of the steps identically or with the same detail. Depending on the clinical location, an evaluation may be different for quickly completing an initial emergency assessment as opposed to a full-length psychosocial history. However, regardless of the circumstances, the first clinical steps always are the most important, and a working diagnosis and a risk assessment must be achieved to guide any clinical interventions. The overall outline for a psychiatric evaluation is summarized in Table 7.1.

During a clinical evaluation of an agitated patient, de-escalation should always be ongoing simultaneously as the assessment is progressing, and patient response to de-escalation techniques should provide helpful clues to the diagnostic process (see Chapter 10). Figure 7.1 shows this basic initial paradigm for the psychiatric diagnostic approach in agitated patients.

Table 7.1. Agenda of the psychiatric evaluation

• Initial exploration – history of present illness
• Psychiatric status examination (PSE)
• Physical examination
• Working diagnosis, differential diagnosis
• Risk assessment
• Completion of psychiatric history
• Definitive diagnosis

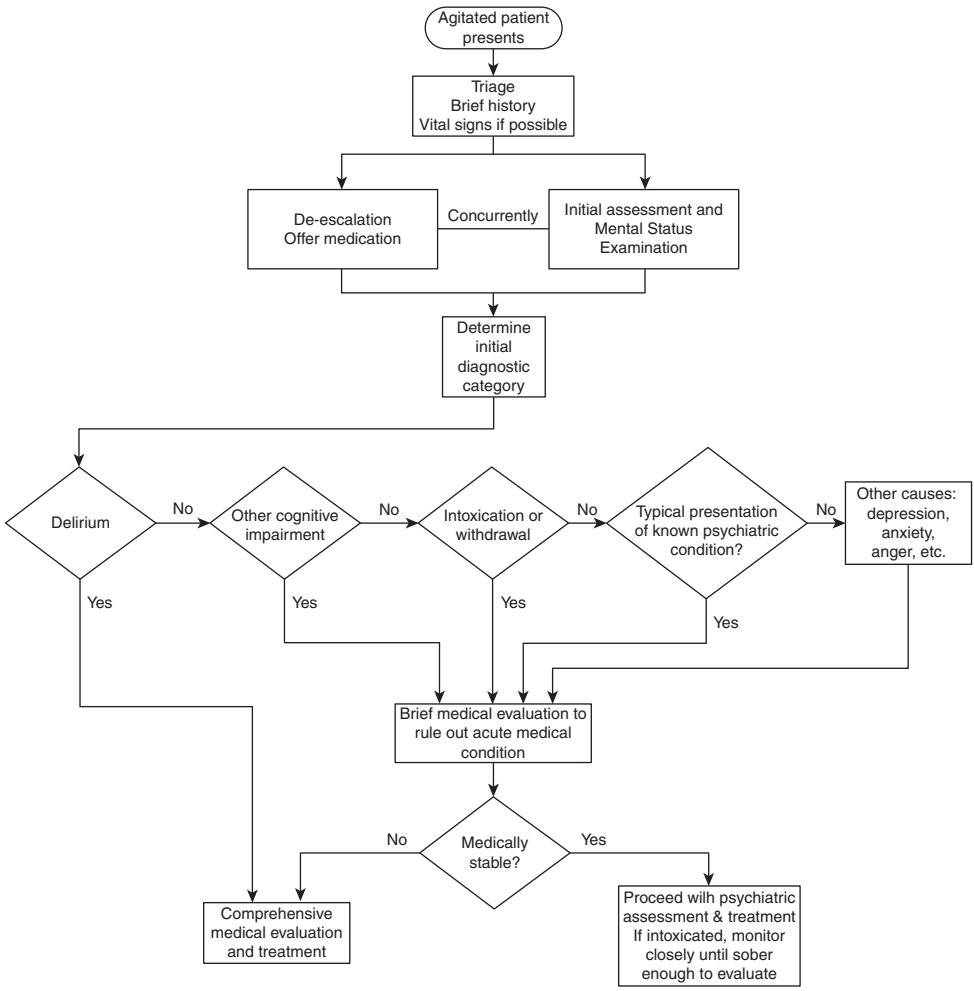

Figure 7.1. Algorithm for psychiatric assessment of the agitated patient (used with permission from Stowell et al., 2012).

Case Presentation

In the following, a psychiatric assessment process is demonstrated using a case report. For the purpose of this discussion, it is assumed that the triage and medical screening examination for urgent medical concerns has already been completed (see Chapter 3) and the patient is considered stable for a psychiatric evaluation.

Case Report

A male patient aged about thirty years is brought to a psychiatric urgent care center by police, according to mental health statutes. He presents as psychotic and agitated, and is obviously hallucinating; his speech is rambling with loose associations, at times very incoherent. He is pressured and labile. He has difficulty answering most questions, being unable to give meaningful answers. According to police, he was found in a public transportation area yelling nonsensically and frightening other passengers, who reported him to police. Police attempted crisis intervention and de-escalation in the field with little improvement. The police then felt he was acutely in need of a psychiatric assessment, placed him into custody and brought him to the hospital emergency department, where a medical screening examination deemed him medically stable for transfer to the psychiatric urgent care center at the other end of the building. Blood draws for chemistry and complete blood count were within normal limits, but a serum toxicology screen was positive for methamphetamine.

Chief Complaint, History of Present Illness, and Mental Status Examination

At the very start of the evaluation process, clinical professionals are often confronted with acute patients with very limited information. Patients in a state of agitation may also be violent and unwilling or unable to cooperate. Despite this, at the very least, basic information should be obtained urgently for immediate management and treatment decisions. In the beginning, it is important to ascertain one simple thing: What is the patient's chief complaint? In other words, why is she or he here right now?

Basic details about a patient may sometimes need to come from police and/or paramedics, or from accompanying friends and relatives (who can often be invaluable sources of data). Such personal contacts should never be dismissed before being interviewed for all relevant collateral information or any valuable knowledge about the patient and his situation they can provide. Often, a fellow staff member can be simultaneously obtaining collateral history (to be promptly reported, especially if there is compelling, pressing information), while the clinician is doing a primary evaluation of the patient, to minimize delay in ascertaining diagnoses and beginning treatment if appropriate.

Once a basic overview of the situation, including a chief complaint, has been obtained from the patient, along with collateral reports from paramedics, police, family, or others, the focus should be to determine if the patient's condition is serious enough to initiate treatment immediately. Does the current presentation rise to the level of emergency concern, such that preventing a dangerous outcome for the patient or others at this point merits a quick presumptive diagnosis, so that treatment may begin without delay? If this is the case, the clinician should draw on the limited amount of information already ascertained, especially focusing on any past diagnoses and medication history of the patient, to determine a working diagnosis and facilitate prompt intervention.

If the situation is not so extreme as to jeopardize life and limb and merit urgent treatment, medical staff should make an effort to establish a basic therapeutic relationship with the patient and start a diagnostic interview. This initial examination should preferably take place in a quiet room, absent from turmoil and disturbances. However, caution should be taken not to isolate the patient and interviewer away from other personnel; it is usually prudent to have at least one other staff member nearby and within sight. This can help to maintain the safety of the interviewer, as well as to provide a level of comfort for the anxious or paranoid patient who might be frightened to be alone with a stranger.

The examining clinician should stay calm and patient. This may sound trivial, but it is of utmost importance for objectivity and effectiveness. Whenever possible, the interviewer should introduce him- or herself and clearly explain the clinician's role in the evaluation process. While this might seem difficult in a tense and chaotic admission situation, if a rapport can be established, the crisis patient is more likely to become comfortable and relaxed and less prone to aggression (Aminur and Saria, 2007; Platt et al., 2001).

The examination itself comprises both questioning and observation. It is often best to initiate the examination with open questions (e.g., "What brings you to the hospital?" "What can I do for you today?"), subsequently switching to more specific questioning to fill in the gaps in the history (e.g., "What medications are you currently taking?"). Attention, empathic listening, encouraging comments ("Tell me more . . . "), clarification ("Did I get it right?"), and summarization ("So you are telling me that . . . ?") are useful means to continue the interview. However, even if the questioning is unsuccessful because of issues with the patient's willingness or ability to verbally communicate, ample information can be gained from interactions and observation alone.

All information obtained, the "subjective data" can be documented as a history of present illness, a brief and concise report on the beginning and development of symptoms, problems, and circumstances leading to the patient's presentation. Focus should be on recent events and relevant details, main or presenting complaints (e.g., Why has the patient been admitted? What's new? What has changed, here and now, in the past few days, recently?). Written reports derived from subjective data can be flexible according to the individual patient's specific situation and needs. However, given that this is an emergency setting, the clinician should be precise and concise, always trying to focus on the issues relevant to evaluation, treatment, and disposition.

Characteristics of the patient's appearance and behavior, thoughts, and feelings and any observed or inquired symptoms and signs, the "objective" data, should be documented as the Mental Status Examination. The process of the assessment itself should not be regarded as separate from the clinical interview. If the clinical interview is conducted in a proper and thorough manner, plenty of data and information should be accumulated that can subsequently be fortified by a few additional questions.

Topics of the psychiatric status examination are summarized, and selected mental status vocabulary are defined in Table 7.2 and Table 7.3, respectively.

In documenting the mental status of a patient, the clinician should note the main domains: Consciousness, Appearance, Attention, Memory, Mood, Affect, Thought Content, Thought Process, Perception, Insight, and Judgment. All categories should be listed, even if the particular domain is completely within normal limits. The "normal" condition should be stated (e.g., "The patient is awake and alert, attentive and responsive . . . mood is euthymic . . . judgment is unimpaired . . . .").

Table 7.2. Topics of the psychiatric status examination

Section	Modality	Quality or Form	Comment
Consciousness		Hypervigilant, alert, drowsy, stuporous, comatose	Level of arousal; the normal condition is alert
Appearance	Body habitus, physical characteristics, grooming and attire, posture and gestures		Features that make patient distinguishable in a group; relevant are observations that give clinical clues to the working diagnosis
Speech	Fluency, prosody, volume, articulation, phonation		
Attitude		Cooperative, hostile, inappropriately familiar, facetious, suspicious	
Cognition	Attention	Attentive, inattentive, distractible . . .	
	Concentration	Able/unable to concentrate	
	Registration	Able/unable to register	Assessed via immediate recall of material presented to the patient
	Orientation	Oriented/disoriented to time, to place, to one's person, to one's situation	
	Memory	Immediate memory	
		Remote memory	Ask for life events (e.g., school, jobs)
		Confabulation	
	Abstraction	Concreteness	A useful means to determine concreteness: proverb interpretation.
Activity	Level of activity	Calm, hyperactive, restless, agitated, bradykinetic, akinetic	

	Qualitative abnormal activity	Tremor, dyskinesia, dystonia, tics, mannerisms, posturing, echopraxia, waxy flexibility	If unsure about what it is that you see, best give a description (an advice valid for the whole PSE)
	Compulsion		
	Habitual behaviors	Kleptomania, pyromania, paraphilia	All sorts of – manias and – philias
Mood		Euthymic, euphoric or elated, dysphoric, melancholic, anxious, angry	
Affect	Range	Restricted, blunted, flat, expansive	
	Mobility	Stable, labile, fixed, immobile	
	Appropriateness	Appropriate, inappropriate, incongruous	
Thought Form	Disordered connectedness and organization	Flight of ideas, loose associations, tangentiality, word salad, incoherence	
	Other peculiarities of thought	Clang associations, echolalia, neologism, perseveration, thought blocking	
Thought Content	Overvalued ideas		
	Delusion	Fragmented or organized, bizarre or plausible, persecutory, grandiose, nihilistic, folie à deux	Describe organization, form and content of the delusion
	Obsession		
	Phobias	Agoraphobia, social phobia, panic attacks	
	Feelings of being externally controlled	Thought broadcasting, thought insertion, thought withdrawal	First-rank Schneiderian symptoms, indicative of schizophrenia
	Violent or suicidal ideation		

Table 7.2. (cont.)

Section	Modality	Quality or Form	Comment
Perception	Illusion		
	Hallucination	Auditory	Differentiate between sound, commanding or insulting voices, and voices commenting or discussing patient in third person
		Visual	Usually suggest "organicity"
		Somatic	Bodily sensations, e.g., in psychosis, often hear: "There is a microchip implanted (to control me!)."
		Others: olfactory, gustatory, tactile	
	Depersonalization or derealization		
Insight		Capable/incapable to achieve insight	Provide arguments for your estimation
Judgment		Competent/incompetent to make sound judgments	Provide arguments for your estimation

PSE = psychiatric evaluation.

Table 7.3. Definitions of selected mental status vocabulary

Affect	Moment to moment expression of feelings, usually reactive to stimuli
Attention	Ability to focus and direct cognitive processes
Clang Associations	Words and phrases are connected by sound rather than by meaning
Concentration	Ability to focus and sustain attention for a period of time
Concreteness	Missing ability to perform abstract thinking
Confabulation	Patient with memory gap fills in false memories
Compulsion	Unwanted impulse to perform certain motor behavior (see *obsession*)
Delusion	Objectively incorrect beliefs that are not culturally determined and cannot be shaken by contrary evidence
Depersonalization	Patients feeling that there is something strange about themselves
Derealization	Patients feeling that there is something strange about their surroundings
Echolalia	Patient repeats statements and questions made by the examiner, often more than once
Echopraxia	Uncontrolled mimicking of another's movements or posture
Flight of Ideas	Topic of a conversation rapidly changes before elaboration of each thought can occur
Folie à deux	A delusion shared by two usually closely connected people
Hallucination	Perceptual distortion without external stimulus
Illusion	False impression from a real stimulus (e.g., a shadow taken for a monster)
Insight	Ability to be aware of internal and external realities (i.e., be aware of one's illness)
Judgment	Problem-solving ability on the basis of consideration and formulation
Loose Associations	No obvious or completely illogical topical connection between statements
Mannerisms	A consistent, characteristic, apparently purposeful, highly stylized way of doing things; often seems very exaggerated or bizarre
Mood	Consistent, sustained feeling state

Table 7.3. (cont.)

Neologism	Production of novel idiosyncratic words or, in form of *contaminations*, unusual fusions of otherwise meaningful words
Obsession	Unwanted thought that cannot be suppressed (see *compulsion*)
Posturing	Sustaining an apparently purposeless, non-resting position
Perseveration	Illogical and seemingly uncontrollable repetition of an idea or action
Tangentiality	Topic of conversation strays down another path or direction without returning to the original topic, the examiner must frequently redirect the patient
Thought Blocking	A thought is lost in midsentence, usually leading to a noticeable pause in speech; patient often experiences and expresses a "*thought disruption*"
Thought Broadcasting	Belief that one's thoughts are no longer private, can be overheard by anyone
Thought Insertion	Belief that one's thoughts are alien and placed in one's mind from outside
Thought Withdrawal	Delusional belief that thoughts are being lost or stolen by some external force
Waxy Flexibility	A limb or another body part is kept in any position, in which another person places them
Word Salad	Extreme form of loosening of associations, sometimes termed "incoherence"

For an agitation patient, the mental status should attempt to focus on the cause of the agitation. Is the patient very paranoid, feeling that others are trying to cause him or her pain? Is the patient hearing auditory hallucinations commanding him or her to assault others? Is there profound confusion that is making the patient lose self-control? A sound understanding of the major issues of the agitation is very useful for determining the course of treatment.

With the history and Mental Status Examination complete, the basis for a differential diagnosis is now provided, and the first important step of the evaluation process has been accomplished. The resulting diagnostic considerations from this first evaluation step, however, are preliminary, and should be considered a starting point for further assessments.

Diagnostic Manuals

No further contributory oral report could be obtained from our patient. Police and paramedics had little additional history due to the circumstances of the patient being found wandering alone in a public area, without much identifying information. Our

working diagnosis was acute psychotic disorder (ICD10:F23.1), with a differential diagnosis (based on an amphetamine-positive toxicology screen) including mental and behavioral disorder due to use of stimulants, acute intoxication with delirium (ICD10:F15.03), or mental and behavioral disorder due to use of stimulants, psychotic disorder, primarily hallucinatory (ICD10:F15.52).

To elaborate a diagnosis, it is important to fit the information gained during the first assessment step into a consistent structure. Psychiatry provides physicians with diagnostic manuals defining descriptive criteria regarding symptoms or syndromes and time duration requirements to qualify patients for specific diagnoses. These criteria afford a high reliability of diagnoses, and these manuals should, therefore, be utilized. This chapter refers to the ICD-10 (Simms, 1992), but DSM-IV (American Psychiatric Association, 2000) or DSM-V (American Psychiatric Association, 2013) are related. For the reader using ICD-10 in the United States, be aware of the coding differences between ICD-10 and ICD-10-CM (National Center for Health Statistics, 2013). ICD-10 itself will soon be replaced, with ICD-11 in starting position due by 2018.

Assessment of Risks, Suicidality, and Violence

Meanwhile, the patient shows signs of increasing agitation. He appears to be unwilling to stay and is looking for the doors, trying to leave the ward.

As a part of the diagnostic process, and as a basis for urgent treatment decisions, it is important to evaluate if the patient poses dangers to himself and/or others. If so, the program might be obliged to keep the patient in the center against his or her will, and there may be a need to apply coercive measures or forcible medication (see Chapters 12 and 13).

At this point of the psychiatric evaluation, the clinician requires a thorough knowledge of local legal procedures and requirements. Staff should be well acquainted with these concepts to be able to focus on relevant details of various situations, while still endeavoring to provide appropriate, compassionate care. There are many potential legal issues regarding not only coercive measures against patients, but also questions of confidentiality, statutory reporting requirements, and duty to warn, among others (see Chapter 17).

Legal procedures and ethical considerations relevant to this situation are based on two important principles: the ability of the patient to make competent decisions (informed consent, see Chapter 16) and the urgency of the patient's medical condition.

The definition of urgency is based on the seriousness of potential consequences if the patient is not treated. In a psychiatric setting, the definition for urgency is closely related to, or even consistent with, the concept of risk for self-harm or danger to others.

Though actual suicide is very difficult to predict, major risk factors for suicidality have been fairly well established, and screening for these risk factors is a standard part of all acute psychiatric assessments (see Tables 7.4 and 7.5). A clinician should never hesitate to ask questions related to suicidality. Such questions do not increase the suicide risk or introduce ideas in the patient just by asking, as is sometimes assumed and feared by inexperienced interviewers (Hirschfeld and Russell, 1997).

Another essential component of a psychiatric diagnostic evaluation is a screening for risk of violence and aggression risk factors (Rocca, Villari, and Bogetto, 2006) (see Tables 7.6

Table 7.4. Basic risk factors for suicidality

• Older age or youth and early adolescence
• Being widowed or divorced, unemployed, socially isolated
• Male gender
• Suicide of a first-grade relative
• Prior suicide attempts
• Severe prior suicide attempts
• More than one prior suicide attempts
• One or several of the following diagnoses: schizophrenia, substance dependence, depression, emotionally unstable, narcissistic or antisocial personality disorder, bipolar disorder or bipolar disorder mixed state
• Chronic medical illness, chronic pain

Table 7.5. Dynamic risk factors for suicidality (sorted due to relative importance)

• Suicidal thoughts and impulses
• Feelings of guilt, hopelessness, perceived entrapment regarding life situation, perceived loss of chances and possibilities
• Agitation
• Episode of mood disorder (especially in the beginning)
• Psychotic state
• Intoxication (especially alcohol)
• Access to suicide means (weapons, medication, altitude)

Table 7.6. Basic risk factors for violence

• History of violence, history of verbal threats
• Male gender
• Younger age (15–24 years)
• One or several of the following diagnoses: substance dependency, organic brain disorder, psychosis, personality disorder with prominent instability, impulsivity or antisocial behavior
• Being uneducated, unemployed, without social support
• Being part of a violence-devoted subcultural group
• Having experienced early abuse, emotional deprivation, victimization
• Low tolerance for frustration
• Low self-esteem
• Having a tendency toward projection and externalization

Table 7.7. Dynamic risk factors for violence

• Auditory hallucinations (especially commanding), paranoid delusions, and suspiciousness (especially if directed against specific persons)
• Agitation
• Poor impulse control
• Acute intoxication (especially alcohol or stimulants)

Table 7.8. Imminent predictors of violence

• Loud or excited speech
• Angry gestures
• Increased movements
• Hostile facial expression
• Fixed gaze or avoidance of eye contact
• Refusal to talk
• Behavior of looking for an escape
• Physical signs of stress (e.g., hyperventilation, sweating, tremor)

and 7.7). Additionally, there are signs indicative of an imminent violent outbreak (Table 7.8).

De-escalation and Communication Issues

The patient is exhibiting poor judgment by trying to exit locked doors and has been increasing his motor activity. He is demonstrating a number of risk factors for danger to self and others. Engaging the patient with a goal of helping to calm him and accept treatment is now a top priority, and the on-duty psychiatrist has interrupted her other duties to attend to this case immediately. The psychiatrist begins using de-escalation techniques to help the patient relax and regain control, while continuing to ask pertinent history questions that can assist with the diagnostic process.

De-escalation techniques are an essential component of working with an acute patient, and can help to reduce the patient's level of agitation while also allowing him or her the ability to make choices and concentrate on questions, both of which can allow a patient to begin to regain self-control. These techniques will be covered in Chapter 10.

While using de-escalation techniques, the diagnostic evaluation should be continuing simultaneously. Questions about past medications or previous hospitalizations might assist the patient to focus, and thus improve his or her control of his or her thought processes, while the patient's specific answers may guide the clinician to a more specific diagnostic category.

For a patient who is in better control, several communication techniques can be used to further the diagnostic interview (Berlin, 2013). Motivational Interviewing (Miller and

Rollnick, 2013) will be introduced in the Substance Use History section later in this chapter. Another helpful approach is Shared or Participatory Decision Making (Duncan, Best, and Hagen, 2010). Shared Decision Making is about involving the patient (as much as possible) in the process of medical decision-making. This is achieved by coming to a mutual understanding of the examiner's and the patient's perspectives and interests and by considering all accessible information to facilitate largely autonomous decisions.

De-escalation approaches help the patient to become more communicative, and he can answer some basic questions. He states his name and birthdate, and a nurse goes to research if the hospital has previous records for him. We learn from him that he has been in psychiatric hospitals before, and he recognizes the names of several antipsychotic medications.

The nurse returns and informs the psychiatrist that the patient has a previous diagnosis of schizophrenia. While the psychiatrist had previously been considering diagnoses ranging from uncomplicated stimulant-induced psychosis to a chronic psychotic illness with symptoms exacerbated by methamphetamine, the latter now appears to be the most likely presumptive condition. If the patient had been antipsychotic medication-naïve and the consideration was toward pure substance-induced symptoms, the clinician might have prescribed only a benzodiazepine as primary treatment, and the symptoms might dissipate with time to rest and detoxify. However, since the patient has underlying schizophrenia, the symptoms will likely need more than just rest to improve; and with a known history of toleration to and improvement on antipsychotic medication, the psychiatrist believes that a neuroleptic prescription is indicated.

Since a good therapeutic alliance has been established at this point, the patient accepts the psychiatrist's offer that he inhale a dose of loxapine. Several minutes after the inhalation, the agitation rapidly decreases.

Full Psychiatric History

The patient lies down and takes a short nap while the psychiatrist attends to other duties. Later, he has awakened and is eating a snack, and the psychiatrist can return to complete her psychiatric evaluation.

As soon as time and circumstances allow, the second step of psychiatric evaluation should be undertaken. The patient's full psychiatric history should now be completed to allow for a more thorough diagnosis. Some relevant information has already been presented or obtained in the initial evaluation, but commonly there will still be substantial data pieces missing that should be pursued.

At this point, first treatment decisions on the basis of the working diagnosis may have been effective, and the patient might be better accessible, perhaps relieved from agitation and florid psychotic symptoms, and is now more willing to cooperate and be forthcoming in the interview. Also, any further sources for additional or collateral information should be pursued to help complete all aspects of the patient's story.

The History of Present Illness has already begun to be documented during the first evaluation step, but now any further relevant information can be added. Next, as much data as possible should be gathered, with a focus on past psychiatric history, past medical history, social and personal history, family history, and substance use history (Table 7.9).

The Past Psychiatric History comprises any information regarding the longitudinal course of any psychiatric condition the patient ever experienced. Age of onset, first and early manifestations, changes in symptomatology, recurrence, or chronicity of the disease,

Table 7.9. Topics of psychiatric history

• History of present illness
• Past psychiatric history
• Past medical history
• Social and personal history
• Family history
• Substance use history

first contact with the medical system, hospitalizations, treatments, and treatment outcomes are all points that should be discussed and documented. Other relevant topics to ask about include past adherence to treatment, incidents of self-harm, suicide attempts, and episodes of violence or assault.

The Past Medical History should give an account of all relevant and serious medical conditions, treatments, and hospitalizations. Birth complications and developmental problems should be queried. Of particular interest is debilitating, painful, or otherwise burdensome medical conditions as possible impairments of quality of life. All information regarding allergies, hypersensitivities, and ongoing treatments should also be included in the medical history. Current non-psychiatric pharmacological treatment should be recorded and later reviewed for potential pharmacokinetic interactions and as possible sources of anticholinergic, serotonergic, and dopaminergic side effects.

Social and Personal History gives the patient's background, including the highest level of education, employment, and current relationship status. It should include, when possible, information about parents, siblings, marriages, divorces or breakups, partnerships, and children. Furthermore, the clinician should subtly and non-judgmentally inquire about significant life events, traumas, accidents, losses, and any instances of abuse or other painful past episodes. Be aware that delving into traumas and abuse might be tough for the patient, and therefore, the interviewer should try not to be overly inquisitive, but rather wait for the patient to find enough confidence to talk about such experiences.

Family History should focus on any psychiatric or relevant physical disease running in the family, emphasizing biologically related family members. Conditions of first-degree relatives are more important than more distant relatives. Drawing of a family tree should be considered.

Finally, Substance Use History should be obtained. It is often best to not put this discussion at the beginning of the interview since this is a point where people often tend to be evasive. To avoid such a reaction, it is often helpful to employ the technique of Motivational Interviewing. Motivational Interviewing is about doing an assessment in a way that best confers the chances for the patient to recognize, and perhaps change, any distressing substance abuse habits. Miller and Rollnick (2013) described five basic principles to guide practice: express empathy, develop discrepancy, avoid argumentation, roll with resistance, and support self-efficacy.

To assess important treatment guiding facts, ask for first exposure to the substance of abuse, first period of continuous intake, periods of heavy use and periods of abstinence, routes of administration, treatments and treatment outcomes, and the impact of substance

use-related problems in daily life. Special emphasis should be laid on the assessment of withdrawal symptoms, including seizures.

After the interview, the patient states that he is feeling much better and that he is ready to leave the hospital and return home. His speech is logical and coherent, and he is showing no further evidence of delusions or hallucinations. He is fully oriented and can describe what medications he takes on a regular basis, when his next outpatient psychiatrist appointment will be, and how he can get home. The patient regrets his methamphetamine use and volunteers that he would like assistance getting into an outpatient substance-abuse program. The psychiatrist arranges for the social worker to assist the patient with a referral appointment to a local substance abuse clinic. At this point, the psychiatrist has completed a history and has a satisfactory treatment plan, the patient is safe, in good spirits, not showing any signs of dangerousness to himself or others, and is appropriate for discharge to home. The completed psychiatric evaluation is stored in the hospital's medical record.

Conclusion

As detailed earlier, psychiatric evaluation for acute patients can be a complex endeavor requiring substantial expertise and effective communication skills. Whereas the knowledge to do such an examination can be acquired by reading and learning, real-world competencies typically have to be acquired by real-life experiences. An effective clinician will improve his or her assessment, diagnostic, and interventional techniques more with each new patient, and the journey toward perfecting these abilities continues over a lifetime of professional practice.

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Chapter 8

Psychiatric Causes of Agitation: Exacerbation of Personality Disorders

Paul R. Borghesani, Sharon Romm, and Jagoda Pasic

Introduction

Personality-disordered patients often demonstrate impaired distress tolerance and interpersonal dysfunction, making them prone to agitation in the emergency department (ED). We discuss the association between agitation and personality disorders (PDs), the influence of comorbid substance abuse, and the medical treatment of agitation. Standard and alternative DSM-5 criteria for PDs are reviewed and case illustrations of patients with borderline, antisocial, and narcissistic PDs and their management employing evidence-based psychotherapeutic techniques are offered. Modalities such as dialectical behavior therapy, motivational interviewing, and problem-solving therapy are outlined for use by ED providers to aid in the management of agitation.

Key Concepts

- Hostility, agitation, and violence are commonly seen in patients with personality disorders (PDs).
- Substance abuse is associated with PDs and intoxication is a frequent destabilizing event.
- Standard sedating agents and calming medications can be effective, but their use should be minimized.
- The DSM-5 offers two ways to classify PDs. The standard method lists ten familiar diagnoses identical to the DSM-IV. An alternative model uses a severity scale, pathological personality "traits," and fewer overall diagnoses.
- Patients with borderline PD may present to the ED suicidal and demanding treatment. Case A illustrates the utility of dialectical techniques as developed in dialectal behavioral therapy (DBT) in managing mood lability and aggression in these patients.
- Patients with antisocial PD are often brought to the ED after becoming agitated and aggressive in the community. Case B illustrates the utility of motivational interviewing (MI) approaches in managing these patients.
- Patients with narcissistic PD become problematic when they disagree with medical staff management and recommended treatment plans. Case C illustrates the use of de-escalation and problem-solving approaches to address their refusal of care.

Agitation, Violence, and Personality Disorders

Hostility, agitation, and violence are a common occurrence in emergency departments (EDs). A recent survey suggests that more than 50 percent of ED nurses are verbally or physically threatened during a seven-day period (ENA, 2011). Personality disorders (PDs), defined in

the Diagnostic and Statistical Manual (DSM™) from the American Psychiatric Association (APA), are an "enduring pattern of inner experience and behavior that deviates markedly from the expectations of the individual's culture." The behaviors should be enduring over time, pervasive in multiple situations, and relatively inflexible. PDs are common, with an estimated 9 percent of the population having both PD symptoms and significant distress or impairment (Trull et al., 2010). Patients with PDs frequently seek care in EDs and having a PD predicts recurrent ED use (Richard-Lepouriel et al., 2015). Moreover, patients with PDs are six times more likely to present for emergency mental health issues (Pasic, Russo, and Roy-Byrne, 2005), while greater than 15 percent of patients who present four or more times for mental health issues may suffer from a PD (Chaput and Lebel, 2007). They may initially present agitated in the context of worsening anxiety, depression, psychosis, intoxication, or suicidality. On the other hand, they may present calm and cooperative with these or other issues, only becoming agitated during their ED evaluation. This distinguishes them from grossly agitated patients, involuntarily sent for evaluation, in that they may be initially calm and cooperative, potentially increasing the risk of unexpected violence.

Personality disorders have been unambiguously linked to violence and criminal behavior (Yu, Geddes, and Fazel, 2012), and there is a very high rate of PDs in the forensic population (Fountoulakis, Leucht, and Kaprinis, 2008). It has been estimated that 65 percent of men and 43 percent of women who are incarcerated suffer from a PD (Fazel and Danesh, 2002). Although antisocial PD may be over diagnosed in the incarcerated population (Howard et al., 2008), it is the most common PD identified in this population. More than 80 percent of repeat women offenders, who were originally incarcerated for homicide, can be diagnosed with a PD, in contrast to less than 10 percent experiencing psychosis (Putkonen et al., 2003). Severe psychopathology increases the risk of aggression and violence (Howard, 2015), but the details of this link remain unclear given the incertitude of PD diagnoses (see next section), the heterogeneity of violence, and the comorbidity of PDs, substance abuse, and other mental health issues. For example, the comorbidity of borderline and antisocial PD may be as high as 50 percent in men with somewhat lower comorbidity in women (Tadić et al., 2009), and thus attributing agitation to antisocial PD, but not borderline (or vice versa) is statistically difficult. Important, PDs are not only predisposing factors for violence, but are thought to contribute to the enactment of disordered behavior. Stated differently, not only are agitation and hostility common in PDs, but having a PD contributes to further escalation of agitation (Coid, 2002). Overall, the risk of violence has been proposed to depend on four personality dimensions, including impulse control, affect regulation, narcissism, and paranoia (Nestor, 2002) – dimensions commonly affected by PDs. Not insignificantly, those with PDs also report being the victims of crime at a high frequency, with 20 percent of those with antisocial PD reporting being a recent victim in contrast to 1 percent of those with psychosis (Coid et al., 2006). In summary, a significant association exists between PDs (especially antisocial and borderline) and violence (Fountoulakis et al., 2008), but the exact psychological reasons for this remain poorly understood (Howard, 2015).

DSM Diagnosis of Personality Disorders

The Standard DSM Model of PDs

For the past several decades, the DSM has divided PDs into three general clusters: cluster A – those who are odd or eccentric (schizoid PD, schizotypal PD, and paranoid PD);

cluster B – those who are dramatic, emotional, and erratic (borderline PD, narcissistic PD, antisocial PD, and histrionic PD); and cluster C – those who appear anxious or fearful (obsessive-compulsive PD, avoidant PD, and dependent PD). Criteria for specific PDs can be found in the DSM-IV™ or DSM-5™ and they are essentially unchanged from the earlier to newer edition. Most important, symptoms of PDs must lead to "clinically significant distress or impairment in social, occupation or other important areas of functioning." Therefore, traits such as suspicion, emotionality, or eccentricity in a well-adjusted individual would not qualify as identified pathology. In most cases, PDs should not be diagnosed in the ED given that mania, depression, psychosis, substance use, and anxiety can all lead to dramatic changes in personality that can often mimic PDs. A diagnosis is made more accurately in the outpatient setting where a longitudinal view of the patient's symptoms can be appreciated. Nonetheless, it is often helpful in the ED to recognize patterns of maladaptive personality as described by DSM PDs such that the ED encounter can be tailored to best help the patient.

Criticism of the current DSM structure for assessing and diagnosing PDs include i) arbitrary diagnostic thresholds, ii) high level of comorbidity, and iii) lack for formal severity assessment (Bornstein, 2011). As is the case for most DSM disorders, PDs are typically diagnosed by the presence and/or absence of subjectively assessed character traits. Any combination of five out of nine symptoms may be sufficient for the diagnosis of a borderline PD, yet any two patients could have nearly non-overlapping symptom profiles. The high level of comorbidity among PDs (Sinha and Watson, 2001) has led some authors to argue that current diagnoses represent more of a continuum rather than distinct entities (Ekselius et al., 1993). Clinically, this manifests itself in charting where terms like "cluster A traits" or "borderline-ish" are used when a clinician wants to document his or her discomfort in choosing a specific PD diagnosis. Finally, current DSM PD diagnoses do not formally include any severity assessments. This precludes both cross-sectional discussions about current severity differences between patients and also compromised longitudinal assessment of individual patients whose overall level of function may vary considerably from month to month and year to year.

The Alternative DSM Model of PDs

Given the criticism of the standard DSM categorization of PDs, an alternative model for PDs is presented in Section III of the DSM-5, "Emerging Measures and Models" (DSM-5, 2013). This can be used in place of the ten current diagnoses (as outlined earlier), and while it offers several advantages, it uses many familiar terms and descriptions. In this alternative model, PDs represent impairment that is relatively inflexible and pervasive, stable across time, and cannot be better explained by other mental or medical disorders. Developmental stage and/or sociocultural factors should also be taken into account. The alternative model was not included in DSM-5's main section describing mental disorders given concerns regarding its complexity and feared impact on clinical practice and research (Skodol et al., 2015). However, it is a useful alternative means to classify patients, and, in the following case discussions, we highlight its utility to describe patients' maladaptive personality.

In contrast to the standard DSM-IV/DSM-5 categorization, assessment using the alternative model relies on logical and distinct steps (Skodol et al., 2011a, 2011b). First, severity of impairment in personality and interpersonal functioning within the areas of **identity, self-direction, empathy**, and **intimacy** is rated on a 0 to 4 point scale, with 0 signifying no impairment and 1 through 4 signifying some, moderate, severe, and extreme impairment,

respectively. Severity ratings aid in both cross-sectional comparison of patients and the longitudinal assessment of functioning within a patient. This provides for clear documentation of recovery, regression, and stability and is in concordance with research suggesting that severity of dysfunction is an important predictor of current capabilities and future recovery (Hopwood et al., 2011). Per the alternative model, a patient must have moderate or greater dysfunction in two of the four areas to have a PD. After characterizing the severity of impairment, the second step in the alternative model is to assess for the presence of twenty-five pathological personality traits. These are organized into five broad domains; **negative affectivity, detachment, antagonism, disinhibition, and psychoticism** are assessed (Table 8.1; see *Online Assessment Measures* freely available on the APA web site www.psychiatry.org). The third step in the alternative model is to determine the overall pattern of pathological traits and whether the patient should be diagnosed with one of the six prototypic PDs (Figure 8.1), or, "Personality Disorder – Trait Specified." This later diagnosis is appropriate when the composition of pathologic traits is atypical for one of the prototypic PDs. Patient-specific pathological traits are then simply listed after the "Personality Disorder – Trait Specified" diagnosis. Regardless, moderate or more impairment in personality and interpersonal functioning is still required for "Personality Disorder – Trait Specified," and thus simply having pathological traits does not qualify one for having a PD unless personality functioning is compromised. This orderly approach allows for the assessment of personality dysfunction and individual pathological traits even if the assignment of a PD would be inappropriate (e.g., when personality and interpersonal dysfunction is only mild). Per the DSM-5;

> *"The utility of the multidimensional personality trait model lies in its ability to focus attention on multiple relevant areas of personality variation in each individual patient. . . . Knowing the level of an individual's personality functioning and his/her pathological trait profile provides the clinician with a rich base of information and is valuable in treatment planning and in predicting the course and outcome of many mental disorders in addition to personality disorders. Therefore, assessment of personality functioning and pathological personality traits may be relevant whether an individual has a personality disorder or not."*

Table 8.1. DSM-5 personality disorder trait domains

Negative affectivity (vs. emotional stability)	Detachment (vs. extraversion)	Antagonism (vs. agreeableness)	Disinhibition (vs. conscientiousness)	Psychoticism (vs. lucidity)
Emotional lability	Withdrawal	Manipulativeness	Irresponsibility	Unusual beliefs and experiences
Anxiousness	Intimacy avoidance	Deceitfulness	Impulsivity	Eccentricity
Separation insecurity	Anhedonia	Grandiosity	Distractibility	Cognitive and perceptual dysregulation
Submissiveness	Depressivity*	Attention seeking	Risk taking	
Perseveration	Suspiciousness*	Callousness	Rigid perfectionism	
Depressivity*	Restricted affectivity*	Hostility*		
Suspiciousness*				
Restricted affectivity*				
Hostility*				

* traits that are listed under multiple domains

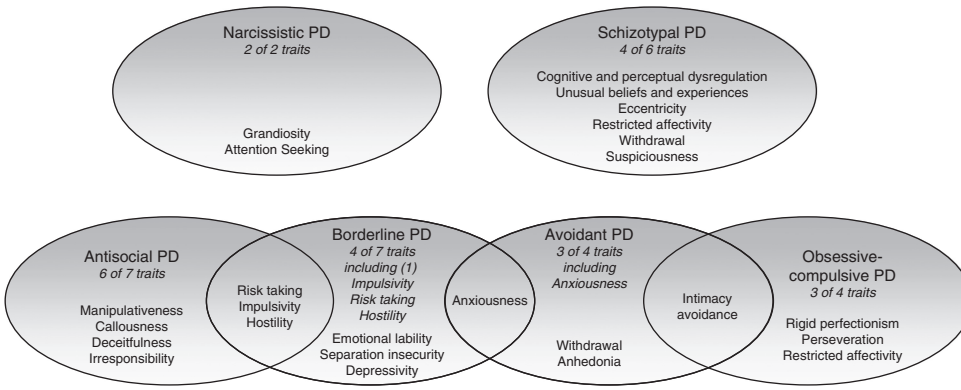

Figure 8.1. Personality Traits.

General Approach to Managing Patients with Personality Disorders

Initial Assessment of Agitated Patients with PDs

General protocols are applicable during therapeutic encounters with agitated and disruptive PD patients (Holloman and Zeller, 2012). Sedating medications can be used, intoxication and withdrawal should be treated, and medical causes of agitation must be evaluated (Nordstrom et al., 2012). However, after completing the medical evaluation and it is determined that the agitation is secondary to a PD, the clinician should establish rapport and begin to plan disposition. Several principles must be kept in mind. First, minimize potential harm to the patient and staff with adequate staffing and judicious use of medical and physical restraints. Second, in contrast to intoxicated or overtly psychotic patients, patients with PDs may have rapidly changing presentations. They can appear calm and organized one minute and then become agitated and aggressive the next. Such behavior is a hallmark of labile personality and is often seen in destabilized patients with PDs. Finally, personality-disordered patients are prone to anxiety and are often dissatisfied with their treatment in the ED. This directly contributes to misunderstandings and conflict between patient and staff. Providers must monitor their own emotions during the encounter. They should note their "countertransference," that is, the way they feel about the patient. Becoming overly involved and parental can be as easy as becoming irritated and dismissive. Providers should monitor such responses in order to ensure proper and expedited medical care.

Personality disorders are often comorbid with other psychiatric diagnoses, including psychosis, anxiety disorders, mood disorders, and substance abuse, and thus all ED evaluations must include a comprehensive assessment of these potential medical emergencies. Moreover, even if the full criteria for a PD are not met, the alternative model formally provides for the documentation of dysfunctional personality traits. For most PDs, outpatient treatment is recommended; though, unfortunately, few patients will meaningfully engage with outpatient care, and thus the ED provider is often called upon to simply manage PD patients rather than provide definitive referral. Managing dangerous behavior and

supporting the patient's own self-efficacy should be central to the ED providers' goal, facilitating rational, safe decisions. Finally, if the etiology of a patient's agitation is psychological in origin, then it stands to reason that psychological approaches may be useful in managing the encounter. We offer three psychotherapeutic methods helpful in managing patients with PDs in the ED.

Approaching the Agitated Patient with a Personality Disorder

It is best to be non-confrontational when approaching hostile patients and to immediately assess your own safety and that of the patient and staff (Nordstrom et al., 2012). The provider should make clear that he wants to see the problem from the patient's point of view and listen to the patient's (angry) complaints in a calm and non-judgmental fashion. It can be enlightening to ask whether the patient has had a difficult experience with past providers or whether he has anger against physicians or hospitals because of the experiences of a friend or family member. The provider should negotiate ways in which the current interaction can be more productive and, as trust develops, should explain how the medical staff has interpreted the patient's actions. Needless to say, the provider should not put himself in the position of undercutting other staff members or agreeing to things that are dangerous or counterproductive. Patients can display hostility when they feel physically threatened or when they feel that their self-esteem is suffering. Focusing on complaints and angry feelings serves the patient in that he does not have to face his fear or sense of loss of control. Becoming an ally is usually beneficial, but not always possible.

Verbal de-escalation involves three steps as described by Project BETA (Best Practices in Evaluation and Treatment of Agitation) (Holloman and Zeller, 2012). First, rapport is built with the patient through verbal engagement; second, a collaborative discussion ensues; and, third, a reduction in agitation will result as a consequence of this discussion (Richmond et al., 2012). To build rapport, it is recommended that a single provider be the primary verbal contact, even if several staff members are needed in the immediate proximity to ensure safety. Careful attention must be paid to respecting the patient's personal space. Do not corner the patient or get within two arm lengths. Avoid provocative behaviors such as staring, crossing arms, or looking disinterested or dismissive. A collaborative discussion is facilitated by concise discourse with short, direct statements, repetition, frequent summary statements, and careful listening. Finally, de-escalation is most likely to occur when understanding is accompanied by clear limit setting and optimism (see Table 8.2) (Richmond et al., 2012). The overall goals of verbally de-escalating patients include diminishing the risk of physical harm to the patient and providers and, ultimately, reducing the length of ED stay and the likelihood of psychiatric admission. Moreover, restraint use is viewed negatively by the Joint Commission and the Centers for Medicare and Medicaid Services, who view limited restraint use as a measure of care quality.

Approaching Patients with Specific Dysfunctional Traits

Patients with dysfunction in the domain of **detachment** (Table 8.1: *emotional lability, anxiousness, separation insecurity, suspiciousness, and hostility*, see Section 4**: Case A**) need to have firm limit setting and require considerable validation. These patients can behave very differently with different providers and thus "split" staff by collaborating with one

Table 8.2. Ten domains of de-escalation [1]

Respect personal space
Do not be provocative
Establish verbal contact
Be concise
Identify wants and feelings
Listen closely to what the patient is saying
Agree or agree to disagree
Lay down the law and set clear limits
Offer choices and optimism
Debrief the patient and the staff

1. Richmond J. S., et al. Verbal De-escalation of the Agitated Patient: Consensus Statement of the American Association for Emergency Psychiatry Project BETA De-escalation Workgroup. *West. J. Emerg. Med.* 2012;13:17–25.

while antagonizing another. Beware of providing patients with conflicting information about their care such as medications ordered, access to visitors and the telephone, and disposition regarding release or hospital admission.

Patients with dysfunction in the domains of **antagonism** and **disinhibition** (Table 8.1: including traits of *manipulativeness, deceitfulness, hostility, irresponsibility, and impulsivity*, see Section 5**: Case B**) must be approached with caution as they are prone to agitation escalating to violence when the provider does not meet their needs. Manipulativeness and impulsivity will contribute to the providers' sense that suggestions and comments go unheard. A firm, clear stance is also beneficial with these patients. Monitor countertransference and avoid unplanned confrontation and verbal challenges.

Approach patients with dysfunctions in the domains of **detachment** and **psychoticism** (Table 8.1: including traits of *withdrawal, intimacy avoidance, suspiciousness, restricted affectivity, unusual beliefs and experience, and eccentricity*, see Section 6**: Case C**) by taking a non-confrontational but firm stance. Clear explanation for tests and hospital procedures should be provided. Maintain patient privacy by pulling curtains, minimizing intrusions by other staff, and using a private room once safety is established. *Withdrawal* and *intimacy avoidance* in these patients may make them seem indifferent to the situation, but, in fact, they may be highly sensitive to personal slights and evaluations. Explaining exactly what needs to be done to accomplish an evaluation or what the consequences of their statements are may be helpful as patients' reality testing may be fragile and thus prone to misunderstanding the situation.

Substance Abuse, Aggression, and Personality Disorders

Comorbidity of substance abuse and other mental illness is well documented (Hasin and Kilcoyne, 2012). Greater than 40 percent of personality-disordered patients abuse alcohol, while 19 percent abuse other drugs (Trull et al., 2010). Upward of 25 percent of individuals

with antisocial PD may abuse drugs. Moreover, PDs are more strongly associated with persistent substance abuse than other mental illnesses, including schizophrenia and mood disorders (Hasin et al., 2011). Antisocial, borderline, and schizotypal PDs are all associated with increased odds of persistent alcohol, cannabis, and nicotine abuse over a three-year period. For instance, the odds ratios for three-year continued substance use in antisocial PD are 3.5, 2.5, and 3.2 for alcohol, cannabis, and nicotine, respectively (Hasin et al., 2011). Substance use often contributes to the patient's inability to deal with stress and leads to agitation and behavioral dyscontrol. In national surveys, hazardous drinking has been associated with greater than 50 percent of all violent incidences (Coid et al., 2006). In fact, repetitive violence correlates with substance abuse but not mental illness, in general (Hagelstam and Häkkänen, 2006).

Using Medications in Individuals with Personality Disorders

When medications are necessary for controlling agitation in an individual with suspected or known PDs, follow general guidelines to attain calm without excessive sedation (Holloman and Zeller, 2012). Eliminate medical causes of delirium, make a provisional psychiatric diagnosis, and seek patient cooperation, as possible (e.g., in choosing a medication and whether it be PO over IM). A second-generation antipsychotic – olanzapine, risperidone, or ziprasidone – is generally recommended over first-generation antipsychotics such as haloperidol, although for intoxicated patients, haloperidol is still considered a first choice because the sedating qualities of atypical agents may not be judicious (Wilson et al., 2012). Details of medication recommendations are beyond the scope of this chapter, though aripiprazole appears somewhat less efficacious and higher doses of quetiapine, necessary for sedation, are not recommended because of possible orthostatic hypotension. With all medications, extrapyramidal and cardiac (e.g., QTc prolongation) side effects should be monitored, as appropriate. If possible, document patients' willingness to take a medication and their contribution in choosing the agent administered. Finally, it is widely recommended that outpatient medication regimens for personality-disordered patients not be changed during crisis unless toxicity is an issue. Changing medications in the ED can reinforce maladaptive behavior and contribute to more frequent ED visits.

There are no specific guidelines for pharmacotherapy in borderline PD (or any other PD). Specific agents that have been tried with agitated borderline patients in the ED include olanzapine (Damsa et al., 2007), ziprasidone (Pascual et al., 2006), and, more recently, inhaled loxapine (Kahl et al., 2015). Long-term pharmacotherapy (months to years) with antidepressants is not useful overall (Saunders and Silk, 2009), although there is some suggestion that mood stabilizers are helpful (Feurino and Silk, 2011). However, recent findings suggest that greater than 80 percent (90% if there are comorbid mental health diagnoses) of patients with emotionally unstable PDs (equated to the DSM diagnosis of borderline PD (Silk, 2015)) are taking medications; with 28 percent taking medications from two classes and 40 percent taking medications from three or more classes (Paton et al., 2015). Thus clinical-practice and evidence-based recommendations are disparate. Recent clinical trials have shifted from antidepressant to mood-stabilizers (including atypical antipsychotics) where only one of fourteen studies since 1998 has included an antidepressant (Abraham and Calabrese, 2008).

Using Dialectical Behavioral Approaches in the ED

Case A: Suicidal Behavior and Impulse Control Issues

Ms. A. is a thirty-four-year-old tourist brought to the ED against her will after her fiancé called 911 as she tried to overdose on pills. She refused to cooperate with the EMTs until police intervened, and in the ED she yelled profanities, disregarded directions, and demanded to be taken out of restraints. Because of ongoing agitation, lorazepam 2mg IM was administered and she subsequently calmed. Upon interview, she was calm but irritated, and demanded the provider tell her fiancé that she is depressed and needs more support from him. She stated, "I wanted to die when I took the pills," but then said, "I was not feeling suicidal yesterday or earlier in the day." When asked if there may have been an alternative to overdosing, she responds, "No, I had to do it!" She admitted to having been given the diagnosis of borderline PD and has undergone numerous medication trials and therapies, including dialectical behavior therapy (DBT). She is requesting admission to the hospital for "a day or two" before she continues her travels with her fiancé.

Her fiancé reported they were in the midst of a financial disagreement. She wanted to spend money on an expensive hotel while he was reluctant to do so, prompting him to leave the hotel room. He confirmed that she has been suicidal on multiple occasions in the past, but that today's behavior was "perhaps more extreme" than normal. He is ambivalent about the need for hospitalization. He explained that she has a therapist in their hometown who knows her well that she had agreed to follow-up with when she returned home.

Case Discussion and DSM Conceptualization

This case illustrates a patient with a self-reported mental health history presenting with intermittent suicidal ideation in the context of a psychosocial stressor. The patient reports a history of borderline PD and her fear of abandonment (overdose after her fiancé walked out), unstable interpersonal relationships, impulsivity around spending and entertainment, affective instability, anger, and recurrent suicidal gestures are all congruent of this diagnosis using the traditional DSM structure. Using the alternative DSM model, she would also be diagnosed with borderline PD with maladaptive traits in the domains of **negative affectivity, antagonism**, and **disinhibition** (see Table 8.1). Specifically, Ms. A. has issues with *impulsivity, hostility, emotional lability, separation insecurity, depressivity*, and *anxiousness* (see Figure 8.1). Of note, one could also argue she shows manipulativeness and irresponsibility as characteristic of antisocial PD, which is not surprising considering the comorbidity of the two disorders (see **Introduction**). This mix of hostility, lability, and irresponsibility frequently contributes to strong negative countertransference in providers when they interact with patients with borderline PD. Care should be taken not to appear dismissive or unaccepting, given that this can harm rapport and lead to the patient's escalation, as validation is the cornerstone of working with borderline patients.

Linehan (1993) proposes three dialectic themes in borderline PD that are immediately apparent in the case of Ms. A.; i) emotional vulnerability versus self-invalidation, ii) active passivity versus apparent competence, and iii) unrelenting crisis versus inhibited grieving. First, Ms. A. is emotionally vulnerable and thus, when feeling unsupported, she regresses to experiencing the intense guilt and shame that likely contributed to her suicidal act.

Demanding that her fiancé solve her "depression" reflects her active passivity and seeming inability to care for her own emotional needs. In justifying her suicidal behavior, she gives an example of the "apparent competence to handle this situation," which, of course, is not viewed as a healthy response to stress and coping. Finally, Ms. A. is in the midst of an unrelenting crisis: she has gone from being depressed, to being upset with her fiancé, to being suicidal, to being upset with the police and emergency staff, to now her current anger at her fiancé for being unsupportive. Her inability to feel appropriate sadness, anger, or even embarrassment while this scenario unfolded directly contributed to her ineffectual, maladaptive behavioral pattern resulting in her suicidal gesture.

Using Aspects of Dialectical Behavioral Therapy in the ED

No evidence-based crisis interventions are currently routinely recommended for managing those with borderline PD (Borschmann et al., 2012). Brief inpatient hospitalization is not effective in reducing para-suicidal behaviors (Soomro and Kakhi, 2015; Waterhouse and Platt, 1990), and should not be considered standard-of-care. On a brighter note, some authors propose use of techniques employed by dialectical behavioral therapy (DBT) in the acute setting as helpful (Sneed, Balestri, and Belfi, 2003). DBT is an empirically validated psychotherapy developed for borderline PD now being adapted for other mental health issues (Linehan, 1993; Lynch et al., 2007). From a clinical perspective, DBT finely balances encouraging patients toward healthier functioning while conveying that they and their behaviors are accepted in the moment. Validation is central to this process as it communicates understanding and acceptance. Linehan has outlined levels of validation (Linehan, 1997) that may be useful for the ED provider. Level 1 is simple listening and observing. There is no better technique to establish rapport with a patient then to actively listen to them. Creating a calm, supportive environment within the ED can facilitate personal connection and should be pursued. Noise, thin dividers, standing while interviewing, answering pages all convey an invalidating environment and should be minimized when interviewing a borderline patient. Level 2 includes providing affirmations and reflections (see Table 8.3). These should not parrot the patient's statements but convey interest and accurate understanding of what the patient is trying to convey. Affirmations can include normalization of the patient's experiences or emotions or simply pointing out connections between the patient's distress and their actions. Levels 3–5 all involve interpretations, or making connections between the patient's current thoughts, feeling, and behaviors (Level 3), their personal experiences and their current feelings and behaviors (Level 4), and normalizing current behaviors and feelings in the context and what might be generally expected for any person (Level 5). The general ED provider could benefit from employing reflections and interpretations in numerous encounters (see Table 8.3).

In contrast to validation, paradoxical methods (i.e., those that challenge the patient) expose the dichotomy that theoretically exists in the patient's mind and can be used to reset or jar the interview onto a more therapeutic path (Linehan, 2014). Paradoxical comments should not be made lightly and should only be used by the attuned ED provider who has established some rapport with the patient using reflections and interpretations as described. It is difficult to "script" paradoxical interaction as each patient-provider dyad will interact differently and thus, what may be appropriate to say to one patient may cause disengagement and anger in another. With that disclaimer, paradoxical interactions that could be considered in the ED are: i) extending, ii) playing the devil's advocate, and iii) irreverent

Table 8.3. Aspects of DBT that may be used in the ED

Basic validating techniques	
Reflections *Simple validating statements about the patient's experience or feelings. They convey acceptance and interest, building engagement.*	"It sounds like it was tense at the hotel." "Being disrespected is hurtful. I can see why you were so upset." "Sounds like you were too upset to use your skills." "Money is so often a source of problems, it would be great if we could just do without it." "So you didn't know your fiancé would call 911. It must have been a surprise to have them at your door."
Interpretations *By linking the patient's statements one can convey greater understanding and provide an acceptable explanation for the patient's behavior.*	"Walking out on someone during an argument is rude. I can see why you felt disrespected and got angry." "After hearing about how you have harmed yourself in the past, I can understand why you feel making the suicide attempt was the only way to grab his attention." "Of course you're upset. Does anyone discuss financial issues without getting emotional?" "Feeling intimidated by the police is pretty common, especially given the trauma you experienced. I can see why that just contributed to your anger."
Paradoxical interventions*	
Extending *Overstating the severity of the situation or taking the patient more seriously than they do. This is helpful when the provider feels manipulated.*	"Treating suicidality takes a long time; I don't think we could help you in just a few days and I would only recommend a week or more." "You're right. He does not deserve a second chance. I think I should ask him to leave the hospital." "Suicidality just doesn't come and go; you must have been suicidal yesterday too."
Devil's advocate *One step beyond extending, this reframes the patient's statements or actions in an extreme manner.*	"It sounds too difficult to patch things up with your fiancé. What about leaving him?" "You're in a really stable spot right now. You don't need to contact your therapist."

Table 8.3. (cont.)

Irreverent communication *Unexpected, extreme statements that, although genuine and respectful, are atypical in the medical setting.*	"Hitting the officer was definitely the right choice. Everyone enjoys visiting jail." "Spending more money definitely shows he's more in love with you." "It's not really a big deal to kick your fiancé out and have him call 911. I am sure it happens to most couples." "You're right, a day or two in the hospital would be exactly what your therapist would recommend."

* Paradoxical interventions should only be used when rapport has been established with validation, reflection, and interpretations. They unbalance the conversation and force a "non-scripted" interaction; often useful when the clinician feels manipulated or trapped into making a certain decision.

communication (Sneed et al., 2003). In extending, the provider takes the patient more seriously than the patient means to be and thus pushes the patient to acknowledge the logical, but exaggerated consequences of their statements and actions. In the devil's advocate, the provider takes an extreme or counter-position that the patient is likely to disagree with, prompting them to offer a more reasonable, and therapeutic solution. Finally, irreverent communication often involves humorous, perhaps sarcastic comments that are intended to derail the patient and hopefully make them snicker or at least smile. Extending and playing the devil's advocate are good for getting the patient's attention, especially if the provider feels manipulated. This can give the patient a way out of the hole they may have dug for themselves without losing self-esteem.

Resolution: Case A

Use of irreverent communication allowed the patient to admit that things were not "status quo" and that she likely was in need of refresher treatment (see Table 8.3). Then we added a validating interpretive statement relating to her how her fear of abandonment set the stage for her suicidal gesture after the argument with her fiancé and his walking out. She de-escalated and agreed to return home with her fiancé, and we left a message with her outpatient provider so that she would be scheduled for a follow-up appointment.

Using Motivational Approaches in the ED

Case B: Aggression and Threatening Behavior

Mr B. is a thirty-four-year-old male brought in by police from a local shelter after becoming verbally threatening toward staff when he was denied access to a computer. Per shelter staff, "Mr. B. is usually gruff and irritable, but today he just went off, yelling, throwing trash and papers, and generally creating such a situation that we had to call the police." Mr. B. has a long history of homelessness, minimal involvement with mental health care services,

sporadic drug use, frequent ED visits for minor medical complaints (six per year), and past diagnoses, including schizophrenia, alcohol use disorder, and antisocial PD. On arrival he was irritated and verbally challenging, but not assaultive. He demanded release, told staff to leave him alone "or else," and cursed but made no specific threats. Given his flight risk from the ED, he was placed in restraints prior to mental health assessment. Vitals were unremarkable. Routine bloodwork, including CBC, electrolytes, creatine kinase, and TSH, was normal, while his blood alcohol level was 0.145 percent by volume. He refused to provide a urine sample for toxicology, but denied drug use other than cannabis. CIWA monitoring was started and the patient was given lorazepam 2 mg PO for agitation. Three hours later, he was upset but calm. He had been reduced to two-point restraints given continued flight risk despite calm behavior, and was still asking to leave. He stated, "I didn't do anything wrong . . . they just pissed me off!"

Case Discussion and DSM Conceptualization

In this all too typical scenario, a familiar, but arguably poorly known individual was brought in by police after becoming agitated in the community. Although the EMR may indicate a myriad of diagnoses, he was not overtly psychotic and it was unclear how past drug use may have contributed to earlier presentations and chart diagnoses. He was not involved with mental health care, not on medications, and there was no indication of decompensation during the preceding weeks beyond that shelter staff observed just prior to ED presentation. As is common in the ED, his BAL confirmed drinking, and it is likely that his inebriation contributed to his outburst, but was not necessarily causal, given that he was frequently intoxicated at the shelter.

In the traditional DSM model, Mr. B. meets criteria for antisocial PD given his failure to conform to social norms, impulsivity, irritability, recklessness, and lack of remorse. Likewise, in the alternative DSM model, individuals with antisocial PD fail to conform to lawful and ethical behavior and have maladaptive traits in the domains of **antagonism** and **disinhibition** (see Table 8.1). Specific traits include (see Figure 8.1) *manipulativeness, callousness, deceitfulness, hostility, risk taking, impulsivity, and irresponsibility*. Common definitions of these terms coincide with DSM usage, but *risk taking* deserves special attention. *Risk taking* is defined as goal-directed behavior during which an individual shows no insight into his or her own limitations and the consequences of his or her behavior. In this case, Mr. B. clearly shows *risk taking* in that he was not specifically trying to be hostile or deceitful; he only wanted something and acted in disregard to accepted social conventions. Patients with ASPD are difficult to manage in the ED and may provoke anger and potentially disrespectful behavior by providers (Groves, 1978).

Patients with antisocial PD develop primitive coping mechanisms that cause difficulties for the staff, in the context of life-long psychosocial stressors (Black, 2015). They often have long-standing conflicts over dependency, and when placed in a challenging scenario, such as an ED evaluation, they fear that they will completely lose control. Given underlying impulsivity and risk-taking behaviors, they may react in a maladaptive manner with over-independent behavior to try to reestablish control. By relinquishing control of some areas of the patient's care, limited control can be restored. For example, in asking for permission to discuss certain topics (see sections on MI that follow), one can build rapport and facilitate treatment. They frequently idealize some staff members and devalue others. This sets the stage for a more complicated ED course. Unproductive arguments about patient

management may follow with the idealized staff member identifying the patient as misunderstood, while the others see the patient as deceitful and manipulative. Patients can use this situation to their advantage and try to bend the rules. This may progress to patients harassing physicians and nurses and disrupting their own clinical care. If they perceive mistreatment, they may demand to be discharged against medical advice, but, when deemed unsafe for discharge, they may escalate, becoming agitated and violent.

Given the preceding discussion, it is imperative that the entire staff huddle to talk about disagreements and decide on the treatment plan for that patient. Above all, the staff must agree to remain consistent. When clinicians interact with the patient, they can acknowledge the difficulties that the patient is having, but should not be pressured into bending the rules or making promises that are normally not made. Conversely, irrespective of how exasperating these patients may be, it is important to refrain from showing outright hostility or acting in a punitive manner. From a non-confrontational stance, the clinician may be able to point out the goals of medical treatment.

Using Facets of Motivational Interviewing in the ED

Mr. B. was brought in to the ED by the police after causing a disturbance in the community, but once removed from the acute situation was calm but irritable, and lacked remorse for his behaviors (trait of *callousness*). His alcohol use likely contributed to his disinhibition and aggression, but after sobering for several hours, he no longer made specifically hostile comments. Per assessment, he was not psychotic, did not appear to be in the midst of an acute mood episode, and his goal was to leave the hospital. However, his safety and the safety of others had to be adequately assessed prior to release from the ED. We believe aspects of motivational interviewing can be helpful and therapeutic during encounters such as this.

Motivational interviewing (MI) is an evidence-based therapy that utilizes a collaborative, person-centered approach to elicit and strengthen motivation for change (Miller and Rollnick, 2012). In simple terms, it is a non-confrontational conversation about a person's behavior that explores the patient's ambivalence about change given self-identified motivations, obstacles, and commitment. It is neither telling the patient to alter his or her behavior, nor simply stating reasons why you think he or she may want to change (Miller and Rollnick, 2009). Most widely used in substance use disorders, it has been found effective in a myriad of clinical situations (Rubak et al., 2005). It is proposed as helpful in convincing patients to use long-acting injectable antipsychotics (Kisely et al., 2012), in increasing self-efficacy in partner violence (Saftlas et al., 2014), and in reducing violence and alcohol use in teens after an ED visit (Cunningham et al., 2012). In ED settings, it reduces staff frustration and improves effectiveness of interventions (Arkowitz, 2008), and authors have encouraged its use by ED nurses (Baumann, 2012). Three concepts underlie MI: i) that it is a collaborative wherein the therapist is a partner in the conversation rather than an expert providing direct advice; ii) that it is evocative wherein the patient must identify the reasons for change while the provider must refrain from imposing his or her own values and reasons for changes; and iii) that it promotes autonomy wherein patients are challenged to come up with their own solutions/approaches to their problems such that they also gain competence to do this in the future. A five-step approach to MI is routinely suggested and includes: i) asking for permission; ii) eliciting change talk; iii) importance check; iv) ability check; and v) a closing summary statement (Miller and Rollnick, 2012).

Table 8.4. Ingredients of motivation interviewing: OARS

Open-ended questions *Not easily answered by yes/no. This invites elaboration and challenges the patient to clarify their concerns and possible solutions.*	"How can we help you tonight?" "What are the good things about staying at the shelter?" "What's the downside to being sent to the hospital?" "You tell me what the advantages of not getting angry would be?" "What would be the advantages (disadvantages) of changing?"
Affirmations (MI) *Statements that point out the patient's strengths, by emphasizing the "good news" that they report followed by the evidence.*	"You showed some real restraint after getting angry; someone with less maturity would likely have lost it." "With your experience, it's no wonder you feel you know more about computers then the staff does." "You've put up with a lot. You deserve some help rather than going to jail." "You're an assertive person because you ask for what you want." "You're saying you don't need people to tell you the rules. You're street savvy. You know how to take care of yourself." "You've done a nice job explaining yourself to me without getting angry."
Reflections *Empathetic statements that are aimed at resolving the patient's ambivalence often by restating the problems with their current behavior and the benefits of change.*	"I hear you saying that protecting your pride is more important than the consequences of getting into a fight. Do I have that right?" "Avoiding the police sounds important to you, and it seems like you're frustrated that you keep running into them." "You have a conundrum . . . on one hand, you get angry easily, and on the other you don't like talking with the police." "It feels as if you are trying your best to change, but just haven't found the right skills to use." "I hear you saying all this could have been avoided if they had bent the rules for you, yet following the rules allows you to stay there. Are you willing to consider acting differently?"
Summary statements *Convey interest and empathy and can help when shifting the topic or ending the interaction.*	"So you'd like to be able to stay in the shelter and you recognize that your anger gets you into trouble. You also see a link between your pride and your anger and are willing to consider being more tolerant of other folks if it means fewer hassles with the police. Sounds like that would be helpful for you."

A useful approach that incorporates the aforementioned concepts of MI is to follow a four-component "OARS" model during the clinical encounter (see Table 8.4). **O**pen-ended questions, **A**ffirmations, **R**eflections, and **S**ummaries are used to actively engage the patient with the intent of fostering engagement and encouraging change talk (Kisely et al., 2012). Open-ended questions facilitate evocative "deep thinking" by the patient and promote *self-efficacy* by reducing the frequency of leading questions made by the provider. Affirmations are genuine remarks by the provider that help convey *empathy*. In essence, they identify patients' strengths, often recasting seemingly negative behaviors in a more positive light, and then offer evidence that the statement is true. Offering evidence for the affirmation is essential in that it conveys genuineness. A statement such as "next time you'll be different," although supportive and empathetic, does not offer any factual data that you are being genuine or that the statement is true. Patients with antisocial PD are sensitive to loss of control and disrespect and thus may be prone to perceive comments as disingenuous. Use caution when making affirmations such that the patient does not feel belittled or challenged. Reflections or reflective listening is when the provider modifies an affirmation such that it points out the patient's ambivalence to change or uncertainty in his or her convictions that he or she is behaving appropriately. Reflections include statements that paraphrase the patient's comments and then go a step further to connect him o her with motivations and commitment for change. Finally, Summaries are used to recap the discussion and ensure that the patient and provider are on the same page about the issues surrounding change. Summaries are also useful to develop discrepancies, that is, acknowledgments by the patient that some of his or her behaviors are interfering with desired goals. They can also be used when the provider decides to change the direction of the discussion. Examples of these concepts in the case of Mr. B. are detailed in Table 8.4.

Resolution: Case B

After calming in the ED, Mr. B. was evaluated for safety and provided with information for mental health and substance abuse treatment. Open-ended questions were used to engage and orient Mr. B. within the therapeutic encounter while reflections and summaries encouraged behavioral change (see Table 8.3). Specifically, he identified how his wounded pride contributed to his anger and that by being less hostile he may avoid future unwanted interactions with the police.

Using Problem-Solving Methods in the ED

Case C: Agitation and Refusal of Medical Care

Mr. C. is a sixty-nine-year-old male with no known mental health history who was brought in by ambulance after calling 911 with chest pain. He was assessed in the medical ED and labs, including CBC, chemistries, TSH, and urine toxicology, were normal or negative. An EKG revealed non-specific ST-segment and T wave abnormalities and his troponins were not elevated. The ED provider felt he likely suffered from unstable angina and recommended that he follow up with his outpatient provider. However, after learning that the patient did not have a primary care doctor, lived alone in a rural home, and was ambivalent about making a follow-up appointment, the ED provider recommended admission for further evaluation. Upon hearing this, Mr. C. became upset, stating that he would

not stay in the hospital and that staff were "crooks." The ED physician attempted to explain the hospital's perspective, but Mr. C. became dismissive and demanded a second opinion and transfer to another ED. Without any therapeutic alliance, Mr. C. was informed that, prior to leaving the hospital, he was required to undergo a decisional capacity evaluation by a mental health care provider. At this point, Mr. C. became highly agitated, threatening, and required restraint.

Case Discussion and DSM Conceptualization

This case illustrates how a seemingly benign encounter can become problematic. Mr. C. was calm when he presented to the ED and he had valid reasons for seeking medical assessment. Difficulty ensued when he did not like the treating provider's recommendation of hospital admission. This ED provider was unaware that Mr. C. had fragile self-esteem and felt invalidated and threatened by the provider's well-intentioned concerns. The situation further escalated when the ED provider countered Mr. C.'s unreasonable request for transfer to another ED with "threats" of a decisional capacity evaluation by a mental health care provider. It would have been more productive to take a non-confrontational, yet firm approach to this mistrustful patient.

Using traditional DSM categorization of PDs leaves the diagnosis for this patient somewhat ambiguous. Although he manifests symptoms of both paranoid PD and narcissistic PD, too little is known about his history and current thinking to label him as either. Supporting a diagnosis of paranoid PD is his suspicion of others, his doubts about peoples' intentions, and his reluctance to open up to ED staff. However, we do not know if he finds hidden meanings in others' actions, frequently bears grudges, or perceives attacks that would suggest a lifelong paranoid PD character. Even less is known about his narcissism. The alternative DSM model may be more helpful because even if we cannot identify a specific PD, individual maladaptive traits can be noted and recorded. For instance, in the alternative model, individuals with narcissistic PD have vulnerable self-esteem, with either overt or covert *grandiosity* and *attention seeking*, and have maladaptive traits in the domain of **antagonism** (see Figure 8.1 and Table 8.1). The overt grandiose character of traditional narcissistic PD is widely appreciated and is exemplified by the successful grandiose individual who craves being the center of attention, feels entitled, and cannot tolerate criticism. However, in the alternative model, narcissistic PD can have covert narcissism that includes self-loathing, isolationism, and poor vocational history (Caligor, Levy, and Yeomans, 2015). Brittle self-esteem and defensiveness can make them exceedingly hard to interact with as normal conversations may be viewed as antagonistic or demeaning. Overall, when interacting with individuals with extensive narcissism, it is essential to be non-judgmental and inquisitive. Avoid subtly paternalistic or dismissive comments. In the case of Mr. C., the suggestion that he may not appropriately follow through with care and that he required a decisional capacity evaluation were significant insults to his fragile self-esteem.

Using Problem-Solving Approaches in the ED

Problem-solving treatment (PST) is a form of cognitive therapy that specifically targets anxiety generated by everyday life experiences and helps patients conceive of rational, helpful plans to address this (Mynors-Wallis, 2005). The anxiety it targets may have been

Table 8.5. Aspects of problem-solving therapy

Engagement and problem clarification *Build rapport and mutually identify specific problems that are interfering with advised treatment.*	"I think I can help you, but I do need to understand what's upsetting you right now." "Mr. P., you seem very upset; I'd like to help you get what you want." "Just so I can better understand you, let's list the reasons you are asking to leave." "What is your biggest concern about staying in the hospital?" "What is your next biggest concern about staying in the hospital?" "Let's work together to figure out a solution to this." "Given how complicated this is, can we spend a few minutes together talking about options – from your perspective and mine – because I think there may be some common ground?"
Generate solutions *Collaboratively brainstorm multiple solutions to the agreed-on problem; discuss the pros and cons as appropriate.*	"Is adequately evaluating your heart in the next few days a goal we can agree on?" "How would you want us to evaluate your chest pain?" "What would you be willing to do?" "What do you absolutely *not* want to happen?"
Choose and implement the plan *Get a commitment from the patient and summarize the mutually agreed on plan.*	"OK, your goals are to not lose money and get home to care for your cat. I think we can accomplish that by . . .." "You've told me you'd be willing to stay as long as financial services comes to speak with you first, that, as best we can, we limit the number of times we collect blood, and that we work quickly in the morning to get necessary tests done. I can promise that we will do our best to accomplish this." "So after going over all this with you, you are still adamant about leaving, but you recognize the need to have more tests, and you'll call your niece and ask her to take you to an appointment tomorrow. Let's set that up before you go."

caused by typical daily stresses such as financial, relationship, or chronic medical stresses, or, more severe, less frequent occurrences such as job loss, death of a loved one, or the new diagnosis of a terminal illness. PST is helpful with depression (Hickie, 2000; Mynors-Wallis et al., 2000), generalized anxiety (Seekles et al., 2011), suicidal ideation, relationship difficulties, and PDs (Mynors-Wallis, 2001). In the primary care setting, PST may be as effective as other forms of therapy and medications for anxiety (Bell and D'Zurilla, 2009), and it has been suggested that it be included in the general training of primary care providers (Franke et al., 2007).

The basics tenets of PST include creatively generating means to deal with problems, fostering effective decision-making, and accurately identificating barriers that may impede success (see Table 8.5). Statements made by the provider are reminiscent of both reflections used in dialectical approaches (see Section 4**: Case A**) and affirmations used in motivational approaches (see Section 5**: Case B**) and illustrate practical similarities between many of the psychotherapeutic approaches. As always, it is essential to develop a collaborative and therapeutic relationship with patients, and this, more than any other specific facet of the methods presented, is essential. Giving advice to patients does not constitute PST. Simple statements such as "Let's work together to . . . ." and "I would like to help you to . . . ." quickly and effectively convey a sense of partnership. Overtly authoritative statements such as "You need to . . . .", "You must calm down!" or "I cannot help you with that issue," although perhaps true at the time, are rarely helpful. In formal PST, it is important to identify stressors that trigger emotions and learn to reduce or avoid them. However in the ED, the goal is to help manage negative emotions and impulsive decisions that compromise appropriate treatment. Both real change and the perceived empowerment have been suggested as therapeutically beneficial in PST for depression, but the true mechanism remains unclear (Mynors-Wallis, 2002).

Resolution: Case C

In Mr. C.'s case, the ED provider took a problem-solving approach. He first built rapport by using affirmations and clarifying the clinical situation and problems (see Table 8.5). Rapport was buttressed by asking for permission to discuss the issue of decisional capacity with clear explanations of what needed to happen for Mr. C. to leave the hospital. Once engaged in a collaborative discussion, the ED provider and Mr. C. generated solutions that inevitably would demonstrate Mr. C.'s capacity to understand the situation and the need for medical evaluation. Finally, a plan could be chosen, permanently de-escalating the patient. By identifying mutual goals, Mr. C agreed to be admitted to the observation/short stay unit after being appropriately educated about the expected hospital course and how he would be kept informed of his medical status.

Summary

We have introduced psychotherapeutic approaches that may be helpful in the ED when managing patients with PDs. The short descriptions of DBT, MI, and PST are intended to stimulate interest and encourage providers who feel these methods may be useful to review the material referenced. We also presented the alternative DSM model of PDs with the intent of conveying the value of identifying individual maladaptive personality traits in addition to full PDs.

Acknowledgments

We would like to thank Chris Dunn, PhD, and Katherine Comtois, PhD, for their advice and expert perspective on motivational interviewing and dialectical behavioral therapy, respectively. We thank Sharon Romm, MD, for her close reading and editing of this chapter.

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Chapter 9

Psychiatric Causes of Agitation: Exacerbation of Mood and Psychotic Disorders

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Case Report

Case Presentation: Agitation in a Patient Suffering from Mania with Psychotic Features in the Ward Setting

In June 2015, Mr. B. was brought to the emergency department by the police after being found outside their department displaying "bizarre behavior."

Past Medical, Psychiatric, Substance Use History

Mr. B. is twenty-two years old, single, and studying at college. He lives with his parents and his brother. Neither our patient nor his family had any history of psychiatric or medical disorder. Premorbid personality was described as well adjusted.

Current Clinical Situation

When he arrived at the emergency department, Mr. B. reported auditory hallucinations consisting of communications with God. Upon presentation to the emergency department, he was combative. Police also reported that the patient was discovered screaming in public, he was agitated with rapid speech, had delusional ideas about being God´s son, and demonstrated grandiosity.

Once the family was contacted, they reported that Mr. B. was well until May 2015, when he developed an unusually "optimistic" state, followed by a decrease in the need for sleep (two to three hours in twenty-four hours), decreased appetite, and increased religious activities. Later in his course, he was noted to have irritability and was frequently found "walking around."

Mental Status Exam at Admission

Upon assessment of his mental status, Mr. B. was alert and well oriented. Dress and hygiene were fair. He appeared preoccupied and anxious. During the interview, he was impatient and restless, frequently changing seats. Despite these observations, Mr. B. reported that today was the best day of his life because he had decided to reveal that he was God's son. His speech was loud, pressured, and over-elaborative. He exhibited loosening of associations and flight of ideas. Mr. B. described grandiose delusions regarding his healing skills. He also reported auditory hallucinations (God had told him to quit his job and become a spiritual healing leader) with religious delusions about being God's son. He presented with elevated mood, decreased sleep, and demanding behavior with irritability, suspiciousness, and assaultive and hallucinatory behavior (talking to himself). He denied suicidal and homicidal

ideation. He refused to participate in intellectual or memory-related portions of the examination. Furthermore, he had become socially isolated and had no interpersonal relationships. Mr. B. was considered an unreliable historian and exhibited poor judgment. Insight was absent.

Summary Differential Diagnosis and Treatment Outcome

Mr. B. was admitted to the acute psychiatric unit, and his routine laboratory tests and brain imaging were normal. The Young Mania Rating Scale (YMRS) and Positive and Negative Syndrome Scale (PANSS) were evaluated weekly during the hospitalization.

Because of the severity of his symptoms, Mr. B. was initially treated with lithium, risperidone, and a benzodiazepine. During the first days of hospitalization, the patient suffered from severe psychomotor agitation despite the high dose of antipsychotics, requiring physical restraint at times. The patient's poor insight did not allow him to recognize his current situation as clinically significant, and delusional ideas of him healing other mental health patients in the ward became prevalent.

After two weeks of psychopharmacological treatment, there was a marked reduction in the agitation and behavioral problems, and the improvement was maintained throughout his stay in the hospital. Despite this improvement, there were still other remaining symptoms like elevated mood, increased level of activity, and decreased hours of sleep. Religious and grandiose ideas persisted, and doses of risperidone were increased.

The patient remained hospitalized for forty-two days. The day before discharge he was completely euthymic and free of all mood symptoms that led to admission. At discharge, he met a Diagnostic and Statistical Manual-5 (DSM-5) diagnosis of bipolar disorder, mania, severe current episode, with psychotic features.

At the time of discharge, Mr. B.'s risk evaluation of behavioral problems and agitation were reduced significantly.

Introduction and Etiology

Introduction

Psychomotor agitation in patients with psychiatric conditions represents a frequent phenomenon and a clinically relevant issue in psychiatry, not only in emergency settings, but also during hospitalization or in outpatient psychiatric settings (Garriga et al. 2016).

Despite different attempts in defining agitation, it remains a broad and multifactorial syndrome, and there is still a lack of clear agreement. Classically, Lindenmayer described the key features present in patients with agitation, including restlessness with excessive or semi-purposeful motor activity, irritability, heightened responsiveness to internal and external stimuli, and an unstable clinical course (Lindenmayer 2000). More recently, the DSM-5 defines agitation as an excessive motor activity associated with a feeling of inner tension (APA 2013). However, all types of agitation include common factors: agitation is an emergent situation that is temporary, breaks the therapeutic alliance, and is in need of a prompt and immediate intervention (Garriga et al. 2016). Even if aggression and violence are not core features of agitation, a progression of severity of agitation can also lead from anxiety to aggressive and violent behaviors (Nordstrom and Allen 2007; Zeller and Rhoades 2010).

Acute agitation is a serious medical problem that may be present in various psychiatric disorders, including schizophrenia (Osser and Sigadel 2001) and bipolar disorder (BD) (Alderfer and Allen 2003; Pratts et al., 2014; Popovic et al. 2015). Agitation associated with psychosis is a frequent reason for emergency department visits, admission to a psychiatric inpatient ward, and continued hospitalization.

Epidemiology

Little information on the epidemiology of agitation is available, but reported prevalence rates range from 4.3 to 10 percent in psychiatric emergency services (Huf, Alexander, and Allen 2005). Thus, the economic burden of agitation episodes has not been sufficiently studied, given that agitation is a syndrome that may increase the use of hospital resources (Peiró et al. 2004; Warnke, Rössler, and Herwig et al. 2011). Agitation in bipolar disorder (BD) occurs very frequently, with an incidence of 87 percent in patients suffering from BD I and 52 percent in those with BD II (Swann 2013).

Risk Factors for Aggressive Behaviors in Agitated Patients

The presence of both psychotic symptoms and the diagnosis of BD have to be considered when assessing risk factors for psychomotor agitation in mental health patients (Nourse et al. 2014). In addition, younger males with a history of previous violence, multiple psychiatric admissions, comorbid substance use, and comorbid personality disorder are more at risk for agitated and/or aggressive behavior (Nourse et al. 2014).

Agitation is a dynamic situation that may rapidly escalate from anxiety to aggressive or violent behaviors (Citrome and Volavka 2014). In this regard, it is important to consider not

Table 9.1. Examples of potential early signs and risk factors of escalating agitated behavior (Adapted from Garriga et al. 2016)

Classification	Description
Demographic	• Young age • Male gender • Not being married • Aggressor and victim of the same gender
Diagnostic	• Schizophrenia or bipolar disorder (especially when positive psychotic symptoms and/or comorbidity with substance use disorder are present)
Clinical	• Greater number of previous admissions • Extended length of hospital stay • Non-voluntary admission • History of self-destructive behavior • History of suicidal attempts, • History of substance use • Occurrence of previous aggression/violence episodes • Presence of impulsiveness/hostility • Disturbing clinical symptoms • Provocative situations • Verbally demeaning or hostile behavior

only causative factors, but potential early signs and risk factors of escalating agitated behavior. Different reviews have proposed a list of early signs and risk factors that can be classified in three ways: demographic, clinical, and diagnostic (Table 9.1) (Cornaggia et al. 2011; Hankin, Bronstone, and Koran 2011; Kasper et al. 2013).

As mentioned, acute agitation is common in the course of schizophrenia, and may be accompanied by destructive and/or violent behaviors (Noble and Rodger 1989; Krakowski and Czobor 1997; Buckley et al. 2011). Patients with schizophrenia show agitated, aggressive, or violent behavior, mostly related to psychotic or other symptoms (e.g., threatening behavior or anxiety) (Hasan et al. 2012). It has been estimated that the 14 percent of hospitalized patients with schizophrenia showed agitation and agitated or violent behavior on admission (Soyka 2002) and that around 20 percent have episodes of agitation during their lifetime (Pilowsky et al. 1992).

Schizophrenia patients are thought to account for 900,000 annual visits to psychiatric emergency services in the United States (Piechniczek-Buczek 2006). Other studies report that 24–44 percent of agitated or aggressive behaviors committed by individuals with schizophrenia occur during an acute phase of the illness (Citrome and Volavka 2011). Incremental increases in the hostility symptom score of the PANSS positive subscale are also associated with agitation in schizophrenia (Swanson et al. 2006).

Psychomotor agitation in BD is a component of both major depressive episodes and excited polarity episodes (manic or mixed). Agitation in BD patients presents as a prominent clinical manifestation most frequently during mania, and particularly during mixed states (Perugi et al. 2001; Pacchiarotti et al. 2013; Vieta and Valentí 2013; Perugi et al. 2015), but also during any affective episode in the presence of mixed or depressive features (Shim et al. 2014; Vieta et al. 2014; Popovic et al. 2015). Agitation during a major depressive episode may indicate the presence of an underlying BD (Angst et al. 2009) and may predict a high risk of mood switching (Iwanami et al. 2015). Important, the presence of agitation and racing/crowded thoughts during mixed depression were associated with a higher risk of suicidal ideation (Sani et al. 2011; Popovic et al. 2015).

Neurobiology

An excessive reactivity in the amygdala, coupled with inadequate prefrontal regulation, has been defined as a trigger to increase the likelihood of aggressive/agitated behavior (Siever 2008). Developmental alterations in prefrontal-subcortical circuitry, as well as neuromodulator abnormality, also appear to play a role. Alterations and dysfunctions of the normal bioamine neurotransmission function of different brain areas are found in mental illnesses.

Serotonin, dopamine, and GABA neurochemical systems are the most studied in relation to agitation. However, a variety of other neurotransmitters has also been implicated in agitation, including noradrenaline, neurosteroids, testosterone and estrogen, the neuropeptides vasopressin and oxytocin, and endogenous opioids (Nelson and Trainor 2007; Siever 2008). In all cases, further work is needed to establish a behavioral specificity of these effects. Despite this, in general, agents that reduce dopaminergic or noradrenergic tone or increase serotonergic or GABAergic tone attenuate agitation, often irrespective of etiology (Lindenmayer 2000). In the specific case of agitation in psychotic and manic episodes, substances that reduce the dopaminergic tone are useful to manage agitation. (For more on this topic, please see Chapter 2.)

Regarding genetics, no gene of major effect for aggression/agitation has been defined to date. Therefore, the use of genetic markers for risk prediction, to mitigate clinical or injury consequences, or to determine the treatment or management of specific individuals is questionable (Vassos, Collier, and Fazel 2014).

Etiology and Differential Diagnosis

In the assessment process, a Mental Status Examination should be performed as promptly as possible, aimed at determining the most likely cause of agitation and guiding the initial interventions to calm the patient. Once the patient is calm, a more extensive psychiatric assessment can be completed (Garriga et al. 2016). A definitive diagnosis is not considered a primary goal. On the contrary, ascertaining a differential diagnosis, determining safety, and developing an appropriate initial management are the main goals of the assessment (Stowell et al. 2012).

Agitation can be caused by a variety of etiologies, both medical and psychiatric (Yildiz, Sachs, and Turgay 2003; Nordstrom et al. 2012). Agitation has been classified in four etiological groups: a general medical condition, substance intoxication, a primary psychiatric disorder (where schizophrenia and BD are classified), and undifferentiated agitation (Nordstrom et al. 2012).

In the initial assessment, and as a general rule in an individual with no previous history of psychiatric illness, the agitation should be attributed to a general medical condition until proven otherwise. In emergency settings, it is not uncommon for a diagnosis of delirium to be overlooked during an initial screening. The patient may be mistakenly diagnosed as psychotic, based on the fact that physical signs and symptoms of delirium may be subtle and easily go undetected (Stowell et al. 2012).

The next issue regarding the differential diagnosis is whether the patient is agitated due to a primary psychiatric condition. Little to no testing may be needed to confirm this in a patient with preexisting psychiatric disease who presents with symptoms similar to previous psychiatric episodes and with normal vital signs (Nordstrom et al. 2012). Once an acute medical cause of agitation is excluded, an accurate psychiatric and mental status evaluation should be performed. Agitation may present with different clinical manifestation across many psychiatric illnesses, and there is no established standard psychiatric assessment (Stowell et al. 2012). However, an initial psychiatric assessment should include not only the interview with the patient, but also collateral information (medical records, interview with families, friends, outpatient care providers) when possible. History of the present illness, past psychiatric history, past medical history, substance use history, social history, family history, and the Mental Status Examination should also be covered. Affective state, thought process, suicidal and homicidal ideation, the presence of psychotic symptoms, judgment/insight, executive functions, and reasoning and reliability must ultimately also be assessed (Stowell et al. 2012). Additionally, clinicians may find auditory hallucinations (rarely visual hallucinations), persecutory and/or paranoid delusions (schizophrenia and related disorders), grandiosity (mania), inappropriate mood (elation or irritability), hostility or aggressive behavior, and loud, rapid, or pressured speech (Hasan et al. 2012). Although acute agitation is commonly associated with psychotic diseases, such as schizophrenia, schizoaffective disorder, and BD, several other psychiatric disorders should also be considered in the psychiatric differential diagnosis, including agitated depression, anxiety disorder, personality disorders, adjustment disorders, and autism spectrum disorder.

Clinical Features and Diagnoses

Specific Clinical Features and Differential Diagnosis

Given the clinical relevance and the global impact of agitation in psychiatry, a prompt evaluation of causative factors and immediate management are essential, since this may allow control over a potentially dangerous behavior that could progress to violence.

Several difficulties complicate the assessment of an agitated patient. Uncooperativeness and/or the inability to give a relevant history often forces clinicians to make decisions based on very limited information. Usually, a complete psychiatric assessment cannot be completed until the patient is calm enough to participate in a psychiatric interview (Stowell et al. 2012). Further complicating things, administration of psychiatric interviews and self-rating scales may exacerbate and escalate agitated behaviors (Huber et al. 2008).

An early identification of warning signs that could predict agitation would no doubt be helpful (Hankin et al. 2011). Unfortunately, there is still a lack of controlled studies comparing different methodologies or tools, and thus, most information regarding screening comes from expert recommendations and consensus based on clinical experience.

Differential diagnosis of agitated behavior in a person with known schizophrenia or BD can be complex as there can be multiple causes, any of which can be present at the same time, and can also differ from episode to episode (Nolan et al. 2005; Volavka and Citrome 2011). Some specific and common triggers in these two kinds of patients might be comorbid substance use or intoxication, neuropsychiatric deficits that result in overall poor impulse control, a chaotic environment that lends itself to behavior dyscontrol, or frank psychopathology. An underlying somatic illness may also be present, resulting in a delirium in schizophrenia or BD patients. These patients are also more vulnerable to iatrogenic causes of agitation, including akathisia (a distressing sensation of being unable to sit still), that can be induced by antipsychotics and antidepressants (Citrome et al. 2001; Advokat 2010).

In psychomotor agitation during schizophrenia or manic/mixed psychotic episodes, there is a dearth of literature that investigates the causal pathways from delusions to agitation or violence. However, some hypotheses have been described: agitation or violence on basis of a delusional belief could be directly due to the content of the delusion by itself (direct pathway), driven by affective symptoms that are another component of the psychotic illness, explained by underlying personality traits (e.g., anger), or explained by the content and the characteristics of the delusion that result in a negative effect (Coid et al. 2013).

Regarding clinical clues that would help in the diagnosis of agitation in patients suffering from schizophrenia and BD, clinicians should consider basic differences in the clinical presentation. Agitation in schizophrenia patients is commonly found in the acute phase of the illness, and may commonly be present in first episodes. Also, schizophrenia patients are at most risk of psychomotor agitation if they present with treatment noncompliance and/or higher rates of hospitalizations. A clinical profile of those agitated schizophrenia patients could be defined as patients suffering from positive psychotic symptoms (e.g., auditory hallucinations, persecutory or paranoid delusions), conceptual disorganization, suspiciousness and disorganization, and/or assaultive speech. On the other hand, it is very rare that psychomotor agitation in schizophrenia appears when there is a predominance of negative symptoms (e.g., reduced speech, low motivation, narrowed range of affect, social withdrawal).

Table 9.2. Agitation in schizophrenia and BD: differential characteristics

	Agitation in Schizophrenia	Agitation in Bipolar Disorder
Phase of the illness	• Acute phases • First episodes	• Manic state > mixed state > depressive features
Predominance of symptoms	• Psychotic symptoms: auditory hallucinations, persecution, and paranoid delusions • Disorganization, confusion, suspiciousness • Speech: disorganization, assaultive	• Grandiosity delusions • Elation, irritability • Speech: loud, rapid, pressure • Depressive mixed states
Clinical implications	• Noncompliant patients • Higher rates of hospitalization	• Predictor of mood switch (indicator of polarity)

When agitation is present in a BD patient, it is more frequently found in manic states, mixed states, though depressive episodes can also include agitation. Moreover, as previously discussed, psychomotor agitation in BD has also been considered a predictor of mood switching in those suffering mixed or depressive states (Iwanami et al. 2015). BD with psychomotor agitation is more frequent when patients present with elated or irritable moods, but also in depressive mixed states. In addition, agitation is more frequent when grandiosity delusions or loud, rapid, or pressured speech is part of the clinical presentation.

Psychomotor agitation presenting in depressive states could occur as a product of inner tension and anxiety without being related to the increased goal-directed activity that is present in manic states (Table 9.2) (Swann 2013).

Assessment Methods

Available expert consensus and literature reviews agree that a prompt assessment of the agitated patient is critical for successful management (Allen et al. 2005; Marder 2006; Stowell et al. 2012).

When agitation is present – even in known schizophrenia or BD patients with typical clinical features – standard assessment, and management with serial neurological and psychiatric mental status examinations, are appropriate. For those with atypical features, especially where other diagnoses are suspected (e.g., delirium, history of trauma, overdose, fever, headache), additional diagnostic tests should be considered to rule out comorbid medical conditions, including neuroimaging, lumbar puncture, serum chemistry panel, complete blood count, endocrine tests, and toxicological screens. However, more recent guides and expert recommendations propose that even when a comorbid condition is not apparent, the routine medical examination should include vital signs, blood glucose (finger stick), and oxygenation level (Allen et al. 2005; Stowell et al. 2012; Garriga et al. 2016).

Further, several psychometric tools have been used during clinical physical assessment of patients and the psychiatric mental status evaluation to measure the severity of agitation,

Table 9.3. Assessment tools for psychomotor agitation (Garriga et al. 2016)

	Characteristics	Target Settings
Psychometric tools assessing psychomotor agitation in psychiatric settings		
Agitation Severity Scale (ASS) (Strout 2014)	• Observer-rated • Twenty-one items • Assess severity • Rapid	Acutely agitated psychiatric patients
Behavioral Activity Rating Scale (BARS)(Swift et al. 1998)	• Observer-rated • Single item, seven levels of severity • Measures severity • Easy and valid to assess treatment efficacy	Agitated patients with psychosis
Brief Agitation Measure (BAM) (Ribeiro et al. 2011)	• Self-rated • Three-item inventory, seven-point Likert scale • Assess severity • Easy and reliable	Non-clinical samples and psychiatric outpatients
Clinical Global Impression Scale for Aggression (CGI-A) (Huber et al. 2008)	• Observer-rated • Single-item, five-point Likert scale • Assess severity • Easy to generalize and extensively used in clinical trials	Agitated psychiatric patients (schizophrenia, substance use, mood, and personality disorders)
Cohen-Mansfield Agitation Inventory (CMAI) (Cohen-Mansfield, Werner, and Marx 1989)	• Observer-rated • Twenty-nine agitated behaviors, seven-point Likert scale • Assess severity in a long observational period (two weeks) prior to administration	Elderly patients in long-term care facilities and agitation in psychiatric wards
Overt Aggression Scale (OAS) (Silver and Yudofsky 1991) / Overt Agitation Severity Scale (OASS) (Yudofsky et al. 1986)	• Observer-rated • Classifies into four severity types • Easily applicable	Adults and pediatric psychiatric patients in clinical and research settings (schizophrenia)
Positive and Negative Syndrome Scale Excited	• Observer-rated • Five individual PANSS items	Acute psychotic patients (schizophrenia, BD)

Table 9.3. (cont.)

	Characteristics	Target Settings
Component (PANSS-EC) (Kay et al. 1987)	• Simple and intuitive • Extensively used in clinical trials.	
Staff Observation Aggression Scale (SOAS) (Palmstierna and Wistedt 1987)	• Observer-rated • Five columns rating • Assess the nature and the severity	Psychiatric inpatients
Checklists assessing agitation and aggressive/violent behaviors		
Broset Violence Checklist (BVC) (Linaker and Busch-Iversen 1995)	• Observer-rated • Six items of aggression/violence • Predictive tool of a violent episode in the next twenty-four hours	Psychiatric inpatients
The Historical, Clinical, Risk Management-20 (HCR-20) (Webster et al. 1997)	• Observer-rated • Twenty items of aggression/violence potential	Clinical psychiatric, forensic, and correctional settings among acute episodes of major mental disorder
The McNiel-Binder Violence Screening Checklist (VSC) (McNiel and Binder 1994)	• Observer-rated • Five-item of aggression/violence potential • Assess the short-term risk of aggression/violence	Psychiatric acute inpatients in short-term units

the risk of escalation to aggressive behaviors, and treatment response (Zeller and Rhoades 2010). Diagnostic assessment tools for the agitated schizophrenia or BD patient may be an important adjunct to the patient´s records. Some assessment tools in agitation are checklists designed to screen warning signs of aggression/violence in patients with agitation (Table 9.3). However, for agitated patients, rapid clinical decision making is a priority, and action often must be taken to protect the safety of patients and staff before administering any standardized assessment tool.

Management

Agitation requires prompt and safe intervention. Traditional methods for treating agitated patients, for example, routine physical restraints and involuntary medication, have been progressively replaced by non-coercive approaches (Richmond et al. 2012; Garriga et al. 2016). In general, the available literature has classified four approaches for the management of the agitated patient that are neither mutually exclusive nor absolute in their order of implementation: environmental manipulation, de-escalation techniques, physical/

mechanical restraint or seclusion, and pharmacological interventions (Marder 2006; Richmond et al. 2012; Garriga et al. 2016). Pharmacological strategies have evolved in the past years with the introduction of better-tolerated and more patient-friendly formulations (Popovic et al. 2015). Ineffective management of agitation can result in an unnecessary use of coercive measures (involuntary medication, restraint, and seclusion), escalation to violence, adverse outcomes for staff and patients, and substantial economic costs to the health care system (Hankin et al. 2011).

Prior to the first contact with psychiatric services, there is considerable evidence that initial psychotic and manic episodes are associated with an increased risk of agitation and/or violence (Coid et al. 2013). When managing agitation in schizophrenia or BD, clinicians should also remember that an episode of agitation often leads to the first visit of these patients to an emergency psychiatric setting. Schizophrenia and BD patients are likely going to need long-term mental health care services and an important factor in acceptance and alliance for long-term care is how well clinicians can minimize coercive measures in this first intervention. Strategies such as environmental modifications, creating a therapeutic alliance, implementing verbal de-escalation techniques, and considering patients' medication preferences could also be favorable in the context of long-term care patients.

Nonpharmacological Interventions

Environmental Modifications

Current literature supports the idea of "safety of the patient and those nearby" as the initial concern in the management of psychomotor agitation (Marder 2006; Schleifer 2011; Richmond et al. 2012). In this regard, some environmental and safety measures should be in place, even before the patient is evaluated (see Table 9.4).

Verbal De-escalation

As a second step, verbal de-escalation and calming techniques are a necessary component to any clinical involvement with psychomotor agitation. These nonpharmacological approaches are important to use not only initially, but throughout the management of an agitation episode. Verbal de-escalation, originally defined by Stevenson and Otto (1998) as "talking the patient down," has shown the potential to decrease agitation and reduce the risk of associated violence. Project BETA proposed ten specific domains of verbal de-escalation techniques (Fishkind 2002; Richmond et al. 2012) that are considered the non-coercive interventions of choice to calm the agitated patient, by gaining his/her cooperation (Table 9.4) (Knox and Holloman 2012). (For more on de-escalation, see Chapter 10.)

Restraint and Seclusion

The third nonpharmacological intervention to consider is physical or mechanical restraint and seclusion. These interventions are traditionally used, but there is much controversy regarding the use of restraints and seclusion for the agitated patient (Fisher 1994). Coercive measures, in general, might involve negative psychological and physical effects on patients, staff, and the therapeutic relationship they may have (Mohr et al. 2003). The use of these techniques should include a good knowledge of local regulatory policy (Jarema 2015).

Although restraints should be avoided whenever possible and never used for staff convenience or as a disciplinary intervention, there may still be clinical situations in

Table 9.4. Nonpharmacological interventions in psychomotor agitation

Intervention	Description
Environmental Modifications and Safety Concerns	Physicians and other staff precautions: • Try to visit patients not alone • Disarm patients • Remove conflict partners (e.g., family members, other patients) • Avoid unsafe situations (e.g., closed rooms or where access to doors is blocked, compromising locations)
	Physical space considerations: • Use moveable furniture • Remove objects that can potentially be used as weapons • Use rooms with two exit doors • Minimization of sensory stimulation • Ensure that the patient is physically comfortable
	Examination and exploration of clinician attitudes: • Maintain a safe distance and respect the patient's personal space • Avoid prolonged or intense direct eye contact • Minimize body language positions that can be considered confrontational and threatening (e.g., crossed arms or hands behind the back or hidden) • Minimize prolonged waiting time • Communicate in a safe, respectful, and caring attitude • Adequate number of trained staff in psychomotor agitation
Verbal De-escalation	Principles of de-escalation techniques: • Respect personal space • Do not be provocative • Establish verbal contact • Be concise • Identify wants and feelings • Listen closely to what the patient is saying • Agree or agree to disagree • Lay down the law and set clear limits • Offer choices and optimism • Debrief the patient and staff
Seclusion and Restraint	• Used as last strategy and for the shortest period possible • Never as a means of punishment, for the convenience of staff, or as a substitute for a treatment program • Medication should be administered • Efforts in verbal de-escalation should continue • Sufficient trained staff available • Monitoring: to assess response to medication and to prevent complications

which verbal techniques are not effective and the use of restraint and/or seclusion becomes necessary to prevent harm to the patient and/or staff (Knox and Halloman 2012). Agitation in patients with medical conditions, personality disorders, and psychotic syndromes (schizophrenia, manic, or mixed patients) are common targets of restraints or seclusion. Quality standards do exist for the use of restraints in these situations (Petit 2005; Marder 2006) (see Table 9.4).

Recent guidelines indicate that if a patient is an immediate danger to others but not to him or herself, locked seclusion alone might be sufficient to separate the patient from potential victims. However, restraint may be appropriate if the patient becomes a danger to him/herself while in seclusion, such as hitting himself or pounding his head against the wall (Knox and Halloman 2012). In either locked seclusion alone or with the addition of restraints, medication will typically also need to be administered, and verbal de-escalation efforts should continue.

All staff members in emergency departments and acute psychiatric settings should be familiar with the types of restraints used in their programs, and how they should be appropriately applied and monitored, as well as how to assess potential bodily injury that might result from the application of the restraint.

Pharmacological Intervention

In patients for whom nonpharmacological treatments for acute agitation fail or are not indicated, medication can be an effective treatment strategy (Baker 2012). The ideal medication for the acute management of agitated patients should be easy to administer and nontraumatic; provide rapid tranquilization without sedation; have a fast onset of action and a sufficient duration of action; and have a low risk for significant adverse events and drug interactions (Allen et al. 2003; Ng, Zeller, and Rhoades 2010; Zimbroff et al. 2007).

The pharmacological management of acute agitation in psychiatry has traditionally employed three classes of medications: first-generation antipsychotics, benzodiazepines, and second-generation antipsychotics (Marder 2006). During the past few years, treatment options have grown considerably with the development of new intramuscular (IM) second-generation antipsychotics and novel, patient-friendly oral, sublingual, and inhaled formulations (Baker 2012; Jarema 2015; Popovic et al. 2015). Nevertheless, none of the current pharmacological options fulfills all of the criteria for an ideal anti-agitation medication.

In general, with the emergence of second-generation antipsychotics, the expert consensus-based guidelines (Allen et al. 2001 and 2005; Hasan et al. 2012; Kasper et al., 2013; BETA group; Garriga et al. 2016) preferentially recommend second-generation antipsychotics as first-line therapy. Oral, sublingual, and inhaled formulations have also been recommended as the first choice, as IM and intravenous (IV) applications may devastate the therapeutic alliance (Allen et al. 2001 and 2005; Hasan et al 2012; Kasper et al. 2013; BETA group; Garriga et al. 2016).

When treating psychomotor agitation in schizophrenia and BD (mainly manic episodes) patients, a common pharmacological pathway should be most commonly attempted. In addition to the goals described previously, these key points should also be considered: the desire to achieve a quick relief of agitation and/or aggression to self or others; reduction of the positive symptoms that may have led to the psychomotor agitation; and the initiation of a therapeutic alliance. The choice of an adequate pharmacological treatment for this population of agitated patients also depends on other patient-related variables such as

Table 9.5. General pharmacological strategies to use in psychomotor agitation in schizophrenia and BD patients

	Schizophrenia/Bipolar Disorder	Special Considerations
Oral Antipsychotics	ODT: olanzapine, risperidone OS: risperidone, aripiprazole, haloperidol, levomepromazine Sublingual: asenapine Inhaled: loxapine	Will need patient's cooperation to be administered
IM Antipsychotics	Olanzapine, aripiprazole, ziprasidone, haloperidol	SGA over FGA
Oral Benzodiazepines	OS: clonazepam SL: lorazepam, diazepam	If an extra anxiolytic or sedative effect is needed
IM Benzodiazepines	Lorazepam, diazepam, midazolam	Erratic IM absorption of some BZD
Combinations		Avoid use of BZD with IM olanzapine

BZD = benzodiazepines; FGA = first-generation antipsychotic; IM = intramuscular; ODT = orodispersable tablets; OS = oral solution; SGA = second generation antipsychotic; SL = sublingual.

comorbid disturbances and readiness for cooperation. Antipsychotics are preferred over benzodiazepines. Different formulations of antipsychotics are proposed in this regard, considering second-generation antipsychotics over first-generation antipsychotics, oral formulations (e.g., tablets, oral-dissolving tablets, oral solutions, sublingual, inhaled) for when patient cooperation is present, and IM (or even IV) for when patients are unable to cooperate. Table 9.5 further delineates these pharmacological approaches.

If benzodiazepines are needed in these patients, they are most commonly used in combination with antipsychotics, when a sedative and anxiolytic effect is required (important also in those mixed or depressive states of BD). One benzodiazepine and antipsychotic pairing to avoid is a benzodiazepine given within one hour of administration of IM olanzapine, because of the higher risk of respiratory depression (Garriga et al. 2016).

As an option for an oral second-generation antipsychotic, olanzapine is supported by data from a large number of positive trials with flexible doses (up to 40 mg/day) (Zeller and Rhoades 2010; Garriga et al. 2016). For risperidone, both the oral-dissolving tablet and the oral solution might be appropriate in this population, and oral aripiprazole has been compared to placebo with positive results (Buckley et al. 2011). Asenapine was also better than placebo in the management of agitation, and it is a good option in BD (Zeller and Citrome 2016). No high-quality trials of oral benzodiazepine monotherapy have been published. Concerning the new aerosolized inhaled formulations, loxapine 10 mg has shown superiority to placebo in the management of agitation in all studies reported (Zeller and Citrome 2016).

For IM first-generation antipsychotics, neither haloperidol, levomepromazine, nor chlorpromazine were superior to other IM second-generation antipsychotics (e.g.,

olanzapine 10 mg). Results from the trials also revealed similar results when IM first-generation antipsychotics were compared with IM aripiprazole (9.75 mg) or ziprasidone (10–20 mg) (Citrome et al. 2001). Among IM second-generation antipsychotics, several trials have evaluated olanzapine, aripiprazole, and ziprasidone against placebo with positive effects (Citrome et al. 2001). IM benzodiazepines, such as lorazepam or midazolam, in general, showed equal effectiveness results in comparison to other IM first-generation antipsychotics. However, when benzodiazepines were compared with other IM second-generation antipsychotics, they were inferior to olanzapine but as effective as aripiprazole (Zeller and Rhoades 2010; Garriga et al. 2016).

Conclusions

Psychomotor agitation is a frequent condition in both medical and psychiatric emergency settings (Yildiz et al. 2003; Battaglia 2005; Nordstrom et al. 2012). Agitation might escalate from anxiety to agitation and aggression (Zeller and Rhoades 2010). Despite common neurobiology and genetics, further research is needed to clarify its neuropathological basis.

To perform an adequate assessment of psychomotor agitation, the first consideration is to rule out medical etiologies. Once a medical condition has been excluded, schizophrenia and BD are the most frequent psychiatric conditions that might present with psychomotor agitation.

Appropriate management of agitation is of utmost importance. Despite the lack of controlled studies comparing nonpharmacological and pharmacological interventions, current guidelines recommend the first-line use of verbal de-escalation techniques. Whenever verbal techniques (or even pharmacological treatments) fail, physical restraint or seclusion may be considered, but constitutes a "treatment-of-last-resort." The most recent guidelines and expert recommendations preferentially recommend second-generation antipsychotics as first-line pharmacological therapy, although first-generation antipsychotics and some benzodiazepines continue to be effective treatment choices.

Key Points

- Schizophrenia and BD patients are the most prevalent psychiatric patients that present psychomotor agitation aggressive behavior.
- Younger males, previous psychiatric admissions, positive psychotic symptoms, and comorbid substance use disorders are important warning signs of agitation or escalation to aggressive behavior in this population.
- The whole therapeutic approach in psychomotor agitation should involve three important steps:
  - Establish safety for patient and others
  - Adequate differential diagnosis
  - Treatment started with verbal de-escalation > oral, sublingual, inhaled medication > IM medication > physical restraint/seclusion
- Pharmacological choices in schizophrenia and BD with psychomotor agitation: second-generation antipsychotics over first-generation antipsychotics; benzodiazepines could be also used in combination with antipsychotics.

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Chapter

10

Collaborative De-escalation

Jon S. Berlin

Introduction and Nomenclature: A Reconsideration

There are different ways to refer to this subject. To "de-escalate" is to "reduce the intensity of (a conflict or potentially violent situation)" (*New Oxford American Dictionary*, 2016). In the clinical setting, involuntary medication and physical holds are considered measures of last resort for de-escalating agitation. Therefore, as a title for our topic, the unmodified term *de-escalation* is not exclusive enough.

The familiar term *verbal de-escalation* conveys the general idea much better, but is not inclusive enough. It leaves out important accompaniments to verbal intervention, including voluntary medication and time out, the provision of physical comforts, and skillful non-verbal behavior. Examples of the latter are a strong, calming, non-reactive presence and maintenance of an altruistic and non-authoritarian yet authoritative demeanor.

Non-coercive de-escalation is a good term for encompassing both verbal and nonverbal interventions, as well as for emphasizing the key attitudinal shift away from power and control toward engagement and cooperation. However, when combative, uncooperative individuals are brought to emergency settings on a mental health detention, the phrase "non-coercive" fails to capture the tacit continuation of a coercive posture. We should have no illusions about the fact that, even if we never use physical force, we initially preserve the legal hold and urge these patients to engage with us against their will. Our approach is benevolent and emphasizes the use of soft power, but our insistence on safety is unyielding, and hostile customers do feel like our prisoner. This clash of agendas – ours to be helpful, and theirs to be left alone – is anything but non-coercive, and to progress beyond this seeming impasse, the drama must be acknowledged and addressed.

The atypical term *nonviolent de-escalation* is interesting. It captures the patient's perspective that, on the receiving end, clinical force and coercion, no matter how respectfully applied, feel like a form of violence, even trauma (Allen et al., 2003). Of course, by the same token, the term unfairly disparages practitioners who responsibly use physical force only as a last resort, that is, when dangerous individuals fail to respond to verbal and nonverbal, non-coercive de-escalation techniques. But in the heat of the moment, it is a good phrase to latch onto; and a spoken declaration about "nonviolence" and "nonviolent conflict resolution" can be a useful way to sum up for a client and our staff what we believe in and what we are committed to practicing.

The newer term *collaborative de-escalation* is similar in many respects to "non-coercive de-escalation." Its special appeal is that it names the outcome we are striving for, not what we are trying to avoid. The amount of patient–clinician collaboration in cases of agitation exists on a continuum, and it is probably the single most important factor in determining the degree of difficulty of the de-escalation procedure. In the easier cases, collaboration is

a given. Such cases are seen more often in the psychiatrist's office than the acute setting. In the hardest cases, collaboration is a good goal to set for future occurrences, but unlikely to be a realistic hope for the current episode of illness. In the intermediate cases where a patient's self-control is touch and go, working quickly to secure his or her participation is the secret to success. This chapter focuses on the techniques for engaging these borderline cases.

Emerging Standards of Care

Collaborative approaches to de-escalation have long been the gold standard, and have only become more in demand with the growing emphasis on participatory decision making in medicine. Multiple authors advocate it (Richmond et al., 2012). But I think there is now the added expectation that, on the front lines in the clinical arena, the best-trained doctors and staff take the lead, not the least trained. There appear to be four reasons for this.

One is the growing recognition that, analogous to emergency department (ED) protocols for stroke and sepsis and myocardial infarction, the protocol of having experts intervene with agitation early, at the front door if possible, produces better outcomes. The merit of this approach for agitation is yet to be empirically validated, but consumer satisfaction reports, naturalistic observation, and anecdotal evidence strongly support it. When a modicum of mental functioning is preserved, individuals previously thought unreachable can be engaged, if we seriously consider their thoughts, feelings, and needs, and find a goal of theirs with which we agree. In this new paradigm, psychiatry residents and other trainees need to learn this science and art by working alongside senior staff, rather than by trial and error alone.

Two, as psychiatric emergency services (PESs) increasingly become a linchpin of the mental health care system around the country, and as the discipline of emergency psychiatry approaches maturity, a consistently high level of practice is called for. Like what law enforcement is experiencing nationally, coercive practices in psychiatry are coming under ever-increasing scrutiny.

Three, in keeping with the biopsychosocial model of diagnosis and treatment, psychiatric agitation is a syndrome of the brain, the mind, and the interpersonal field. It responds best to a skillful blend of the biological, psychological, and humanitarian dimensions of psychiatric practice. Psychiatric residents and other trainees have not mastered all of these or developed a style that smoothly integrates them. They need to see experts at work and to have experts see their work.

Four, since de-escalation procedures can deteriorate rapidly, and mistakes or less-than-perfect moves are inevitable, another emerging standard of care is to follow up with the patient afterward as soon as possible. There is an art to this kind of conversation; trainees and hospital staff can benefit greatly from observing how senior practitioners handle it. This form of debriefing is detailed later in this chapter.

Five Fundamentals of De-escalation (see Table 10.1)

De-escalating the extreme types of agitation seen in ED and PES settings is like batting in the major leagues. Didactic instruction and observing the performance of others both have their place. In the end, it just takes a lot of practice. Even then there will be strikeouts. However, it does help to have a good intellectual framework to build on, refer to, and ultimately tailor to one's own personal style and preferences.

Table 10.1. Five Fundamentals of De-escalation

I.	Prepare to engage
II.	Engage early and safely
III.	Be authoritative, not authoritarian or permissive
IV.	Engage the person around medication, if indicated; don't rush or delay
V.	Learn from mistakes and repair any damage

What follows is a format successfully used to orient general psychiatrists, psychologists, psychiatry and emergency medicine residents, nurses, social workers, and security to the key concepts of de-escalation. It is a distillation of the literature, shoptalk, feedback from consumers, and four decades of front-line, personal experience in multiple acute care settings, beginning with my time as a child care worker in a residential treatment center for psychotic and assaultive adolescents. Fifteen thousand is a conservative estimate of the number of agitation cases personally managed or supervised in a hectic, state-of-the-art, inner-city PES.

I. Prepare to Engage

As one embarks on a new agitation case, it is helpful to prepare cognitively and emotionally. First, review briefly the reasons why collaborative de-escalation is a good idea (see Table 10.2).

Next, anticipate that charged atmospheres provoke intense negative emotions and reactions in oneself and others. The goal is to experience them and process them internally without acting on them. Consider that whatever feelings one might be having, for example, fight or flight, the patient is undoubtedly having them even more. If a patient seems threatening to *us*, when we hold all the cards (police, security, show of force, restraints, intramuscular injections, involuntary treatment law), imagine how threatening we appear to *him*.

A useful scheme for remembering the affects that get generated in oneself and the patient is to review the disaster reactions that we ameliorate with Psychological First Aid (Center for the Study of Traumatic Stress, 2016) (see Table 10.3).

An interesting feature of psychotic agitation is that the likeable and human aspects of a person may be submerged in mental illness. Be prepared initially not to see any aspect of the agitated individual that is accessible to engage with. But be resolved to actively search out preserved areas of functioning or to shift quickly to support another member of the team with whom the patient might have a rapport.

By the same token, be prepared to avoid the temptation to dismiss everything the agitated person says as without merit and as a symptom of illness. Very psychotic individuals sometimes make sense, and individuals may remember how they were treated even when their agitation is very biologically driven, as in cases of delirium. A common example is patient complaints. When a patient is agitated, the way complaints are verbalized may be excessive or distorted, but they may have a kernel of validity that needs to be acknowledged and addressed.

Table 10.2. 10 Reasons Why Collaborative De-escalation Is a Good Idea

1. Increases staff & patient safety; reduces injuries
2. Reduces overall staff involvement and documentation requirements
3. Models nonviolent problem solving and self-control, rather than imposing it
4. Engages patients in treatment, rather than alienating them from it
5. Increases disposition options, such as transfer to private or subacute crisis facility
6. Fosters the ED/PES agenda of turning an acute patient into an outpatient
7. Potentially reduces the frequency of return visits
8. Increases patient satisfaction
9. Lowers the risk of lawsuits over excessive use of force
10. Lowers restraint rates, which are a quality indicator for Joint Commission and CMS

Table 10.3. Reactions and Helpful Responses

Expect the patient feels	Respond wiith
fear of being physically hurt	promises to do everything possible to ensure safety
overstimulation	calming statements and actions
feelings of being disconnected with one's support system	well-timed re-connection with key social supports
helplessness and lack of self-efficacy	fostering self-efficacy by asking such questions as "What do you need?"
hopelessness and defeatism	using hopeful statements such as "You can do this. We are committed to helping people get through this without getting physical. Work with us. This is what we do."

II. Engage Early and Safely

One of the most common errors is to omit the step of engaging the agitated individual and jump ahead to medication. It is an understandable mistake when seeing someone so symptomatic and probably under-medicated. But it falsely assumes that the affected person will have no useful ideas of his or her own, which only agitates the person further and diminishes his or her receptivity to the doctor's ideas.

Note that with every case of agitation three semi-independent variables are at work: illness, dangerousness, and therapeutic alliance or engagement. A rapid estimate of the status of each will guide where efficient practitioners should first direct their efforts. Office practitioners without ED experience may fail to appreciate how much they take engagement for granted and similarly fail to appreciate how lacking it is at the front door of an ED. Likewise, ED and PES practitioners without much ambulatory care experience may not appreciate what a difference a strong therapeutic alliance makes, and therefore give short shrift to developing it immediately at the outset.

Case Example 1

A delightful, retired business woman with a bipolar disorder has a heated argument with her son about the current presidential campaign. Years earlier, she had decided never to discuss politics with him again, but now she thinks it's time to stop being so passive. He notices excessive irritability, tangentiality and pressured speech, which are her usual warning signs of an impending manic episode, and calls her psychiatrist. The psychiatrist calls the patient and they talk briefly. She is in an expansive mood, but friendly, rational, and very glad to hear from him. She has been sleeping only two hours a night and spontaneously describes herself as "agitated." Dangerousness is not an issue – never has been – but she is clearly hypomanic, and she readily agrees to his suggestion to increase her medication that evening and come in the next day for a brief appointment. In the office, she begins with a rambling, detailed account of the entire political argument with her son. The psychiatrist keeps bringing the conversation back to what she wants help with, and she keeps changing the subject to her son, whom she describes as dogmatic and condescending. He persists, and within ten minutes, she agrees with his assessment that she is variably euphoric and irritable, but disagrees that her thought process is less focused than usual. She is just excited about a contract for a new project that will be a feather in her cap. Nonetheless, she has trusted and enjoyed seeing her doctor for twenty years, and she agrees with his recommendation to increase her medication and the frequency of office visits. Without hesitation, she takes her pill bottles out of her purse and starts the higher dose. Total length of visit: twenty minutes.

To illustrate this point, consider a typical office case where the individual with mental illness is agitated, but not dangerous or opposed to professional help.

Emergency practitioners rarely see such cases, where engagement and alliance are this strong and dangerousness is nonexistent. In this scenario, it is fine to proceed directly to the subject of medicine after a brief assessment. Had this woman turned out to be a danger to herself or others, she would have also accepted a referral for a voluntary hospitalization or community crisis center stay without hesitation. Emergency practitioners do not see many of these cases, either. The classic ED or PES agitation case is an individual on an emergency police detention, where the sine qua non is hostility and uncooperativeness, in addition to mental illness and dangerousness. The person has refused help before coming in and continues to refuse it. Therefore, the initial focus of de-escalation should be to try to engage people to participate in their own de-escalation.

One's own personal safety is an equally important consideration. These individuals resent being forced. They may have been combative with police and been treated roughly. They may complain their handcuffs are too tight. They view doctors as jailers and can be intimidating. Most beginning staff tend to avoid such cases out of fear. A few may happily answer the call but then physically sit or stand too close, forgetting that initially they are seen as the enemy, not the ally. Supervisors must remind them to approach the agitated patient cautiously, with security and staff back up, and begin the process of engagement from a safe distance.

Beginners should be reminded that doctors and staff are most at risk for assault when frustrating an agitated patient's most serious requests, which usually revolve around disposition. Typically, there is a demand for discharge or a demand for admission. The practitioner should always reassure the person that one's job is to give them exactly what they need, or find someone who can.

These are hard cases. Having an experienced doctor see agitated patients at the front door is strongly recommended. It leads from the front, communicates genuine interest, and

mitigates iatrogenic escalation in multiple ways. Strong anecdotal evidence suggests it is as pivotal to a good outcome as early intervention for stroke or myocardial infarction or sepsis. Agitation is painful and dysphoric. Making sufferers wait is irritating and tends to provoke either acting up or shutting down.

Next, give the person your undivided attention and listen actively. In the words of Covey, "Seek first to understand, then to be understood" (Covey, 1989). Active listening, non-judgmental and non-probing, is both diagnostic and therapeutic. One should introduce oneself and ask what one can do for the person. Consider that, from the person's perspective, treatment begins at the beginning of the interaction; it's the sum total of how he or she is treated.

If an individual is angry with me, I consider the possibility that I have, or someone on my service has, done something to annoy him. Address valid complaints as one would with any other person one respects.

Highly irrational and psychotic individuals can be unnerving. Respond to paranoid accusations and hate glares by reminding the individual over and over again, as often as necessary, that as his doctor (or his nurse, et cetera) the only thing one wants is to be helpful. Keep asking what the person wants and needs. Find something that makes sense that one can partner with. Find a way to join one's own agenda with the patient's agenda. Begin with the end in mind (Covey, 1989): What goal can you and the patient agree on? Most often, agitated and hostile individuals just want to get out. Reformulate this into the goal of "being safe to go."

Case Example 2

"Ms. Smith," a middle-aged, African American woman in fine clothes and jewelry, is brought into PES on an emergency detention for agitation and verbally threatening her family. She had refused help and was combative with police when they came to the house. She sits down in the nursing triage booth, but refuses to answer any questions or let her vital signs be taken. Her loud, pressured speech, flight of ideas, mocking laughter, and angry accusations fill the room. The triage nurse asks the psychiatrist to see her. The patient is extremely agitated. She glares but avoids eye contact and talks to the wall. The psychiatrist introduces himself and asks what he can do for her. She looks at him briefly, but ignores the question. Her statements are emphatic but hard to follow.

He tries to interrupt her, and finally succeeds in asking her what she needs. She replies, a black doctor. He says that, although they have some black doctors on staff, none are on duty at the present time. Her flight of ideas and loose associations resume, and he interrupts again, asking what does she need? She eventually gives him a haughty look and says she needs someone with some "effen" common sense. He says he thinks he has that and asks again several times what he can do for her.

At this point, he has a pretty good starting idea of her problem and her needs. He has never seen her before, and doesn't know if she has an old chart, but something about her suggests that she is familiar with this kind of situation and has been here before. She looks physically healthy and alert. She isn't perspiring or disoriented or showing fluctuations of attention or consciousness. He realizes organic mania is a possibility, but suspects manic psychosis in the context of bipolar disorder. He keeps all of these ideas to himself for now. He has many other questions for her pertaining to mental status, treatment history, history of present illness, medical history, et cetera. All of them can wait.

Then he asks her again what she needs. She half comes out of her chair and points in his face and shouts, "I need to get the eff out of here!" He rolls his chair back a little, glad that

when he sat down across from her, he had kept a safe distance. He also looked to make sure that security and nursing staff were paying attention and keeping an eye on them.

He pauses, and then says, "Great. That's my job, to jumpstart the process of your getting out of here. To do that, *we* just need to show people that it's *safe* for you to go." He pauses again, and then continues, "What works for you when you're feeling like this?" She stares off into space again but with less intensity. He has a sense he has her attention and asks the question again. She glares at him and speaks slowly, biting and attacking each word. "I . . . suppose . . . I could take . . . some effen . . . lithium."

He nods. "Great. We have some here. I assume you've taken it before, but maybe not for a while, is that correct?" He pauses. When she doesn't say anything, he goes on, "Good. I'll get some for you." He stands up and starts to walk back to the medication room, but then stops and turns back to her. "You know," he says, "It takes lithium several days to take effect. We recommend combining it with another medicine. We have several to choose from. I'm thinking of something like . . . " She cuts him off. "And some effen . . . Zyprexa!"

He brings her 450 mg of lithium and 20 mg of meltable olanzapine. Ms. Smith takes both without hesitation. In twenty minutes, she is significantly calmer. She allows the nurse to complete the triage interview. The old chart arrives and confirms the diagnosis of bipolar disorder. Family is contacted and reports a recent history of significant dangerousness and treatment refusal. Ms. Smith does need admission. Orders are written, and she goes to an acute inpatient unit without incident.

This is clearly a case that could have gone either way. Avoidance of forced intramuscular medication and brief seclusion was not a foregone conclusion. The key was to find out what Ms. Smith wanted and how the doctor could work *with her* to get that. Once he had actively listened to her, she was more willing to listen to him, that it was fine for her to go, she just had to be *safe to go.* He deferred sensitive or humiliating subjects, such as diagnosis or formal mental status testing or previous medication noncompliance. He had enough information. And he refrained from making treatment recommendations before pressing her for *her* ideas about treatment. His guess was correct that she was far from treatment naïve.

Some practitioners might have been leery of offering Ms. Smith lithium without first checking a lithium level and baseline labs. Her psychiatrist could have said, "Lithium's a great idea, but starting out we should consider something a little bit different." But the risk of one dose of lithium is very low, compared with the risk of injury in a physical altercation, which she was on the verge of, and the benefit to engagement of trusting her grudging request was considerable. Also, she was obviously an intelligent person who showed no signs of being self-destructive or interest in becoming lithium toxic. Again, once he had listened to her about lithium, she was more willing to listen to him about adding on an antipsychotic. Finally, had she been even more agitated, he would have asked about her preferred route of administration of olanzapine. People who want the fastest results will often request an intramuscular injection.

III. Be Authoritative, Not Authoritarian or Permissive

Unlike being authoritarian, being authoritative implies having expertise, the ability to explain one's rationale, the power to influence or persuade, a thoughtful openness to being influenced by others, and knowledge of one's own limitations. Being authoritative means collaborating without abdicating expertise, and recommending without claiming

infallibility. Being authoritarian is being autocratic and domineering. Being authoritative is being self-assured and decisive.

Authoritativeness is a key to shared decision making and to collaborative de-escalation. In a recent article, Fried makes the counterintuitive but excellent point that the less sure a physician is about which treatment option to pick, the more opinionated the patient might need the doctor to be. Conversely, the more certain a physician is about which treatment option to pick, the more he should solicit the patient's opinion (Fried, 2016). It is the difference between telling someone what to do, and really making a joint decision. The case of Ms. Smith is a perfect illustration of this latter scenario.

Being authoritative also implies the ability to set limits, which is authoritarian. In working with Ms. Smith, the psychiatrist did not overtly set limits, but he did not lift the emergency detention she was on or consider letting her go before she was ready. He insisted on safety but was matter of fact about it. Had she stood up and become behaviorally threatening, he would have said firmly, "Sit down. Please, sit down." Had she claimed to be ready for discharge now, he could have said that, in order to convince people, she would need to demonstrate safety for a longer period of time. He could also have pointed to some of her behaviors that could make people uncomfortable.

Had she continued, like some patients do, to make an issue of "being held prisoner in this hell hole," he might have said they needed to work on finding a nonviolent way to resolve their conflict about this point. And perhaps he would point out that peaceably resolving this disagreement in the here and now would be good practice for handling other disagreements she might have in her outside life. The word "nonviolent" tends to make people feel less threatened. It's useful as an entreaty and a mantra.

Sometimes patients will argue that nonviolence doesn't work on the street. The best response to that is that we need different skills for different situations. There might be situations where you have to defend yourself with violence, but there are many other situations where getting physical makes things worse, where talking things out works best. If the patient continues to argue, one may be forced to point out that violence obviously wasn't working that well or the person wouldn't have been brought here.

In the case of Ms. Smith, the psychiatrist did not let her pick a fight. He understood it provoked her that he didn't immediately drop her protective custody, but he pressed her to collaborate: "What do you need when you're feeling like this? What would make you feel better? What can I do for you?" Had she been unable to answer this question at all, he would consider and/or offer the range of voluntary options such as time out, something to eat or drink, a blanket or couch to lie down on, a peer specialist to talk to, a bit of medicine, et cetera.

Had she seemed hopeless or helpless, he might have chosen to convey hope and partnership: "If we work together, I'm almost sure we can find a way to work this out."

If family or friends had accompanied her to PES, he would have assessed whether they were constructive influences or not, and then approved or disapproved them staying with her.

Had she asked for something that was going to be bad for her, he would not go along with it. To eschew being authoritarian does not mean being permissive. Similarly, when asking someone what he needs, one should take care not to ask in such a manner as to suggest that one has no good idea what to do. If a person says, "You're the doctor, you decide," determine whether this is a sincere request that should be granted, or whether it is being said sarcastically to bait the doctor into being controlling. In the latter case, one says, "Honestly, I mean it, I really want to know what your thoughts are."

IV. Engage the Person around Medication, if Indicated; Don't Rush or Delay

A seminal 2002 paper on the importance of verbal de-escalation is titled "Calming agitation with words, not drugs . . . " (Fishkind, 2002). Fishkind's point is not that medication is unimportant, but that it is essential to talk to people first. Ideas can be powerful. The relationship can be powerful. There is no medicine to stop Ms. Smith in her tracks and make her think about what she really needs. It took the force of personality and an idea conveyed with words, not drugs. People with agitation often need medicine, but they may not. In any case, if we skip ahead to medication, they will not feel heard or appreciated as a real person; they will feel dismissed, and they are much less likely to accept crucially needed medication.

Along similar lines is Diamond's excellent discussion of the importance of engaging the crisis patient concerning medication (Diamond, 2008). Rather than imposing a medicine on them, which makes it feel like an instrument of mind control, he adopts the point of view that it is a tool the patient can choose to take advantage of. To the greatest extent possible, make it a voluntary choice, for it is almost always that after the patient goes home.

Sometimes we see the opposite mistake. A patient comes in asking for an antipsychotic, and instead of giving it to them, we make them wait and wait. In fact, it is very rare for people to come to an emergency setting to ask for an antipsychotic medication unless they really need it. Usually, it is sorely overdue. I learned this from reviewing the chart on several episodes of physical restraint where the patient had come in requesting tranquilizing medication and not received it until after they were in restraints.

When patients come in asking for an antipsychotic, it is also safer and more effective to do an in-depth evaluation after they have received the medicine they need than before. I have reported on a case (Berlin & Gudeman, 2008) where I ill-advisedly broke the rule of "stabilizing before exploring." The patient was asking for medication and hospitalization, but seemed too composed and calm to need the latter. When I pressed him for acute precipitants, I suddenly touched a raw nerve that sent him bolting out of his chair, screaming, and pounding his fist on the desk right in front of me. I then asked if I could get him some medication. He glared at me. "That's what I goddam asked for in the first place!" I was unhurt in this incident, but learned a good lesson.

But the most common error in emergency practice is to bring up "taking your meds" before the patient does. In my experience, patients with severe mental illness have heard people say "Take your medicine" so many times in their lives, and are so sick of it, that they think you've said it to them even when you haven't. They assume that physicians and other prescribers will be pushing pills. In the case of Ms. Smith, the psychiatrist was all but sure that Ms. Smith was supposed to be on medication and had gone off of it for some reason. Manic psychosis almost always responds well to medicine, but had he pushed it, he could almost be guaranteed of hearing a litany of complaints.

However, sometimes a harder sell is required. As adapted from a presentation slide by Zeller (2008), one can use escalating persuasion to engage a person around medication. Sample language:

1. What helps you at times like this? *Fostering autonomy*
2. I think you might benefit from medication. *Matter-of-factly stating a medical opinion*

3. I really think you should consider a little medicine. It can be a nice tool for you to use. *Persuading and fostering self-mastery*
4. You're having a psychiatric emergency. I'm going to get some emergency medicine. It works well and it's safe and you'll feel a lot better. *Authoritatively inducing*
5. I'm going to have to insist you take some medicine. I think you're in grave danger, and we're not coming up with any other options. Would you like it as a pill or a shot? *Coercing, as a last resort, while maintaining some patient choice*

Applying this to Ms. Smith, if in response to question #1 she had come up with a non-medication solution that worked for her, the psychiatrist might have stopped there. Had her alternative solution not been successful, or had she not had any kind of answer to question #1, the psychiatrist would have gradually worked his way up the ladder of persuasion, stopping with the least degree necessary.

Another common mistake that beginners make is in the phrasing of the statements, "I think you might benefit from medication" or "I really think you should consider a little medicine." They are too timid. They see a person suffering from psychotic agitation, but the way they ask "Would you like some medicine?" comes off as reflecting fear and self-doubt.

Trainees sometimes benefit from a medical analogy. I ask them to imagine going to the ED with severe abdominal pain that started in the epigastrium and migrated to the right lower quadrant. They have abdominal guarding, rebound tenderness, mild fever, and an elevated white count. They have failed a trial of antibiotics. What would they think if a surgeon were to come in and say, "You have appendicitis. It's failed to respond to conservative management. Would you like me to take out your appendix?" They would be confused and anxious. They need the surgeon to be decisive. No one wants surgery, but if we need it, we will have it.

V. Learn from Mistakes and Repair any Damage

Agitation is an intermediate diagnosis, with a multitude of underlying etiologies. Agitated patients, especially non-engaged patients, are difficult to evaluate. Ms. Smith refused simple vital signs and undoubtedly would also have refused laboratory studies, brain imaging, or point-of-care screening tests such as a urine drug scene. Had she not been approached in just the right way, she would have refused medicine too. It is very easy to imagine her, and patients like her, escalating further upon arrival in an emergency center, and escalating to the point of needing a brief physical hold and involuntary medication.

The goal of avoiding coercive intervention is made even more difficult by other conditions that impair brain functioning: delirium, intoxication, fulminant mental illness, and brains that are senescent, juvenile, or damaged. There may be trauma history that seriously damages an individual's capacity for relationships and trust. It may be trauma from childhood or adulthood. There may be trauma and ill will due to encounters with previous caregivers. There are also limitations of the treatment setting, such as inadequate physical space, tired staff at the end of a shift, patient volume surges that cut our time short, and overly lean faculty-trainee ratios or simply a lack of expert staff on hand.

Given these frailties and failings, coercive intervention is occasionally necessary. At the same time, it is essential to realize that it generally evokes hard feelings and it may damage the therapeutic relationship. Whenever possible, and as soon as possible, the practitioner should non-defensively follow up with people after they are calm, to discuss what happened,

how it might have gone better, and how to handle it better in the future should the condition arise again.

Patients sometimes make some very good observations and suggestions. The practitioner should be open to constructive feedback. He or she might say, simply, "I wished that had gone better. What thoughts do you have? How do you feel about it? Any suggestions?" This is part of the therapy, and the long-term goals of therapy remain: repairing inevitable ruptures in relationships (Lewis, 2000), talking things through rather than acting out, planning ahead to avoid coercion in the future, and turning oneself from an acute patient to an outpatient. At the very least, a sincere after-event conversation mitigates negative feelings, sets a good example for the rest of the team, and reduces the risk of a lawsuit.

Theoretical Considerations

As described in this chapter, this approach to de-escalation involves rapid, iterative mini-cycles of data gathering, assessment, and treatment. Assessment is approached with the mindset of being useful to the individual in a very respectful, concrete way, essentially wrapping assessment together with treatment. This approach can also be conceptualized as a form of ultra-brief psychotherapy. It is very active yet very sensitive. It combines elements of:

- Psychological First Aid
- Motivational Interviewing
- Stages of Change Model (Engagement)
- Interpersonal Therapy
- Solution-Focused Therapy
- Trauma-Informed Care

Given the crisis nature of the situation, the usual contraindications to brief therapy (Mantosh, Steenbarger, & Greenberg, 2012) do not apply:

- Poor insight
- Severe and persistent illness
- Significant trauma history of abuse and neglect
- High complexity, for example, dual diagnosis
- Poor social support
- Hypersensitivity to the ending of the therapeutic relationship

However, their existence may account for the slowness of psychiatry historically in promulgating an assertive, dexterous, biopsychosocial approach to de-escalation. And, of course, they are helpful prognostic indicators, adding another perspective to the question of why some attempts at collaborative de-escalation fail.

Conclusion

Formerly, collaborative de-escalation in the emergency setting has been left to chance. The questionable tradition in psychiatry of using professional advancement to increasingly buffer oneself from the most acute treatment settings was never more evident than in the psychiatric emergency service. Unsupervised residents once manned the battle stations and simply did the best they could, which was hit or miss.

Now, however, graduate medical education requires the presence of faculty, the private practice environment has become less hospitable, and high-quality psychiatrists are discovering the satisfaction of the most acute care. They are replacing the dread of complex, unknown, agitated, dangerous patients with humanity, intellectual curiosity, verbal virtuosity, and the pleasure of engagement. As might be appreciated from the verbatim case of Ms. Smith, it is very rewarding to help a hostile individual begin to break the habit of violent coping skills and learn the value of trust, self-determination, self-control, and equal partnership. One has to be judicious in deciding how many hours of exposure to have to this kind of work. But the skills learned enhance one's performance in many other settings.

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Chapter

11

Agitation in Field Settings: Emergency Medical Services Providers and Law Enforcement

Thom Dunn and Charles Dempsey

Agitation is commonly the concern of providers working in emergency departments (Wilson, Nordstrom, & Vilke, 2015), critical care areas (Barr et al., 2013), behavioral health services (Kwentus et al., 2012), and those who work with patients suffering from dementia (Livingston et al., 2014). Agitation is also a common presenting complaint (or co-occurring feature) faced by emergency service providers (Weiss et al., 2012). This chapter, in two parts, discusses agitation in field settings. The first section addresses emergency medical service (EMS) providers, the second law enforcement personnel.

Management of Agitation by EMS Providers

EMS providers have a unique role in health care in that they interact largely with the patient in the patient's environment. These field providers are expected to identify and manage a wide number of patient presentations including polytrauma, acute and subacute medical and neurological problems, psychiatric decompensation, drug and alcohol intoxication, and obstetrical emergencies. Likewise, prehospital providers must be proficient in treating patients of all ages, from neonates to the elderly. Patient care is expected to be delivered expediently and in sometimes demanding conditions. Finally, EMS providers may see patient presentations infrequently seen in the hospital, as some conditions rapidly resolve during ambulance transport, or effective field interventions may significantly change the course of illness or injury.

A city's 911 communication center receives a report of a man having a medical problem while sitting in his car. The car is running and in the middle of an intersection. The caller reports that the patient seems confused and is acting strangely. Pagers carried by volunteers beep, sending an EMT to the scene while a second goes to the ambulance barn to pick up a vehicle for transport. Volunteer firefighters trained to the "first responder" level also respond. Based on the call taking information, a single paramedic in a neighboring community is also notified; she starts toward the call in an outfitted sport utility vehicle. The nearest law enforcement officer is more than thirty minutes away and is busy with a domestic dispute.

Approaches to providing EMS vary widely across the United States (Wang et al., 2013), and even more so internationally (Pozner et al., 2004); the approach to the patient described in the scenario just given will be dictated by type of local EMS system. This discussion of agitation will be most salient to systems found in the United States. In some systems, the EMS provider will be an emergency medical technician (EMT) trained in basic life support (BLS) who does not have access to sedating medications. Restraining the patient for safety may be encouraged in some systems, but not permitted in others. Paramedic providers trained to the advanced life support level (ALS) may have access to medications for sedation, but requirements for administering them may vary depending on the system. Some

paramedics may only sedate a patient after verbally consulting with a base physician. In other systems, the paramedic may have access to sedating medicine from several drug classes and may judge the appropriate medication and dose to use without physician involvement. Yet in others, any hint of agitation would trigger a direction to "stage," or retreat to a distant safe location until law enforcement can secure the scene, even if that means a significant delay in patient care. Finally, in rural settings, for example, law enforcement backup for EMS providers may be quite delayed, making reliance on police officers or sheriff deputies impractical. Across the United States, any number of permutations of EMS systems may be found, such as: BLS fire department arriving first and ALS transport ambulance second; ALS first responders arriving before transport ambulance; all-volunteer providers on a ski mountain, a BLS-only transport agency, and so forth.

While there are myriad combinations of EMS systems and differing levels of training of those working in a prehospital setting, all EMS providers share challenges unique to field settings. For example, prehospital providers often contact patients without the benefit of having had the patient screened by a clinician in triage; they operate in a setting lacking the infrastructure found in other health care settings, such as dedicated security personnel and advanced diagnostic tests; they lack knowledge of the environment, such as the locations of weapons within a patient's home; EMTs and paramedics cope with the patient and bystanders in uncontrolled environments; and most patient care is done by a single provider in the back of a moving vehicle.

First-arriving EMS providers find a fifty-year-old male sitting behind the wheel of a pick-up truck. The responders begin to assess the patient in the intersection, while vehicle traffic passes by on each side. The man is shouting incoherently and rummaging around the passenger side of the vehicle. There is nothing to suggest a collision. A bystander reports that the man was weaving across the center line at a slow rate of speed until finally stopping in the intersection.

Agitation as a feature of a patient presentation in the field likely follows a similar distribution to that found in hospital settings, although no definitive studies exist on this topic. Management of agitation is extremely important in field settings, as prehospital providers are often subject to assault (Corbett, Grange, & Thomas, 1998; Mock, et al., 1998). One national study of EMS providers found that at least 85 percent had been spat on or physically assaulted, and one in five urban EMTs or paramedics had to take time off of work because of injuries due to violence (Dunn et al., 2014). It is imperative that EMS providers can properly assess agitation as a medical sign, expediently derive a reasonable differential diagnosis, and manage the agitated patient so that neither the provider nor the patient is harmed.

Alcohol intoxication is routinely encountered in emergency medical settings (Pletcher, Maselli, & Gonzales, 2004) and is often the etiology of agitation in the field (Dunn et al., 2014). Identification of the intoxicated patient is not intuitively difficult, but it is unfortunately a common mimic for other sources of agitation that might be life threatening and/or reversible. Complacent EMS providers have been known to inadequately assess patients by quickly and erroneously believing that the person they are caring for is "just drunk." Such cases have resulted in high-profile instances of poor outcomes (Stout, 2006). The competent EMS provider is capable of identifying a wide number of etiologies of agitation. Table 11.1 includes common sources of agitation and typical signs and symptoms found in the field.

EMTs and the firefighters surround the pickup truck containing the patient. The patient is highly agitated. The keys are quickly removed from the ignition and the wheels chocked. The patient presents as a 40s male who is awake, but not aware. Efforts to communicate

Table 11.1. Common etiologies of agitation, their field presentation, and likelihood for verbal de-escalation

Etiology	Common Presenting Features in the Field	Candidate for Verbal De-escalation?
Intoxication – alcohol	Odor of alcoholic beverage, ataxic gait, slurred speech, family/bystander report of ingestion of alcohol, emotional lability, relatively acute onset	Consider a short trial
Intoxication – amphetamines	Tachycardia, mydriasis, hypertension, delusions, hallucinations, sleeplessness, hyperkinesis, drug paraphernalia found on scene	Consider a short trial
Hypoxia	Altered mental status, changes in skin color, low pulse oximetry readings	No, treat underlying cause
Hypoglycemia	Diaphoresis, pale pallor, confusion, ataxia, declining mental status	No, treat underlying cause
Traumatic brain injury	Physical findings consistent with trauma, other findings of injury (e.g., skier found down), perseverative questions, confusion	Consider a short trial
Seizure/post-ictus	Oral trauma, incontinence, altered mental status that improves over time without intervention	Consider a short trial
Psychiatric decompensation	Disorganized speech and/or behavior (speech may be pressured during manic episode), delusions, hallucinations, these patients are typically free from altered mental status	Consider; may be highly effective in some cases, less so in others
Cerebral vascular accident (CVA)	Acute onset, aphasia, pupillary changes, hemiparesis, confusion, known risk factors for CVA, hypertension	Consider a short trial
Dementia	Typically found in geriatric patients, global intellectual decline, impaired recent memory while remote memory relatively spared	Consider a short trial
Delirium	Altered mental status and agitation with waxing and waning course; common in alcohol withdrawal	No, consider neuroleptic
Excited delirium	Highly agitated, speech limited to nonverbal vocalization, often sheds clothing, combative and destructive, associated with breaking glass	No, sedation early in contact with patient is important
Autism spectrum disorder	History of such provided by bystanders, stereotyped behaviors, odd speech, inflexibility of being out of a routine, hypersensitive to external stimulation	High likelihood of success; use extensively
Intellectual disability	Childlike speech and demeanor, may have caretakers despite being an adult, some intellectual disabilities co-occur with reliable physical findings (e.g., Downs syndrome)	High likelihood of success; use extensively

Table 11.1. (cont.)

Etiology	Common Presenting Features in the Field	Candidate for Verbal De-escalation?
Emotional dysregulation	Free from altered mental status; highly emotional, either angry, frightened, or stressed beyond ability to cope	High likelihood of success; use extensively
Instrumental violence	Agitation used as a tool for achieving a goal; no confusion or underlying medical mechanism; be particularly aware of persons in police custody	Consider a short trial; involve law enforcement

with the man are met with a clenched fist and confrontational stare. His speech is difficult to understand. His skin is noted to be pale and diaphoretic.

Obviously, managing the agitated patient is a high priority. While EMS protocols and training programs often direct prehospital providers to retreat and/or involve law enforcement when a patient becomes agitated, such directives may be ineffective. Law enforcement may not always be available and patients may become agitated after transport to the hospital begins. Indeed, patients have been known to jump from moving ambulances during transport. In one case, the EMS provider followed her training to retreat before the patient leapt to her death from the back of an ambulance traveling at highway speed (Dunn, 2008). Finally, agitation may be an indicator of a life-threatening condition (Nordstrom & Wilson, 2015). It is imperative that EMTs and paramedics be trained to make safety a priority in coping with agitated patients. Unfortunately, a majority of EMS providers report being inadequately trained and having ineffective protocols when dealing with agitated patients who become violent (Dunn et al., 2014).

Clearly, personal safety is absolutely paramount and at no time should prehospital providers jeopardize their (or anyone else's) safety by engaging with an agitated patient unless he or she reasonably feels that they have the knowledge, tools, and skills to do so. An approach to managing the patient that starts with evaluating the patient from a distance may be most effective. The provider can then decide whether the patient is a candidate for verbal de-escalation, if physical restraint is indicated, and when to consider sedation. This approach is summarized in Figure 11.1. Verbal de-escalation is the preferred first step in managing agitation. It is by far the safest method in addressing a patient who is combative and can be employed by any level of EMS provider. There are many approaches to effective verbal de-escalation. Included in this chapter is a model based on Richmond and colleagues' (2012) consensus statement of the American Association for Emergency Psychiatry Project BETA de-escalation workgroup regarding verbal escalation. Many of the core features of this model have been distilled into a five-step approach prompted by the mnemonic "ERASER." The ERASER de-escalation mnemonic can be found in Table 11.2.

The man is contained in the truck by having firefighters stand at the doors and keep them closed. The lead EMT sees packets of cake frosting on the front seat, appreciates the significance of altered mental status with diaphoresis, and astutely suggests that the man is potentially

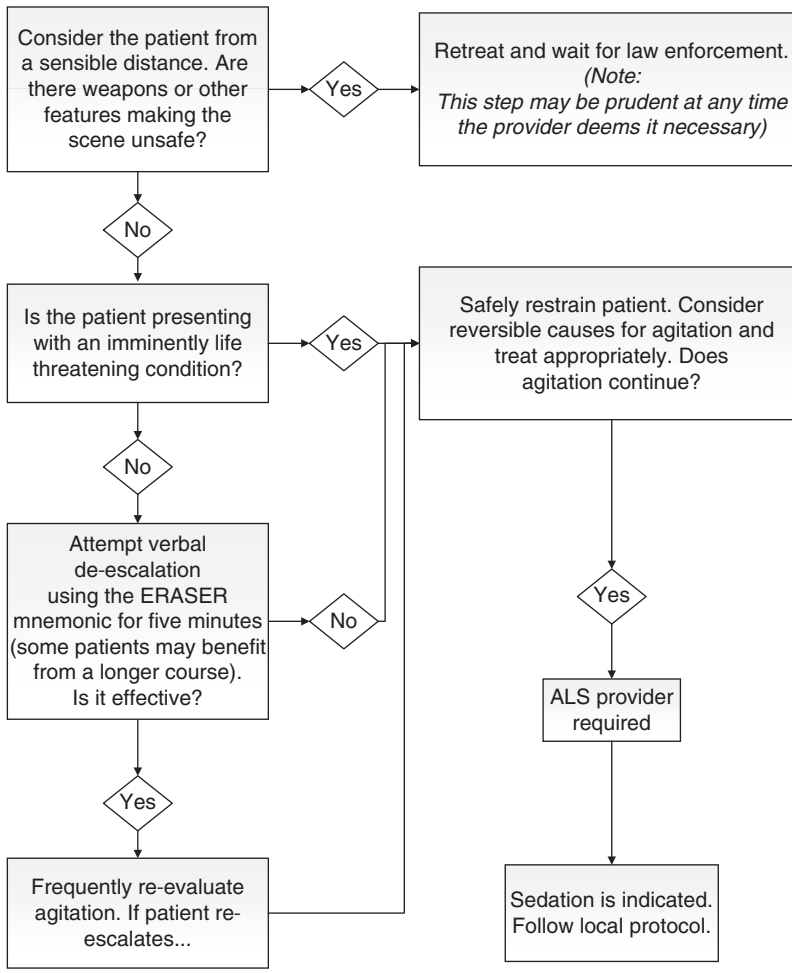

Figure 11.1. Managing agitation in the field.

a diabetic in the midst of a hypoglycemic episode. Roller gauze is looped around the man's wrists as he is too diaphoretic for providers to effectively grab his arms. A "medic-alert" bracelet is found on one wrist declaring the patient to be an insulin-dependent diabetic. Finger stick blood glucose testing reveals a blood sugar of 32 mg/dL.

When dealing with patient who is not an appropriate candidate for verbal de-escalation (see Table 11.1), after failed attempts at verbal de-escalation, or concerning a patient who again escalates after once being talked down, restraint may be required. This is contrary to common protocols inside hospitals where the patient may be offered medication by mouth in hopes of avoiding physical restraint (Knox & Holloman, 2012; Wilson et al., 2012). Given the dynamic nature of the field, the urgency to complete an assessment to be certain that life threats do not exist, and that EMS providers have a duty to act in most states, restraining a patient for safety takes on a greater priority. Certainly, taking this step should be done with the utmost caution and after assurances that the risk of doing so is substantially outweighed by the benefit.

Table 11.2. ERASER mnemonic for verbal de-escalation

Step	Action
E. EYEBALL the patient	Evaluate the patient from a safe distance. Are there weapons or other features that make the scene unsafe? Retreat and wait for law enforcement. Are there signs that the patient will not respond to verbal de-escalation, or may be suffering from an imminent life-threatening condition? It may be prudent to safely and rapidly restrain the patient for further evaluation and treatment.
R. RESPECT the patient's space	Patients may escalate when there is intrusion into the personal space. The provider should maintain a respectful distance while being aware of escape routes should the patient become violent.
A. A single provider does the talking and builds rapport	With multiple providers on a scene, a single individual should be charged with talking with the patient. The provider charged with this task must not become "emotionally involved" in the patient (such as becoming angry or frightened of the patient).
S. SENSIBLE listening	Often, agitated patients want to be heard. The provider making contact with the patient needs to calmly listen to the patient without being drawn into a prolonged conversation or reacting to demands. This step is likely when iatrogenic escalation may occur. Another provider may need to step in and continue if this happens.
E. ESTABLISH expectations and set boundaries	Boundaries should be set with the patient about behavior that will not be tolerated, consequences of actions, and what the patient is likely to expect. Such as, "You may not threaten people," "We need to make sure you are alright, we are going to take some vital signs and ask you some questions." Or, "Unfortunately, we are worried you cannot make informed medical decisions because you are intoxicated. We are going to take you to the hospital so you can be treated for your injuries."
R. REASONABLE choices are given to the patient	By retaining some degree of control, many patients will comply with direction if given reasonable choices. For example, a provider could say, "Would you like to walk over to the ambulance and sit on the bed inside, or do you prefer we bring the bed over here for you to sit on?"

Note: These steps are based on best practices recommended by Richmond and colleagues (2012).

For patients who continue to be combative, sedation may be required. The use of sedation by EMS providers varies greatly by jurisdiction and provider level. Some EMS systems do not have access to ALS providers whose scope of practice permits the administration of sedative medication. Other ALS systems may not include sedating medication as part of the prehospital formulary. In addition, some paramedics may simply elect not to use sedation for agitation, preferring to manage the patient using nonpharmacological interventions. Protocols and training that encourage prehospital sedation (when indicated) are important, as it benefits the patient, the EMS provider, and staff at the hospital who will be receiving an agitated patient (Weiss et al., 2012).

Providers in field settings have practical considerations to contend with, making the pharmacological management of agitation challenging. Among these considerations is that

EMS professionals tend to work without the benefit of multiple staff members managing different parts of patient care. Commonly, a single paramedic may be engaging with an agitated patient, while also establishing intravenous access, unlocking a double-locked medication compartment, drawing up medicine, and monitoring vital signs. Unlike the emergency department, the usual paramedic formulary is typically limited to first-generation antipsychotics (most often haloperidol) and benzodiazepines such as midazolam or diazepam. Lorazepam, a very common agent to treat in-hospital agitation, is not commonly used by paramedics, as the drug is intolerant of wide variations in temperature, making it impractical for use in many EMS systems. Finally (likely because of the history of paramedics intervening only in life-threatening emergencies), most medications on ambulances are parenteral preparations. This, unfortunately, limits the ability for a paramedic to offer sedating medicines to an escalating patient as an early intervention.

The paramedic from the neighboring community arrives in her SUV. She affirms the EMT's findings that the patient in the pickup truck is agitated because of hypoglycemia. She is able to start a 16 gauge IV in the patient's left antecubital fossa and administers 25 grams of 50 percent dextrose. Within a minute the patient stops struggling and yelling and says, "Oh, man, I didn't make it home, did I?"

The scope of practice of prehospital providers has evolved greatly from its inception of delivering early urgent cardiac care (Smith & Bodai, 1985). For example, twenty-first-century paramedics regularly administer antiemetics and analgesics; perform advanced interventions such as cardioversion, rapid sequence intubation, and chest decompression; and some have an expanded scope of practice to provide primary care as so-called community paramedics (Bigham et al., 2013). Critical care paramedics manage patients receiving mechanical ventilation, monitor infused medicines, and provide care to complex patients from one facility to another (Mabry et al., 2012). Despite these remarkable advances in the field, few EMS agencies have evolved their approach to the treatment of the agitated patient. For example, a national study found that fewer than 4 percent of EMS providers have access to an atypical antipsychotic (Dunn et al., 2014). It is imperative that physicians who work with EMS agencies consider the following steps to help modernize the treatment of agitation in the field.

1. **Revision of paramedic protocols.** Many EMS systems do not permit restraining the patient for safety and/or the administration of sedating medications by paramedics. Other systems require contacting a base physician for a medication order before a paramedic may sedate a patient. Not allowing prehospital sedation delays needed intervention and, thus, is detrimental to the patient. Physician contact requirements can put both field providers and the hospital staff who receive patients from them in potential danger due to those delays. Adding an additional step of requiring a paramedic to speak with a physician to give medicine is an outdated model. Protocols that permit restraining patients who are refractory to verbal de-escalation should be commonplace.
2. **Addition of medication with alternate delivery systems to parenteral administration.** As reviewed by Nordstrom and Allen (2013), injectable routes of medication administration have numerous downsides. Not having a "by mouth" option limits the paramedic's ability to offer sedation to interrupt the escalation of a patient. Orally disintegrating tablets of second-generation antipsychotics, such as risperidone and olanzapine, are ideal for prehospital settings. Water is not needed to take them,

"cheeking" the medicine is difficult, and onset of sedation is rapid. The intranasal preparation of medicine is also a viable option for the delivery of sedating medication, as this route has reliably been used for the rapid administration of other drugs in the prehospital setting (Barton et al., 2005). This route is non-invasive, does not require a "sharp" with an agitated patient in a potentially confined space, and can still be administered to a patient who objects to being medicated. Finally, the approval for the first-generation antipsychotic loxapine to be delivered via inhalation opens yet another non-invasive drug route (Keating, 2013).

3. **Ketamine.** With greater recognition of excited delirium (Vilke et al., 2012), and the possibility of sudden death associated with physically restraining these patients (Otahbachi et al., 2010), ketamine has been seen as an excellent agent in reducing severe agitation. It has the advantage of sedating effects without depressing respiratory effort (Hopper et al., 2015). With onset of action within three minutes of intramuscular injection, ketamine has proven highly effective in prehospital settings (Burnett et al., 2015; Scheppke et al., 2014). Ketamine is likely underused for managing agitation by paramedics. Given that it also has utility in analgesia and as an induction agent for endotracheal intubation, ketamine should become commonplace in the paramedic formulary.
4. **Make training in dealing with the agitated patient compulsory.** Physicians often set the standard of practice for EMS providers. Because of the challenges in managing the agitated patient described earlier, training in this area needs to be mandatory. Both BLS and ALS providers can benefit from training to recognize common etiologies of agitation, continuing education in verbal de-escalation, and ALS providers can benefit from learning more about psychopharmacology and indications for sedation.

EMS providers share ownership with their physician colleagues in advancing the field in treating agitation, including:

1. **Adequately assessing the agitated patient**. Agitation is commonly seen with altered mental status. Common reasons for agitation can be quickly ruled out or in by field providers. Hypoxia is easily detected and reversed in the field. Bedside finger stick blood glucose monitoring can confirm hypoglycemia (or its absence), and in many states even EMTs are permitted to reverse this condition with IV dextrose. Acute alcohol intoxication can be deduced from patient presentation and odor, as well as ruling out other etiologies for altered mental status. Traumatic brain injury and cerebral vascular accident can be identified though physical exam and history. Finally, a patient in a post-ictal state following seizure commonly has oral trauma and incontinence.
2. **Becoming proficient in verbal de-escalation**. An agitated patient often responds to de-escalation in a short time (Richmond et al., 2012). Following the ERASER mnemonic and regular training can increase proficiency in its use. It is also particularly important that providers do not allow themselves to emotionally react to patients who are provocative.
3. **EMS training in physical restraint is critical**. Even in EMS systems that direct their providers to stage and wait for law enforcement, EMTs and paramedics can still be surprised by an agitated patient. All field providers should attend a sanctioned training program in the management of the agitated patient.
4. **Consideration of sedation should occur early in the agitated patient's field course**. Given the complexities of managing an agitated patient and preparing sedating

medicine in a moving vehicle, pharmacological intervention should be considered early. If there is a concern about a patient escalating, it may be prudent for the attending EMS provider to ask for additional first responders to ride in the back of the ambulance en route to the hospital (perhaps even law enforcement). Law enforcement can also follow the ambulance and be quickly alerted to an escalating patient. In other situations, preparing sedating medicine before the ambulance leaves for the hospital so it is readily available permits rapid intervention by a single provider alone with the patient.

5. **De-escalated patients, those who are agitated, or who may become agitated should ride on the ambulance gurney.** Simple interventions before a patient requires restraint or sedation can be useful. Patients should always be placed on the gurney (and not the bench) where their center of gravity is at its lowest. Seat belts can be placed above the knees and high around the chest. Buckles to release the seat belt can be inverted to make them harder for the patient to reach. A brief, prearranged signal can be worked out between the attending provider and the one who is driving to indicate the need for the ambulance to be stopped because of patient escalation.

After the administration of dextrose, the man in the pickup thanks the paramedic, EMTs, and firefighters. "I took my insulin and did not make it home in time to eat," he explains. Given that his blood glucose level has normalized, that he was able to eat a toaster pastry he keeps in the truck, and he did not desire ambulance transport, the man signed a "refusal form" and went on his way.

Agitation/Crisis Management – A Law Enforcement Perspective

Police officers arrive to a radio call and see a man with his leg dangling out a fourth-floor window, glass on the ground below. A caller to 911 reports the man is in the process of being evicted and has made suicidal statements. Police enter the building and find the man sitting on the windowsill. He has long grey hair and a flowing grey beard. He looks like a skinny Santa Claus. He is agitated and he yells, "stay back." Fortunately, these officers have been trained in crisis intervention/behavioral health de-escalation techniques.

The mental health crisis begins in the field and can either escalate or de-escalate based on the management of the crisis by first responders. Those in law enforcement perceive a paradigm shift in which they have become ***gatekeepers*** to mental health services. This shift is exemplified by the this excerpt from the Los Angeles Police Department Manual:

- **1/240.30 CONTACT WITH PERSONS SUFFERING FROM A MENTAL ILLNESS** In police contacts with persons suffering from a mental illness, the goal of the Department is to provide a humane, cooperative, compassionate and effective law enforcement response to persons within our community who are afflicted with mental illness. The Department seeks to reduce the potential for violence during police contacts involving people suffering from mental illness while simultaneously assessing the mental health services available to assist. This requires a commitment to problem solving, partnership, and supporting a coordinated effort from law enforcement, mental health services and the greater community of Los Angeles (LAPDonline, Employee Conduct).

This challenge is not new for law enforcement; one only needs to look at historical documents such as Los Angeles Police Training Bulletin, dated November 10, 1948, titled, "How to Handle Mentally Ill Persons – Field Procedures," which states, "*An alert policeman anticipates the unpredictable thoughts and actions of a mentally ill person. He treats the*

patient with understanding and consideration, remembering, however, that the use of protective restraint is often necessary." What has changed is the acuity of the mentally ill population whom first responders are encountering and the options they have in managing these volatile situations. With the advent of de-institutionalization, codified by the Lanterman-Petris-Short Act (Cal. Welf & Inst. Code, sec. 5000 et seq.) in 1967 in the State of California and subsequent legislation across the nation, the chronically mentally ill can no longer be treated in a mental health care facility or sanitarium for the duration of their lives. This concept of a community-based treatment model, in the least restrictive environment, has created a revolving door at most psychiatric emergency departments and medical emergency rooms across the country, in which first responders have become the primary mechanism by which persons in crisis are contacted, de-escalated, detained, and transported for treatment.

This shift in the role of first responders, particularly those working in law enforcement when dealing with a person suffering from a mental health crisis, has ultimately led to several tragedies in which a person with a mental illness died because of that law enforcement involvement. These tragedies led to the birth of two law enforcement-based response strategies or Specialized Policing Responses (SPR).

The first is the Crisis Intervention Team (CIT) model, more commonly known as the "Memphis Model." This is a "first responder" law enforcement-based model. Memphis police (Dupont & Cochran, 2000) developed this model in 1988 in Memphis, Tennessee, as a result of a fatal shooting of a man with a history of mental illness and substance abuse. A community task force consisting of law enforcement, mental health and substance abuse treatment providers, and mental health care advocates sought to develop a means by which to decrease the potential for violence between emergency service personnel and persons with a mental illness. In addition, they sought to divert those same individuals when appropriate, toward much needed mental health treatment and away from the criminal justice system.

The core concept of the traditional CIT model is to provide forty hours of training to a select group of officers, who volunteer for the team, providing them with the skills needed to recognize certain mental illnesses and develop the de-escalation skills required in order to safely manage the mentally ill person in crisis. It also encourages a collaborative relationship between law enforcement, community stakeholders, and mental health care providers, not only as a core component of the training, but in a community effort to engage and properly treat those suffering from a mental illness. The Core Elements and Ongoing Elements of the CIT Model have been published by Dupont, Cochran, and Pillsbury (2007) and are available on the University of Memphis' IT Center webpage (http://cit.memphis.edu/).

The "Memphis Model" or some form of it has been adopted by several thousand communities across more than forty states, and in some states it has been adopted as a statewide initiative, including Maine, Connecticut, Ohio, Georgia, Florida, Utah, Kentucky, Texas, and, most recently, California. In Texas, Senate Bill 1473 (Bob Meadours Act) mandated sixteen hours of crisis intervention/de-escalation training for all Texas peace officers. In California, Governor Brown recently signed into law Senate Bills 11 and 29 (Beall, Peace officer training, mental health) increasing academy training to fifteen hours for crisis intervention/behavioral health-related topics and requiring additional training for all field training officers ranging from eight to forty hours in order to qualify for these advanced positions. This has become the trend nationally to address this growing challenge of providing crisis intervention/de-escalation/ behavioral health training for first responders.

The second law enforcement response strategy is known as the Co-responder Team (CRT). This is a "secondary" response model, in which a specially trained officer and a mental health clinician respond to the person in crisis after being contacted by uniformed field officers. Typically, these teams are dispatched and ride together in a police vehicle. This strategy was first employed by the Los Angeles County Sheriff's Department in 1992, known as Mental Evaluation Team (MET), and in 1993 by the Los Angeles Police Department, when it began deploying the Systemwide Mental Assessment Response Teams (SMART).

The goals of the CRT model are to:

- Prevent unnecessary incarceration and/or hospitalization of mentally ill individuals;
- Provide alternate care in the least restrictive environment through a coordinated and comprehensive systems approach;
- Prevent the duplication of mental health care services; and
- Allow police patrols to return to service as soon as possible.

Today the CRT model is in use in hundreds of jurisdictions across the United States, Canada, England, and Australia; these include San Diego County-California (PERT), Los Angeles County-California (MET and SMART), Baltimore County-Maryland (MCT), Seattle Police Department (CIT), Vancouver Police Department-Canada (AOT), Leicestershire Police-England (Triage-Car), and Queensland Police Service (MHIP). The CRT response model is now the predominant model adopted by the majority of large urban areas in Canada.

The CIT and CRT models are not mutually exclusive; many of the CRT programs utilize CIT as a base concept and have added the CRT as an additional layer of response and call management. In addition, several jurisdictions have added another layer of response, utilizing the CRT as an intensive case management team. These teams of detectives or police officers are co-deployed with mental health care professionals and work closely with the criminal justice and behavioral health care systems to manage high-risk individuals. Jurisdictions who have initiated these specialized CRT follow-up teams include the Houston Police Department – Chronic Consumer Stabilization Initiative (CCSI) and the Los Angeles Police Department – Case Assessment Management Program (CAMP) (Law Enforcement Mental Health Learning Sites). These CRT follow-up teams focus on individuals who are high utilizers of emergency service and at risk for violent encounters with first responders, such as suicide-by-cop scenarios, use of force situations, and access to firearms.

At first glance, there appears to be a lot of work being done nationally and internationally to address this growing problem; however, many communities and jurisdictions have yet to become engaged in the discussion and process of responding to and managing these high-risk mental health crisis calls. In many cases, a tragedy must occur before action is taken to address this public health crisis, which generally falls on law enforcement. However, without a collaborative approach addressing all of the systems of care, efforts will be ineffective.

Call Intake and Triage

Effectively responding to mental health emergencies typically starts with a phone call to a 911 call center. Depending on the jurisdiction, there can be a police dispatch separate from the fire/EMS dispatch. The call for service can create a police response, an (EMS) response, or a combined response to the mental health crisis. Dispatch protocols vary. Agitation regarded as medically based may trigger an EMS response with police co-responding, while

in other instances EMS may not be sent at all. If the agency or jurisdiction has begun to implement a specialized policing response, or has one established, the training of the call takers/dispatchers is critical.

On Scene De-escalation, Evaluation, and Call Management

As police officers work to formulate a plan to engage the man on the ledge, he becomes more agitated, picking up a 2 × 4-inch piece of wood and swinging it back and forth. The officers arrange themselves. One will be the "contact officer" and speak to the man, while a second "cover officer" stands ready to intervene if the man advances. The officers also ensure they have "less than lethal" options available. The conversation begins by establishing personal space. "I promise; I won't come any closer," says the first officer. "Can we just have a conversation as to why we are here?" The man sets the 2 × 4 down and states, "Okay." Rapport is established with the man by identifying his love for the musical group Lynyrd Skynyrd and motorcycles. He relates that his life has taken a downturn lately and when he received the notice of eviction, he just lost his cool, because he has nowhere to go. He talks of depression, but is not "really suicidal." He has several lacerations on his arm and back from the broken window. He says he is very thirsty and would love a Coke. The officer says he will get him one, but he has to step away from the window first.

Arrest versus Hospitalization/Diversion

When police officers contact an agitated individual, they are tasked with the additional consideration of whether that person may have committed a crime. Even for those who have, it may be appropriate to divert them from the criminal justice system to mental health services. Many communities, such as Miami-Dade, Florida, have invested in diversion, keeping those individuals with a serious mental illness out of the criminal justice system (Criminal Mental Health Project). Additionally, with the large number of returning combat veterans, many of whom are suffering from mental illness, veterans' treatment courts have been established to address this specific population (California Veterans Legal Task Force). Nationally the Council of State Governments Justice Center with the assistance of the Bureau of Justice Assistance has established the Mental Health Court Learning Site program to help address this important need (Mental Health Court Project).

The Substance Abuse and Mental Health Services Administration (SAMSHA) has also been involved in this work of diversion and has introduced the "Sequential Intercept Model." This model identifies five key points for "intercepting" individuals with behavioral health issues, linking them to services and preventing further penetration into the criminal justice system.

Many law enforcement agencies have adopted specific policies and procedures on diversion, but in most cases, they give the officers a great deal of discretion (Templin, 2000). An example of a law enforcement policy is cited next in an excerpt from the Los Angeles Police Department Manual:

> **4/260.20 Taking Persons with a Mental Illness into Custody**
> When a person is taken into custody for a criminal offense and the person is suspected of having a mental illness, the Mental Evaluation Unit shall be contacted prior to the person being booked. When a subject is a suspect in a felony or high-grade misdemeanor crime, or

the subject has any warrants, the criminal matters shall take precedence. If the subject is under arrest for a low-grade misdemeanor, misdemeanor warrant, or infraction, and meets the criteria for an Application for 72-hour Detention for Evaluation and Treatment, booking is at the discretion of the Area watch commander (LAPDonline/Line Procedures).

Hospitalization

The man steps away from the window and drops the piece of wood. As the man sits down on the gurney, the officer hands him the promised Coke. While there is some property damage, it is relatively minor. The man is not wanted. The officer believes that he should be transported to the hospital for evaluation. The man does not want to go voluntarily, so the officer fills out an "application for an involuntary mental health hold," and transports him to a local emergency room. The officer relates the event to the intake staff. In particular, while the man stated that he was not suicidal, he was depressed, had broken out a window of a fourth-floor apartment, and was dangling out the window. In addition, he had threatened officers with the 2 × 4; this could have resulted in a use of force. Both the officers and clinical staff agree that this man is an at-risk individual and his presentation warrants further evaluation.

Once the person in crisis has been transported to the treating facility, a report must be provided to the facility staff delineating the reason for the involuntary detention. These required forms vary by state and the Treatment Advocacy Center has a comprehensive listing by each state to include the applicable laws (Emergency Hospitalization for Evaluation). The benefit of adopting the training associated with many of the specialized policing responses is that the training teaches the detaining officers what state law requires and what the treating staff at the medical facility needs. In particular, officers are trained in best practices in describing behaviors observed and statements made that led them to believe the person detained qualifies for an involuntary detention. During training, law enforcement officers are reminded that the report they are completing is a legal document, no different from an arrest report they would complete for a criminal complaint. They are taught the behaviors to look for that are indicative of a mental illness and that they must use clear and concise language, absent of terms and acronyms or terms they would commonly use in a police report. They are also taught the importance of gathering witness and family statements to establish the "probable cause" needed to make the detention.

It is at this juncture, in the management of the person in crisis, when information is critical to properly develop a comprehensive team approach. It is here the federal privacy laws, based on interpretation, may block this flow of information. It is important to understand that, in most cases, limited information can be shared between the health care provider and law enforcement. The U.S. Department of Health and Human Services delineates this in the publication. "When does the Privacy Rule allow covered entities to disclose protected health information to law enforcement officials?" It is also explained in detail in the publication "Information Sharing in Criminal Justice – Mental Health." This is when having a CRT mental health clinician on the response team can be beneficial, as they can communicate with the treating staff at the medical facility. At minimum law enforcement should be satisfied with one-way communication between themselves and the treating/receiving staff at the medical facility, ensuring that the reporting is as complete and accurate as possible to best enable the treating facility to provide the appropriate intervention for the person in crisis.

Discharge Plan – Collaboration and Safety

A specialized policing response program works closely with the county mental health and housing specialists. In conjunction with the hospital social worker, temporary housing is arranged for "Skinny Santa Claus." In addition, it has been determined he is a disabled veteran and follow up services have been arranged with the local Veterans' Administration hospital, ensuring that he will have linkages in the community post discharge.

This is where law enforcement, treatment providers, and community stakeholders must work together to ensure that the person who was in crisis is properly linked, ensuring the safety of the person suffering from a mental illness and the community at large. Many factors go into discharge planning, but safety is the key to a successful outcome. In Los Angeles, at least 60 percent of the crisis calls for service involve individuals who are one-time users of emergency services and will not be seen in an emergency setting again. However, there are those who reconstitute just well enough to no longer meet criteria for involuntary treatment, but still may pose a significant risk to their safety and to society. This is where cases such as *Tarasoff v. Regents* and its subsequent extensions and adaptations across the country present challenges (Ewing, 2005). Treatment providers, dependent on their jurisdictions, must understand the "duty to warn" as it applies to their professional license and their state laws. This "duty to warn" has now been extended to a "duty to protect," and this is where a beneficial relationship with law enforcement can assist a therapist or treating physician in complying with these sometimes confusing and complicated laws (Berger & Berger, 2009). This is where it is important to review the confidentiality exceptions to HIPAA and understand that communications are permissible for reasons of public safety or to report or assist officers in identifying and making an arrest of a person who is wanted for a crime. This must be looked at from the public safety aspect; the vast majority of these cases are not criminally prosecuted, but by intervening we divert a person on a pathway to violence. This is when having an SPR in your community can be beneficial to the discharge and management of these potentially high-risk individuals.

The first responder role in agitation/crisis management is a very important one and sets the tone for all of the subsequent contacts the person suffering from a mental health crisis will have on their journey through a very complicated, regulated, and fragmented system of care. It is only through a thorough analysis of the system, its key stakeholders, and a willingness to work cooperatively in order to provide the best intervention possible, that we can have successful outcomes. We cannot hide behind fabricated or misperceived barriers that prevent this collaborative approach from being successful. We must train all facets of the system, so that there is an intimate knowledge of each other's capabilities and legal limitations. This includes the consumer, for to see the world through their eyes, failure is not an option, and lives are at stake. There are many well-intentioned individuals working diligently in their own silos, not realizing that working together may make the task at hand achievable. Begin the process in your community and if one is in place join it and make it stronger.

Conclusion

Managing agitation in field settings is often more complicated than intervening with the agitated patient in the hospital. Depending on the information conveyed to a 911 call center, an agitated person could be regarded as a law enforcement problem and police officers manage the individual. In another community, an individual presenting with the same type of agitation may be regarded as having a medical emergency and therefore managed by

EMTs and paramedics. With high rates of assaults on vulnerable EMS providers, it is sensible to involve the police. Given the recent national conversation about use of deadly force against agitated individuals who are unarmed, one wonders if EMS should be taking on a greater role in such instances. Likely a partnership between EMS and law enforcement where both are dispatched to an agitated person will achieve the best results.

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Chapter

12

Use of Force in the Prehospital Environment

Yuko Nakajima and Gary M. Vilke

Concepts

Law enforcement officers are increasingly using conducted energy devices (CEDs) in the prehospital setting for severely agitated and combative subjects. Many of these subjects are suffering from a medical emergency and require rapid intervention. We will discuss in this chapter TASERs, the controversy over their use in the prehospital environment, and patients suffering from Excited Delirium Syndrome (ExDS).

Case Presentation

Police are called for a thirty-four-year-old male in a public park who is sweating profusely, naked, confused, and talking incoherently to himself while intermittently yelling and swinging his arms. He states that dragons are setting him on fire. He becomes increasingly agitated and aggressive as police approach him. Although police attempt to verbally calm the patient, their attempts are unsuccessful. At this point, police call for emergency medical services (EMS) standby for a possible case of ExDS and instruct them to prepare for treatment and transportation once the patient is taken into custody and the scene is secured. While EMS is en route, the man's aggressive behavior escalates and he starts running into traffic. The police decide on a rapid takedown using a TASER CED, and the subject is rapidly incapacitated with the device in probe mode. Two officers place the subject in handcuffs. A third and fourth officer attempt to restrain each leg with a loose hobble, but the subject is incredibly strong and difficult to restrain. When EMS arrives, the paramedics begin their assessment and treatment. They note that the subject's skin is extremely hot to the touch. Vital signs indicate a heart rate of 140, a blood pressure of 170/87, a respiratory rate of 32, and an oxygen saturation of 100 percent. The subject is sedated with 10 mg of midazolam intramuscularly as per the paramedic protocols for agitation. He is placed in an ambulance and promptly transported to the nearest emergency department.

Conducted Energy Devices (CEDs)

CEDs are one of the most frequently used less-lethal weapons utilized by law enforcement and military personnel as a means of rapidly controlling combative or otherwise dangerous individuals. The devices offer the advantage of increased distance and larger margin of safety, as well as reduced need for impact firearms and the injuries associated with their use. Recently, CEDs have been modified and made available for use by the public for self-protection purposes. There are, however, controversies surrounding the use of such products in excited delirium patients as they are becoming more widely distributed and available to the public. We will discuss the controversies later in this chapter.

History of CEDs

In 1935, an electric glove for use by police was invented by Cirilo Diaz in Cuba to subdue combative perpetrators. The device delivered a 1,500 V shock, powered by a half-pound battery worn on a belt. Records show that police officials were impressed when the device was first demonstrated (Modern Mechanix 1935). More recently, the commonly used "TASER," an acronym for "Thomas A. Swift's Electric Rifle," is a reference to the Tom Swift science fiction character and childhood hero of Jack Cover, the NASA researcher who invented the device. Cover began developing the TASER in 1969, and completed it by 1974. In 1983, Nova Technologies adapted Cover's patent for the development of Nova XR-5000, its first non-projectile handheld-style stun gun.

TASERs were initially designed for protection against hijackings in pressurized airplanes where projectile weapons cannot be safely discharged. Soon, law enforcement adopted the tool in the 1980s as an alternative to lethal firearm weapons. Original TASER devices used gunpowder as a propellant and so were considered firearms. In 1993, TASER International CEO Thomas Smith and his brother Rick worked with Jack Cover, the TASER inventor, to develop a non-firearm electronic control device. In 1994, the Air TASER Model 34000 was developed, a device boasting a mere seven watts of power and demonstrating an effectiveness of only 86 percent. In 1994, the label of firearm was removed when the device was converted to probes fired with compressed air. Thereafter, the modern TASER became more readily available for public use (Roberts & Vilke 2016). In 1999, TASER International developed the Advanced TASER M-series, a handgun-shaped device that used neuromuscular incapacitation (NMI) technology. The advanced TASER M26 had twenty-six watts of power, and in May 2003, TASER International released a new CED called the TASER X26. In July 2009, TASER International released the X3, which can fire three shots before reloading. Two new designs were released in 2013, the TASER X26p and the TASER X2. The newest TASER X26p utilizes new solid-state arc controllers and measure and can adjust output during discharge. The data logs record every user action, including safety activation and trigger event. Additionally, a camera is mounted in the handle of the device for further protection of both the subject and user. The TASER X2 offers a warning arc of energy with the goal of preventing conflict from escalating. This device has been shown to provide a precise amount of current upon discharge that maximizes safety and effectiveness.

Mechanism of CEDs

When properly used, CEDs will incapacitate subjects regardless of mental focus, training, size, or state of intoxication. These devices do so by administering a high-voltage, low-current electrical discharge with the aim of disrupting superficial muscle functions and causing pain without injury to the subject. The subject feels pain, and is momentarily paralyzed by uncontrollable muscle twitching while an electric current is applied. During a CED activation, subjects remain fully conscious with total recall of the events in spite of having no voluntary control over motor tasks (Roberts & Vilke 2016). Once the discharge has ceased, subjects immediately return to their cognitive and physical baseline. The internal circuits of most electroshock weapons are based on an oscillator, resonant circuit, step-up transformer, or diode-capacitor voltage multiplier in order to achieve an alternating high-voltage discharge or a continuous direct-current discharge (Smith 2003). When properly applied, CEDs cause muscles to contract rapidly at nineteen times per second, functionally resulting in the muscle groups being in a state of tetany.

Types of CEDs

CEDs include TASERs and other electric stun devices such as compact stun guns, stun belts such as the remote activated custody control (RACC) belt, stun shields, and electric shock prods. The electric shield transmits 75,000 volts across metal-conducting plates on a Plexiglas shield that is pressed against a subject. The RACC belt is placed around the waist of prisoners in custody and may be activated remotely from as far away as 200 feet. The belt transmits 50,000 volts, stun pulse rate of seventeen to twenty-two pulses per second, and current of three to six milliamps. Stun guns originally worked by electrical shocks that stimulate sensory nerve fibers and cause significant pain. However, these weapons often could be overcome by focused or altered individuals. Modern stun guns work more like TASERs, causing contraction of muscles and incapacitation of the subject. There have not been any case reports in the medical literature of death attributed to the use of stun guns, electric shields, or RACC belts (Roberts & Vilke 2016).

TASER

A TASER is a specific brand of CED manufactured by TASER International that delivers an electrical discharge of energy through a sequence of dampened sine-wave-current pulses lasting approximately eleven microseconds each. Rather than pure AC or DC, this energy is akin to rapid-fire, low-amplitude DC shocks. The discharge is transmitted from the TASER device through thin copper wires to the end barbs. These barbs, consisting of a thick metal base and thin, barbed metal shaft, are designed to penetrate and stick into skin or clothing. Law enforcement uses several models that can be deployed from up to thirty-five feet away, with a recommended distance of twelve to eighteen feet to obtain the optimal probe spacing for NMI.

Probe location and distance between probes, as well as the underlying condition of the subject, all contribute to the device's effectiveness. Probes located a short distance from each other (<5 cm) will have less of a neuromuscular effect but cause more pain compared with probes spaced further apart. The probes do not have to be directly in contact with the subject's skin, as long as they are within an inch or two.

The TASER's projectile design allows for safe operating distance to be maintained between the subject and officer. This is referred to as "probe" mode. If probe mode is impractical because of close distance or other tactical reasons, a so-called drive stun mode may be used in which two electrode plates at the end of the device are held against the skin. Drive stun mode is intended for pain compliance, not NMI. Advantages over other pain compliance tools include a lower risk of physical injury to the officer and subject that occurs compared with punches or impact weapons.

Frequency/Stats of TASER Usage by Law Enforcement

Since the 1980s, law enforcement has implemented the use of TASERs as an alternative to traditional firearms in order to safely subdue dangerous individuals. According to TASER International, since 1994, more than 850,000 TASER weapons have been sold to more than 18,000 law enforcement agencies. As of September 30, 2015, TASER devices are deployed, on average, 904 times a day. They also report that TASER devices are deployed in more than 17,800 of the 18,250 law enforcement agencies in the United States, and in 107 other countries, including Argentina, Australia, Brazil, Canada, Columbia, France, Germany,

New Zealand, Singapore, South Korea, and the United Kingdom. TASER devices are reported to have saved more than 157,000 lives from death or serious personal injuries – defined as cases in which lethal force would have been used if the TASER device was not available.

As of November 20, 2015, there have been approximately 2,924,000 field applications and 2,009,000 volunteer training activations. There have been no reported deaths in the volunteer population following the use of a TASER. A 2009 police executive research forum study reported that officer injuries dropped by 76 percent when a TASER was used (Taylor et al. 2009).

Excited Delirium Patients in the Prehospital Environment

Excited Delirium Syndrome (ExDS), also known as "agitated delirium," is closely associated with "sudden death in custody syndrome." The term ExDS is used in the forensic literature to describe a subgroup of patients with delirium who have suffered lethal consequences from untreated agitation. Traditionally, the forensic medical community has classified those patients as "excited delirium" who present with altered mental status, aggressive agitated behavior, and a combination of other symptoms such as superhuman strength, diaphoresis, hyperthermia, attraction to glass and light, and/or lack of willingness to yield to overwhelming force (Vilke et al. 2012).

These patients often suffered sudden death where no anatomical cause of the death was found on autopsy. Due to this lack of an anatomic cause of death, there has been continued debate about the validity of the term "excited delirium," as some observers believe the term to be convenient language used to excuse and exonerate law enforcement personnel when someone dies in custody.

Currently, the term "excited delirium" is not recognized by the AMA (American Medical Association) or APA (American Psychological Association). This hinges on the fact that the medical coding references, including the International Classification of Disease (ICD-9), do not recognize the exact term "excited delirium" or "excited delirium syndrome." However, other diagnoses reflect the clinical presentation of ExDS. The National Association of Medical Examiners (NAME), the body representing forensic pathologists in the United States, published a position paper that validated the existence of ExDS for the first time in 2004 (Stephens et al. 2004). In 2009, the American College of Emergency Physicians (ACEP) joined NAME in recognizing ExDS as a discrete medical entity (ACEP 2009).

Table 12.1. Common symptoms of excited delirium

Altered mental status, aggressive agitated behaviors + combination of other symptoms such as:
• Superhuman strength
• Diaphoresis
• Hyperthermic
• Tachycardic
• Hyperthermia
• Attraction to glass and light
• Lack of willingness to yield to overwhelming force

ExDS has been defined as a syndrome instead of a unique disease due to the lack of a clear definition and pathophysiologic etiology. As of today, the actual pathophysiology of ExDS is complex and not well understood. There are no clear explanations as to why some patients progress to death and why some do not, but one possible effect may be kindling from various causes, including stimulant drug use. Use of sympathomimetic substances, especially cocaine, has been strongly associated with ExDS. However, post-mortem toxicological analysis of ExDS fatalities associated with cocaine use demonstrate cocaine concentrations similar to those found in recreational drug users. These levels are less than those noted in acute cocaine intoxication deaths, suggesting a different mechanism of death (Vilke et al. 2012). Post-mortem brain analysis in ExDS patients has also demonstrated a characteristic loss of the dopamine transporter in the striatum of chronic cocaine abusers who die with clinical presentations. This suggests that a potential pathway for the development of ExDS is excessive dopamine stimulation in the striatum, but the significance of this in ExDS unrelated to chronic cocaine abuse remains unknown (Mash et al. 2009). Another fact supportive of central dopamine stimulation as a pathway for development of ExDS is that hypothalamic dopamine receptors are responsible for thermoregulation. If so, abnormalities of dopamine neurotransmission may explain the hyperthermia reported in ExDS patients (Bunai et al. 2008).

Many of the ExDS patients who die typically do so shortly after a violent struggle, usually within minutes after cessation of the struggle. This suggests that severe acidosis may play a prominent role in ExDS-associated cardiovascular collapse, and that there may be some relation with the peaking of catecholamine shortly after increased exertion (Hick, Smith, & Lynch 1999). Recent research suggests that physical exertion may be a greater contributor to a catecholamine surge and metabolic acidosis than any other causes of exertion or noxious stimuli (Ho et al. 2010). Well-documented cases of ExDS deaths without ECD use or maximal restraints are amply in evidence, and the idea that prone restraint may be a contributing factor to death has been discredited by careful studies (Vilke et al. 2012).

The differential diagnoses of ExDS include several specific entities that cause altered mental status. For instance, hypoglycemia has been reported with outbursts of violent behavior and an appearance of intoxication. Heat stroke may manifest as hyperthermia or delirium, and may be associated with neuroleptic use and mental illness. Thyrotoxicosis may manifest a similar clinical presentation. Serotonin syndrome and neuroleptic malignant syndrome (NMS) may also mimic some clinical characteristics of ExDS. These factors are important to consider when encountering a subject who is altered and aggressive.

Many psychiatric conditions including acute paranoid schizophrenia, bipolar disorder, and even emotional rage from acute stressful social circumstances, may mimic presentations of ExDS (Vilke et al. 2012). Some patients exhibit behavioral disturbances due to antipsychotic drug withdrawal. Additionally, substance abuse is also common in psychiatric patients and may present similarly to ExDS.

Symptoms and Signs of ExDS Recognized by Law Enforcement Officers and Prehospital Care Providers

Members of the general public, law enforcement, EMS personnel, first responders, and even trained medical personnel are generally unable to differentiate the etiology of an acute behavioral disturbance by observation alone, nor is it necessary to do so. Providers do not need to make a diagnosis, but rather to recognize the symptoms consistent with ExDS and

Table 12.2. Differential diagnosis of ExDS

Hypoglycemia
Heat stroke
Thyrotoxicosis
Serotonin syndrome
Neuroleptic malignant syndrome
Paranoid schizophrenia
Bipolar disorder
Emotional rage
Antipsychotic drug withdrawal
Substance abuse
Infection
Intracranial lesion

that these symptoms constitute a medical emergency. These symptoms include extreme agitation or aggressive behavior and patients are often resistant to pain. Typically, patients are combative, hyperthermic, diaphoretic, and tachycardic (described in Table 12.1). Many are naked or under-clothed, attracted to water, lights, or glass. Most cases involve stimulant drug abuse, most commonly cocaine, though methamphetamine, PCP, and LSD have also been described (Karch & Welti 1995; Karch & Stephens 1999). The other cohort of ExDS cases and deaths are patients with psychiatric disorders who had abruptly stopped taking their psychotherapeutic medications (Morrison & Sadler 2001).

The ExDS workshop panel, convened in April 2011, designed a useful two-sided pocket card for use by law enforcement officers and EMS personnel. The card identifies major presenting signs and symptoms to assist law enforcement personnel and others, as well as treatment goals of ExDS: Identify, Control, Sedate, and Transport (ACEP 2009; shown in Figure 12.1).

Hopefully, increased awareness of ExDS among law enforcement and EMS personnel through education will lead to better early recognition of individuals experiencing this medical crisis and to early interventions preventing sudden death. Cooperative protocols that combine law enforcement and EMS efforts to manage ExDS patients should be encouraged.

Prehospital Evaluation and Management of the Patient with Symptoms of ExDS

The concept of ExDS is increasingly becoming a concern for law enforcement, EMS personnel, and emergency physicians who encounter and manage these patients (Table 12.2). There is a high fatality rate, best estimated in upward of 10 percent, in subjects who present with signs and symptoms of ExDS (Stratton et al. 2001). Although ExDS is not universally fatal, case presentations in the literature often discuss its lethality, perhaps in part because most of the available publications have come from the forensic literature. Among ExDS patients,

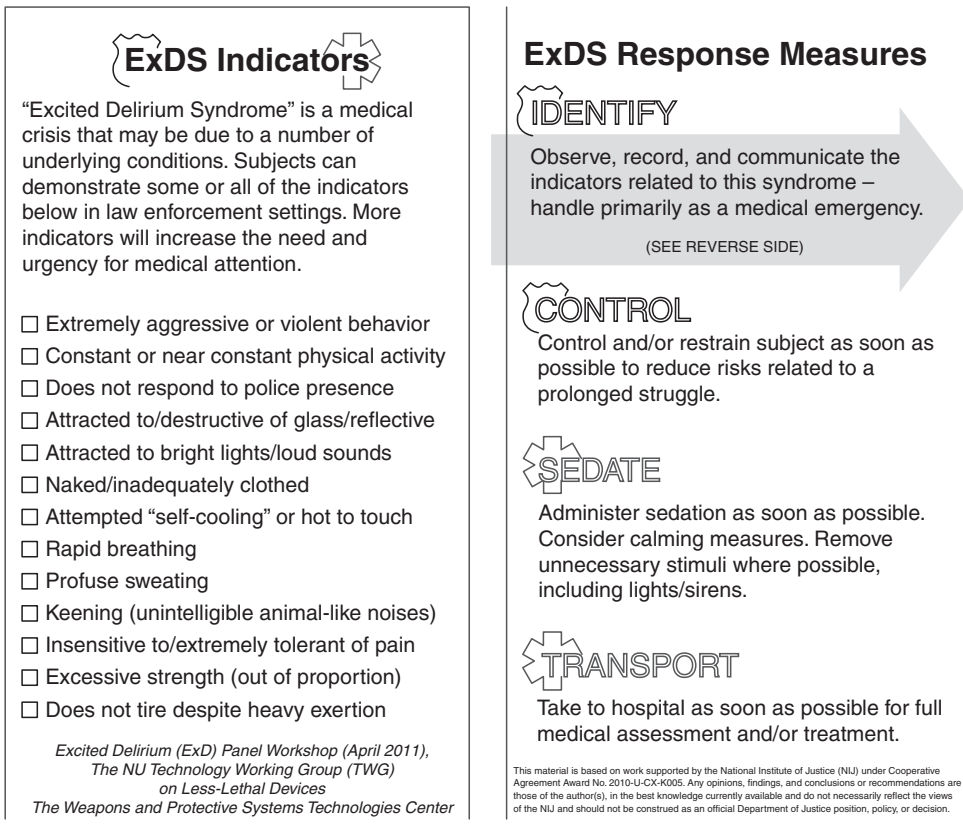

Figure 12.1. ExDS pocket card (front and back) for law enforcement and EMS personnel created by the work of the National Institute of Justice Technology Working Group (TWG) on less lethal devices.

a proportion will progress to cardiac arrest and death as a result of a combination of factors. Even though many of the deaths from ExDS are likely not preventable, there may be a subset of which death might be avoided with an early directed therapeutic intervention.

Quickly controlling an ExDS subject in the prehospital setting to minimize the subject's exertional activity is a priority, while maintaining both the safety of providers and the subject. ExDS subjects typically have altered mental status, are often paranoid, and are essentially impossible to effectively communicate with, making verbal de-escalation of little value. The use of an ECD such as TASER to rapidly gain physical control and restrain a subject is preferable to the approach of going hands-on, as heavy physical exertion may exacerbate acidosis in the subject and contribute to a greater risk of sudden death. Data have shown that exertion and struggle increase acidosis more than use of a TASER (Ho et al. 2010). The goal is rapid control allowing as little struggle as possible by the subject. Once the subject is restrained and scene safety is secured, the medical evaluation and treatment can begin for the patient.

Initial efforts should be made to minimize the subject's fear from the chaotic environment, and verbal de-escalation from a single provider is still recommended. Once the

patient is restrained physically, treatment of agitation with appropriate pharmacologic agents is the most important early patient intervention. When safely feasible, a blood glucose and an oxygen saturation should be assessed. A cardiac monitor should also be placed and ongoing reassessment should occur.

Recommended medications for use in patients with ExDS generally consists of three classes: benzodiazepines, antipsychotics (both first and second generation), and ketamine (Vilke & Bozeman 2012). Benzodiazepines (lorazepam, diazepam, and midazolam) are useful in severely agitated patients and are typically considered a first-line medication. These are particularly useful in ExDS presumed to be due to sympathomimetic intoxication. Benzodiazepines may be administered either by IV (intravenous), IM (intramuscular), or IO (intraosseous) routes. Alternative dosing may be used with IN (intranasal) midazolam, though often it is challenging to administer. Typically, repeat doses may be required to obtain and maintain chemical control. Some disadvantages of benzodiazepines include relatively slow onset, which may be as much as five minutes for midazolam if given IM. Concerns for oversedation or respiratory depression, synergism with alcohol or other sedatives/hypnotics and hypotension are further considerations for benzodiazepines in general, but in patients with true ExDS, these issues rarely if ever arise given the tremendous adrenergic drive of the ExDS patient. Even when a patient is mistakenly thought to have ExDS, it is not unreasonable to obtain initial stabilization with a benzodiazepine to ensure safety for medical personnel. Investigation for differential diagnoses should be done subsequently.

First-generation antipsychotics, such as haloperidol or droperidol, and second-generation antipsychotics, such as olanzapine or ziprasidone, are commonly administered either IM. First-generation antipsychotics such as haloperidol or droperidol are known to prolong the QT interval, and so if a long QT syndrome is suspected based on patient history, usage of antihistamines, diuretics, antibiotics, antiarrhythmics, antidepressants, or antipsychotics should be avoided, as some ExDS deaths have been thought to be related to ventricular dysrhythmias and/or lengthened QT intervals.

Ketamine may be administered IM or IV and rapidly induces a dissociative anesthesia with preservation of airway reflexes. Ketamine has a benefit of rapid onset of action, preservation of airway reflexes, and a large safety margin that allows relatively safe administration of large doses without titration. While ketamine may theoretically worsen hypertension or tachycardia, case reports have indicated excellent clinical results and overall reductions in hyperadrenergic vital signs when used in ExDS patients in the prehospital setting (Vilke et al. 2012). A recent retrospective study examined the efficacy and safety of ketamine in the treatment of acute agitation in an ED setting that focused on any changes of vital signs after use of ketamine, particularly oxygen saturation. Ketamine was used without any significant vital sign changes and 62.5 percent of patients required additional calming medication within three hours. Ketamine has a short onset and short duration, and is expected to gain rapid and safe control of severely agitated patients. As ketamine has not been proposed specifically as a treatment for the underlying cause of agitation, but rather as a means to facilitate an initial work-up of an agitated patient, it is perhaps not surprising to find that the majority of patients required additional medications.

Many practitioners find combination therapy pairing benzodiazepines with antipsychotics or IM ketamine useful. Combination therapies are thought to have synergistic effects and a reduction of side effects. However, one study showed a marked reduction of side effects when haloperidol was combined with a benzodiazepine; however, this study was not performed in patients with ExDS (Battaglia et al. 1997).

Table 12.3. Recommended dosing of pharmacologic agents for treatment of ExDS

Lorazepam	2–4 mg IM/IV
Midazolam	2.5–5.0 mg IM/IV
Haloperidol	2.5–5.0 mg IM
Droperidol	2.5–5.0 mg IM/IV
Olanzapine	10 mg IM
Ziprasidone	20 mg IM
Ketamine	4–5 mg/kg IM or 2 mg/kg IV

ExDS patients are often dehydrated due to decreased water intake associated with their drug use, an elevated temperature, hyperventilation, and diaphoresis. Additionally, drugs that cause ExDS often predispose patients to rhabdomyolysis and electrolyte abnormalities. IV fluid administration is therefore indicated in ExDS patients once an IV can safely be established.

Currently, there is consensus that early medical intervention should include rapid recognition and control, aggressive sedation, hydration, monitoring, and rapid transportation of patients who display signs and symptoms of ExDS. Further research is required to identify disease process, mechanisms, and risk factors for sudden death and optimal therapeutic approaches.

Position Papers, Clinical Guidelines

The ACEP Task Force states that ExDS is a real syndrome with uncertain, though likely multiple etiologies. Presentations include delirium, agitation, acidosis, and hyperadrenergic autonomic dysfunction, typically in acute-on-chronic stimulant drug abuse or serious mental illness (ACEP 2009). The task force recommends rapid physical control and early medical intervention (Table 12.3). They also support the use of TASERs to facilitate getting the subject restrained to minimize physical exertion (Table 12.4).

Vilke and colleagues conducted a structured review of the literature on ED evaluation after CED use upon request of the American Academy of Emergency Medicine (AAEM) Clinical Guidelines Committee and published their findings as a position statement (Vilke et al. 2011).

Four recommendations for emergency department evaluation after CED use were offered. Recommendation 1: Cardiac monitoring and electrocardiogram screening after CED use – Class A recommendation – "Medical literature does not support routine performance of electrocardiograms (ECGs), prolonged ED observation, or ongoing cardiac monitoring after CED exposure in an otherwise asymptomatic awake and alert patient with a short duration (<15 seconds) of CED exposure." Recommendation 2: Laboratory testing after CED use – Class A recommendation – "The medical literature does not support routine performance of laboratory studies, prolonged ED observation, or hospitalization for an ongoing laboratory monitoring after a short duration (<15 seconds) of an otherwise asymptomatic awake and alert patient." Recommendation 3: Evaluation after use of CED in drive stun or touch stun mode – Class B recommendation – "For patients who have

undergone drive stun or touch stun CED exposure, medical screening should focus on local skin effects at the exposure site which may include local skin irritation or minor contact burns." Recommendation 4: Evaluation after use of CED in probe mode – Class B recommendation – "For patients who have undergone probe mode CED exposure, medical screening should focus on probe penetration sites, potential injuries due to muscle contractions, and potential trauma due to falls."

Current expert guidelines on the management of agitated patients recommend that all patients have verbal de-escalation attempted if possible. Although ExDS patients by definition have failed simple verbal de-escalation, a verbal approach is nonetheless likely still useful since it may help partially calm both the patients and the other involved individuals during the takedown to gain control of the patient.

Adverse Effects Reported from TASER Use

Musculoskeletal – In general, there are no permanent lasting effects on the muscular system aside from any injuries associated from an associated fall.

There have been several case reports of vertebral compression fractures that occur when the TASER is used in probe mode in the back region and the strong back muscles compress against some weakened osteopenic bones (Winslow et al. 2007; Sloane et al. 2008).

Central Nervous System – There has not been any published reports of seizures induced in either healthy or epileptic subjects by the use of TASER. There has not been any reports of development or exacerbation of posttraumatic stress disorder (PTSD) or other psychiatric effects.

Cardiac – There has been a number of limited animal studies and human studies. Based on the totality of the review of animal and human studies, the potential for inducing life-threatening cardiac dysrhythmias with current TASER devices appears very low. However, the effect of recurrent or prolonged TASER discharges remain unclear for patients with pacemakers or underlying cardiac disease.

Respiratory – A number of human studies have demonstrated that subjects breathe faster and have a higher minute ventilation when undergoing a TASER activation. However, none of the studies' respiratory changes was clinically significant.

Laboratory – Current literature on humans has not demonstrated evidence of clinically significant laboratory abnormalities of physiologic changes after CED exposures. Human studies have not shown any clinically significant changes in electrolyte levels or renal function in CED activations up to fifteen seconds (Wilson & Vilke 2015).

Others- Injuries at the probe penetration sites, injuries due to excess muscle contractions, and trauma due to falls have been reported. There have also been case reports of injuries sustained from the darts such as ocular, skull, or genital penetration (Rehman, Yonas, & Marinaro 2007; Ng & Chehade 2005). A recent literature review indicates that significant injuries are rare, occurring in less than 0.5 percent of deployments.

The subject and medical personnel who may need to remove the TASER probes are at risk of contracting a blood-borne disease. Methods of TASER probe removal include removal by hand, removing the probe with pliers or similar tools, or using specialized commercial removal systems. Judicious precautions should be taken when TASER probes are being removed from sensitive areas (Cronin 2006).

Table 12.4. Reported adverse effects of TASER use

Musculoskeletal	No permanent effects aside from any injuries associated from a fall. Several cases of vertebral fractures in osteopenic patients when TASER is used in back region
CNS	No reports of seizures, PTSD, or other psychiatric effects
Cardiac	Limited animal and human studies. Potential for inducing life-threatening cardiac dysrhythmias appears very low
Respiratory	Subjects breathing faster and higher minute ventilation seen in a number of human studies but clinically non-significant
Laboratory	No clinically significant laboratory changes demonstrated in current literature
Others	Injuries at the probe penetration sites, injuries due to excess muscle contraction, injuries due to falls. Significant injuries reported to be rare (less than 0.5% of deployments)

Pitfalls in ExDS Patients

There are several common pitfalls in managing ExDS or other behaviorally disordered patients in the prehospital setting (Wilson & Vilke 2015):

1) Failure to suspect medical etiology: EMS providers should always suspect a medical etiology of agitation and never blame the patient's symptoms on psychiatric problems unless other medical problems have been excluded first.
2) Failure to check glucose or oxygen saturation: EMS providers should always check complete vital signs on all behaviorally disordered patients. Hypoglycemia and hypoxemia may cause agitation in many patients and can be discovered easily.
3) Failure to recognize impaired level of decision making: An assessment of mental status is important in all behaviorally disordered patients. These patients, by virtue of substance use, a medical condition, injury, or psychiatric disorder, have impaired reasoning about their condition.
4) Overuse of force: EMS providers should only use the minimum of force to accomplish the primary objective of caring for the patient and should ensure safety for themselves and the patient.
5) Failure to use appropriate amount of benzodiazepines: Patients may need repeat dosing of benzodiazepines. The dose of medication should be enough to sedate the patient without compromising respiration and airway maintenance. Close monitoring is required.
6) Failure to recognize symptoms of ExDS: The signs and symptoms should be recognized as well as the significant risk for sudden death.

Controversies in TASER Use in Excited Delirium Patients

Approval of the original TASER devices was not based on actual human or animal studies, but rather on theoretical calculations of the physical effects of dampened sinusoidal pulses, which the U.S. Consumer Product Safety Commission concluded should not be lethal to a normal healthy person (McDaniel et al. 2005).

ExDS is often considered lethal particularly compared with other behavioral disorders. The presentation of ExDS frequently requires the involvement of law enforcement, and when deaths occur during or after struggle or restraint, the use of force technique used to gain control is often implicated in being the cause of cardiac arrest. This includes cases involving hobble restraints, chemical agents such as OC spray, and TASER devices. Other reports implicate the use of illicit drugs. There has been a controversy over the use of TASER CEDs being associated with sudden deaths. A database run by *The Guardian* newspaper, The Counted, tracking killings by police and other law enforcement agencies, report 48 deaths out of 1,126 killed classified as by TASER (as of December 28, 2015)(*Guardian* 2015). Amnesty International claims 334 deaths after an ECD shock between 2001 and 2008, which increased recently to 540 between 2001 and 2013 (Amnesty International 2013).

There are many case reports of subjects in a state of ExDS who die suddenly. The circumstances of the events often vary. Sometimes a hobble restraint is used. Sometimes OC spray is used. Sometimes there are various uses of force. Sometimes a TASER is used. Often the cardiac arrest occurs well after the law enforcement involvement, like in the back of the ambulance or in the emergency department. In most cases, there is a struggle and all are exhibiting the severely agitated symptoms associated with ExDS. However, when a death occurs after a TASER is used, there is often scrutiny that the TASER played a role in the cardiac arrest, despite when the arrest occurs. There has never been a published human study that concludes that a TASER can kill a human in the drive stun mode or in probe mode with probes located away from the trans-cardiac axis. There are only case series that specifically implicate the TASER as the cause of cardiac arrest and sudden death and hypothesize an etiology.

In a controversially published case series by Zipes, eight cases in which loss of consciousness followed the use of a TASER X26 electronic control device were analyzed in detail to determine whether a CED such as the TASER can result in cardiac electrical capture, thereby provoking ventricular tachycardia (Zipes 2012). Cases were included as part of litigation related to the administration of shock from the TASER X26, with one case collected in 2006, four cases in 2008, and three cases in 2009. Four cases had structural heart disease and/or elevated blood alcohol concentrations at the time of shock. Data analyzed included police, medical, and emergency response records, X26 data port interrogation, automated external defibrillator information, ECG strips, depositions, and where applicable autopsy reports. In all cases, the individuals receiving shocks were reported as previously healthy males between the ages of sixteen and forty-eight who were shocked with barbs in the anterior chest near or over the heart and lost consciousness during or immediately after the shock event. All but one individual died.

Based on these materials, Zipes concluded that shocks from a TASER X26 probes may cause cardiac electrical capture. The proposed method for this is forced rapid pacing of the previous beat, causing disorganized ventricular activation and resulting in a rapid drop in blood pressure and ultimately ischemia. The major limitation of this study is the lack of an ECG recorded during the shock event. Thus, neither the incidence of death nor true cause of death cannot be concluded from this study.

Nanthakumar and Waxman, however, challenge the conclusion reached by Zipes that the TASER 26X may cause ventricular fibrillation (2013). In response, the authors note two mechanisms whereby a TASER shock could lead to asystole and thereby death: hyperkalemia and electrical silence in the epicardial regions. The authors conclude that ECG recordings made long after ventricular fibrillation with surface leads may appear as asystole, as long-duration ventricular fibrillation can seem to be asystole, or may later become asystole.

They also stress the importance of temporality between myocardial capture and CED shock, which is not well studied.

The conclusion that TASERs can cause cardiac dysrhythmias and sudden death was further challenged by Vilke and colleagues due in part to the fact that the phrase "clinically healthy" was not defined and in fact does not appear to be true in seven of the eight cases (Winslow & Bozeman 2007). Not only were the mean heart weights of seven of the eight cases significantly greater than the predicted mean provided by the Mayo Clinic (a risk factor for sudden cardiac death), case one was known to suffer from mental illness as well as chronic alcoholism and illicit drug use, and case five was known to be epileptic. The authors also note that the specifics of the shock event are not elucidated on in the paper by Zipes, and that there was no differentiation between probe and drive stun deployments. Additionally, the studies cited for the mechanism by which TASER shocks may cause ventricular fibrillation do not conclude that CEDs cause ventricular fibrillation or dysrhythmias in humans, as swine are not a good analogue to human conduction systems. Finally, the authors report that of the more than 1 million volunteers who have undergone TASER activation, none has ever lost consciousness or died even with probes placed across the cardiac axis.

Swerdlow and colleagues reported on 200 deaths after a TASER was used (Swerdlow et al. 2009). They found fifty-six subjects who collapsed within fifteen minutes of the CED shock in which the presenting rhythm was recorded. VF was seen in four subjects, and fifty-two had bradycardia, asystole, or PEA. One death was typical of electrically induced VF and occurred almost immediately with the activation of the TASER. For this subject, Swerdlow and colleagues argued that neither drugs nor cardiac disease can be implicated; both the time course and the electrode location are consistent with electrically induced VF. They state this is the first reported fatality suggestive of "CED induced VF" (Swerdlow et al. 2009).

Numerous limited animal and human studies have been used to support both sides of the arguments (Kornblum et al. 1991; Kim & Franklin 2005; Cao et al. 2007; Ideker et al. 2007; Levine et al. 2007; Vilke et al. 2007; Dawes et al. 2008; Eastman et al. 2008; Lakireddy et al. 2008; Sloane et al. 2008; Valentino et al. 2008; Vilke et al. 2008; Bozeman et al. 2009; Ho et al. 2009; Vilke et al. 2009; Moscati et al. 2010; Strote et al. 2010; Ho et al. 2011; Gardner et al. 2012; Kroll et al. 2014). When a sudden death occurs while a patient in custody, there is often the challenge of separating any potential contributions made by restraint and those of the underlying pathology. Hence, an actual connection between the use of the TASER and these fatalities is often controversial. However, research on the effects and safety of TASERs has been growing significantly.

Conclusion

Summary

The TASER is a conducted energy device most commonly used as a nonlethal weapon by law enforcement and military personnel to momentarily incapacitate a subject. TASERs are increasingly becoming a mainstay to ensure the safety of law enforcement officials, as well as an alternative to deadly force in severely altered, aggressive, and agitated subjects. It is crucial for law enforcement and EMS personnel to rapidly identify, control, sedate, and transport the patient who is presenting with signs and symptoms of ExDS. To accomplish this, the TASER's use has been effective in minimizing physical struggle, which is thought to provoke sudden cardiac death by increasing lactic acidosis. The use of a TASER in this population has been

recommended by numerous groups and task forces, both law enforcement and medical, to facilitate the rapid restraint of subjects in ExDS so that medical evaluation and treatment can be promptly initiated. It is this early medical therapy that is felt to optimize the survival of ExDS patients, a condition with an estimated 10 percent mortality rate.

Recommendations

Although definite pathophysiology of ExDS is controversial, there is consensus on the importance of rapid identification, control, sedation, and transport of these patients as a true medical emergency. Law enforcement and EMS personnel play an important role in identification and should be aware of current recommendations and controversies. The benefits of TASER use seem to outweigh the risk, although judicious use is recommended. Avoidance of TASER darts around the chest and sensitive areas and of prolonged firing are recommended to prevent potential unnecessary complications. After restraint is complete and scene safety is secured, initiation of medical therapy with proper sedation is strongly recommended.

Key Points

- TASERs are used commonly in the prehospital setting to ensure safety of personnel and the altered, aggressive, and agitated patient.
- TASERs are increasingly used to control violent and aggressive individuals while maintaining a margin of safety, as well as to reduce the need for impact weapons and injuries associated with their use. They are reported to have prevented many law enforcement personnel injuries as well as subject injuries.
- ExDS is a condition that is a true medical emergency and requires rapid identification, control, sedation, and transport. Further research is required, but adverse effects seem trivial and TASERs have been considered useful in rapid control of these patients.

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Chapter

13

Appropriate Use of Restraint and Seclusion

Naomi A. Schmelzer

Introduction

Restraint and seclusion have long been in use in the medical and psychiatric setting. Drawing on deep historical roots and legal precedent, current practice continues to shape around changing ethical perspectives and advancing psychiatric knowledge. Practitioners should be well trained in the safe and appropriate use of restraint and seclusion, with thoughtful consideration toward the therapeutic impact, when less coercive alternatives have been exhausted.

Case Example

Ben is a twenty-three-year-old man with schizophrenia arriving to an inner-city psychiatric emergency department by ambulance from a nearby supportive residence in a severely agitated state, screaming nonsensical words, and running around the small space knocking over furniture. Ben cannot sit or stand still for an interview, and continues furiously pacing the ER. The psychiatric nurse attempts to engage him in simple conversation, but Ben continues to call out loudly in response to internal stimuli. He begins to climb on the sink, stating his intention to "fly off," and must be helped down by security guards. Ben has refused the offered oral medication and receives an intramuscular injection to assist with his psychotic symptoms, but remains agitated one hour later. He is then seen trying to run his head repeatedly into the wall in an attempt to "knock the demons out." He attempts to physically fight staff and security who have approached to stop him, and does not respond to the nurse or psychiatrist's attempts at verbal de-escalation. As Ben's behavior is acutely dangerous to himself and staff and is directly influenced by delusional thinking, and as he has not responded to alternatives to de-escalation, the decision is made to use four-point restraint as well as provide an additional dose of antipsychotic medication. As the designated leader for this event, the psychiatrist provides Ben with an explanation of the treatment and rationale, and observes him during application of restraints for any signs of distress or difficulty with respiration. After thirty-five minutes of continuous monitoring by staff, Ben is assessed by his nurse to be calm and no longer a danger to himself, and the restraints are discontinued. He can participate in a debrief discussion with his team about this part of his treatment.

Patterns of Use

Historically, various forms of mechanical restraint can be traced back through psychiatric practice. From 1403 at Bethlem, an inventory list of medical equipment includes iron chains and manacles (Winship 2006). During the eighteenth-century Enlightenment, reformers in Europe focusing on principles of humane care in asylums drove the

development of non-restraint alternatives for the mentally ill. In 1815, a parliamentary inquiry into conditions at Bethlem demonstrated the need for increased legislative control over conditions there and resulted in annual inspections, certification, and licensure requirements, as well as improved record keeping (APA 1985). In the nineteenth century in the United States, controversy surrounding mechanical restraint led to John Conolly's invention of the padded seclusion room, and the philosophy of non-restraint was coined "Conollyism" (Colaizzi 2005). In 1844, Benjamin Rush advocated for the abolishment of restraints, instead making use of a restraining chair (APA 1985).

Over the centuries, various forms of mechanical restraint and seclusion have come into use and fallen from favor, including manacles and wristlets, cloth restraints, straightjackets, protection beds, hydrotherapy, chemical restraints, and others. With changing attitudes and advances in care, mechanisms of restraint that were once considered part of compassionate care in overcrowded institutions now seem antiquated and inhumane (see, e.g., Project BETA; Knox & Holloman 2012). However, while clinical practice strives toward reducing restraints and seclusions, it is unlikely their use in psychiatric care settings can be eliminated entirely.

Centers for Medicare & Medicaid Services (CMS) (2006) defines restraint as "any manual method, physical or mechanical device, material, or equipment that immobilizes or reduces the ability of a patient to move his or her arms, legs, body, or head freely." In psychiatric settings today, the four-point restraint is commonly used.

The prevalence of seclusion and restraint varies widely in psychiatric and medical settings, with a meta-review by Beghi and colleagues (2013) showing that use occurred in 3.8 percent to 20 percent of hospitalized patients. In a survey of psychiatric emergency departments, restraints were used in 6 percent to 7 percent of patients in suburban or rural areas and 12.3 percent of patients in urban areas. Overall, 8.5 percent of patients ended up in restraints for a mean duration of 3.3 hours (Allan & Currier 2004). In another survey on the use of coercive measures for agitated patients in both medical and psychiatric emergency departments, 30 percent reported using physical restraints and 30 percent reported the use of combined physical and chemical restraints for management (La Vonne, Zun, & Gonzales 2007). Forster, Cavness, and Phelps (1999) note that 0.4 percent to 9.4 percent of patients will experience at least one episode of seclusion or restraint during an acute hospitalization.

When used in practice, the clinical indication should be clear, within established guidelines, and communicated to the patient. Primary indications for the use of restraint or seclusion include prevention of imminent harm toward the self or others, or prevention of serious destruction to the environment, when other means are not effective (APA 1985). In addition, clinicians may utilize seclusion as a means to decrease sensory overstimulation or upon voluntary request of the patient, though these indications are declining in use (see Table 13.1). Restraint and seclusion should not be used for patients with unstable medical conditions such as those with delirium, drug intoxication, or withdrawal states. Similarly, they are contraindicated as a form of punishment, if they would be viewed by the patient as positive reinforcement for disruptive behavior, or if used for staff convenience (Fischer 1994; Simon 2005).

Risk Factors

Restraint and seclusion practices vary widely across hospital settings, influenced by a variety of patient, staff, and hospital-based factors. Particular characteristics may only be risk

Table 13.1. Restraint and Seclusion Indications and Contraindications

Indications	Contraindications
• Risk of imminent harm to self • Risk of imminent harm to others • Serious destruction to environment • Patient's voluntary reasonable request • Decrease sensory overstimulation[1]	• Unstable medical condition (ex. delirium) • Severe drug reaction or overdose • Punishment • Staff convenience • If experienced by patient as positive reinforcement for violence or disruptive behavior

[1] Only for seclusion

factors under certain circumstances; for example, acute psychosis may be more of a risk factor for restraint on an inpatient psychiatric unit than in a psychiatric emergency department. Overall, several studies have demonstrated that the following patient risk factors should be considered: involuntary hospitalization, younger age, male gender, psychosis (such as schizophrenia), foreign ethnicity, severe functional impairment, impairment in judgment and insight, substance use disorders, and prior experience with restraint or seclusion (Migon et al. 2008; La Rue et al. 2009; Georgieva, Vesselinov, & Mulder 2012; Beghi et al. 2013; Goulet 2013; Knutzen et al. 2007).

Staff characteristics have also been shown to influence the use of restraint and seclusion, particularly as Gerolamo (2006) notes, the varied training and educational experience of the nurses on the psychiatric floors. He points out that the proportion of registered nurses (RNs) to licensed practical nurses (LPNs) and other assistive personnel was significant, and that expert skills including surveillance by RN could not be discounted. Other staff factors include high levels of stress, anger, or aggression (de Benedictis et al. 2011), and negative attitudes toward mental health problems (La Rue et al. 2009). Based on a survey of physicians by Sandhu and colleagues (2010), a physician's lack of knowledge about restraints increased the likelihood of ordering them. Hospital factors generally involve the degree of teamwork, organization, leadership, resources, and prevailing attitudes on the wards (Bowers et al. 2011), and are more difficult to measure. See a summary of risk factors in Table 13.2.

Morbidity/Mortality

Current trends call for the use of restraint and seclusion only when unavoidable, as a last option when all alternatives have been ineffective. However, inappropriately withholding restraint or seclusion when they are needed may also result in adverse outcomes. Being able to weigh the involved risks in using or avoiding restraints is an essential part of caring for patients with agitation or behavioral emergencies.

The Joint Commission reviewed restraint-related adverse event data from 1995 to 2013, collecting events that resulted in death or permanent loss of function, and found 240 events in that time period (Joint Commission 2012). By the same criteria, 121 events were recorded for a ten-year period. The FDA (1992) notes that adverse events seem to result from the incorrect use of restraints, including their use on inappropriate patients, incorrect application, or inadequate monitoring of restrained patients.

Table 13.2. Risk Factors for Restraint and Seclusion

Patient Risk Factors	Staff Risk Factors	Environment/Hospital
• Involuntary hospitalization • Younger age • Male gender • Psychotic illness (ex. schizophrenia) • Foreign ethnicity • Prior experience with restraint/seclusion • Lack of judgment/insight • Severe functional impairment • Substance use	• Staff mix (ratio of RN/LPN) • Training level • Insufficient staffing level • High staff stress • Greater expression of anger/aggression • Physicians: less knowledgeable of restraints • Perception of risk	• Lack of alternatives • Ward culture • Level of unit organization

Patient-related adverse events can range from the mild to severe, and can be both physical and psychological. Staff should be trained to monitor the patient closely and recognize adverse effects early to prevent significant injury or death. Patient death in restraints is commonly caused by asphyxiation, such as when excessive weight is placed on the back in the prone position, when a towel or sheet is placed over the head to prevent biting or spitting, or when the patient's arm is pulled across his neck, leading to airway obstruction (Mohr et al. 2003). For this reason, the APA warns against restraining a patient in the prone position (Nissen et al. 2013). Furthermore, staff should not place towels, sheets, or other cloth items over a patient's head or mouth; rather individual staff members should wear personal protective equipment such as face shields to protect themselves from patients' spit. Other causes of patient death include cardiac arrest, circulatory problems including DVTs, blunt trauma, and additional factors listed in Table 13.3.

Certain characteristics place a patient at higher risk of having an adverse outcome. Individuals with a large abdominal girth or BMI greater than 30 may be at greater risk of developing restrictive pulmonary function. Patients with catecholamine hyperstimulation (such as from blunt trauma due to agitation or other hyperactivity, physiologic stress, hyperthermia or illicit drug use) have greater risk of sudden death (Mohr 2003; Nissen et al. 2013; Rakhmatullina, Taub, & Jacob 2013).

Nurses and other staff involved in placing patients in restraints are at risk for both physical and psychological adverse events as well. They can suffer physical traumas ranging from mild such as skin abrasions to more permanent disabilities such as eye and shoulder injuries. Nurses and other staff must also face the conflicted emotional reactions that come with providing this type of care, which can include feelings of guilt, sadness, and self-reproach (Rakhmatullina et al. 2013).

Regulatory/Legal Considerations

The laws and regulations that govern the practice and procedure for restraint vary by country, state, locality, and hospital. A central principle is balancing the patient's right to autonomy – including here the right to freedom from confinement or intrusive treatment as

Table 13.3. Adverse Outcomes Related to Restraints

Patient-Related Adverse Events	Staff-Related Adverse Events
• dehydration • asphyxiation • choking/aspiration • rhabdomyolysis • thrombosis (ex. PE, DVT) • skin problems (ex. Bruising) • cardiac arrest/death • joint injuries • blunt chest trauma • escaping restraint • escalating agitation • re-traumatization • emotional distress • feelings of humiliation, fear, dehumanization, isolation, being ignored	• spit upon • fracture or skin injury • eye injury • permanent disability • negative emotional reactions (ex. Sadness, guilt, self-reproach, retribution)

well as the right of informed consent – with beneficence and justice – in this case protecting the individual from serious harm to himself or others due to failure to treat. The emergency use of restraint or seclusion is widely accepted as appropriate only when a patient is without capacity for informed consent, when a delay in care would lead to serious injury or death, and when less restrictive means are not effective (Glezer & Brendel 2010). Conversely, failure to treat in this circumstance would be unacceptable according to both clinical standards and societal expectations (Austin, Bergum, & Nuttgens 2004).

In the United States, the landmark 1982 Supreme Court case *Youngberg* v. *Romeo* laid the legal groundwork for restraint and seclusion treatment around the country. The Supreme Court ruled that involuntarily committed patients are constitutionally entitled to "personal security and to freedom from bodily restraint," although these rights were further qualified and it was recognized that there were circumstances in which restraint was necessary. The standard by which restraint was used was deferred to the clinical judgment of the professional (Wexler 1982).

Although most states have had legislation in place to regulate the use of restraint and seclusion, an investigative report published in the *Hartford Currant* in 1998 focusing on restraint and seclusion-related deaths led to an increase in federal legislation and oversight of these practices (Appelbaum 1999). Federal agencies began releasing reports and guidelines regulating the practice of restraint, including the Joint Commission, the American Psychiatric Association (APA), the National Association of Psychiatric Health Systems (NAPHS), the American Hospital Association (AHA), the National Mental Health Association (NMHA), the American Psychiatric Nurses Association (APNA), the National Association of State Mental Health Program Directors (NASMHPD), the Substance Abuse and Mental Health Services Administration (SAMHSA), and the U.S. General Accounting Office (GAO) (Recupero et al. 2011). Since 2007, the Centers for Medicare and Medicaid (CMS) also released its own set of national standards for the use of restraint and seclusion, which include guidelines for the training of staff as well as

reporting of adverse events, and which continue to be updated (Recupero et al. 2011). Staff responsible for administering restraints or placing patients in seclusion should be aware of their hospital policy, as well as all applicable local, state, and federal laws and professional standards of care.

The Experience of Restraint

A review of the literature done by Strout (2010) identifies four themes when summarizing the patient's experience of physical restraint: the negative psychological impact, re-traumatization, perceptions of unethical practice, and a broken spirit. Patients reported feelings of anger, fear, humiliation, demoralization, degradation, powerlessness, distress, embarrassment, and a sense of violation (Meehan, Vermeer, & Windsor 2000; Strout 2010). In a mail survey of individual perspectives following treatment, 73 percent did not perceive themselves to be a danger to self or others at the time of being placed in restraint, and felt that their behavior was inappropriate but not dangerous (Ray, Myers, & Rappaport 1996). In a focused group of patients who were placed in seclusion or restraint, Mayers and colleagues (2010) note that themes emerged regarding feelings of inadequate communication, isolation, a violation or lack of respect for rights, and distress.

The use of restraints in patients with a history of trauma or abuse may lead to re-traumatization. The trauma-informed care perspective (Hammer et al. 2011) teaches providers that patients may experience increased suffering and staff may be at increased risk of injury during these interventions.

The use of restraint and seclusion can have a long-term psychological impact on patients, staff, and the hospital milieu. For example, Currier, Walsh, and Lawrence (2011) note that in one study, patients who were placed in restraints while in the ER had a decreased likelihood of following up with prescribed outpatient mental health treatment. The use of restraints also affects the inpatient milieu by consuming staff resources, diverting staff from other therapeutic tasks, and rousing negative emotions such as anger.

Changing Patterns of Use

There has been increasing emphasis on interventions to reduce the need for restraint and seclusion, and to replace these with alternative methods to manage aggression should behaviors escalate. There are multiple examples in the literature of successful hospital-based programs aimed at reducing restraint and/or seclusion, though these are typically case-based and specific for one hospital and unit type (i.e., acute inpatient or ED). When examining these as a group, common features emerge and can be considered when a hospital-based service is looking to develop its own specific program (see Table 13.4).

The American Association for Emergency Psychiatry Project BETA – Best Practices in Evaluation and Treatment of Agitation – issued a consensus statement on Use and Avoidance of Seclusion and Restraint that included formalized guidelines and a recommended treatment algorithm for the patient presenting to the ED with agitation (Knox & Holloman 2012). Included in the algorithm was the recommendation that unless the patient is physically violent, verbal de-escalation should be attempted first. The clinician should offer medication and attempt to involve the patient in decision making about medication. If the patient remains a danger to self or others, seclusion or restraint is then indicated and the algorithm should then be followed for the most appropriate placement. Additional recommendations included following CMS guidelines (as legally mandated),

Table 13.4. Common Interventions to Reduce Restraint and Seclusion

Staff education and training
Data collection and reporting
Changes to therapeutic setting
Policy/Leadership change
Patient involvement in treatment planning/review
Debrief or post-incident review
Crisis response teams or increasing staffing

which should be incorporated in the program's policies, annual training for clinical staff on verbal de-escalation techniques, as well as the prevention and management of aggressive behavior, staff familiarity with the types of restraints used in their program and potential adverse effects, and debriefs of episodes of restraint and seclusion.

In a national survey of both medical emergency departments and specialized psychiatric EDs, the majority of both (90% and 98%, respectively) make use of alternatives before using physical restraints, and of these psych EDs, 90 percent have a management protocol in place to guide these interventions and 76 percent provide staff education on alternative techniques. The alternative methods reported by the EDs in the survey include verbal interventions (used by 84% of EDs), one-to-one observers (79%), decrease in environmental stimulation (74%), and food or drink (69%) (La Vonne et al. 2007).

Rintoul, Wynaden, and McGowan (2009) stressed that an interdisciplinary approach was necessary to reducing rates of seclusion and restraint while successfully managing aggression in the ED, with a shared philosophy that staff from all disciplines are accountable for early recognition, response, and competent management of aggression. His group additionally noted other interventions that played a part in successful reduction of restraints, including emphasis on early intervention, staff education and training through annual workplace competencies, having a clearly articulated management plan, and aggression management teams.

Scanlan (2009) reviewed the literature of seclusion and restraint reduction programs in the inpatient setting, and identified seven common strategy types that included changes in policy or leadership toward a committed effort, use of debriefing or external reviews, data collection, and reporting that provide staff with feedback and benchmarking, formalized staff training to increase skill at de-escalation and crisis management techniques, patient and family involvement, increased staff ratios and/or crisis teams, and modifications to the therapeutic milieu. Coburn and Mycyk (2009) additionally recommended that every institution have a detailed protocol for the use of restraints for which all team members are trained and familiar, and suggested security measures such as twenty-four-hour uniformed security and alarm systems.

Jonikas and colleagues (2004), based on an inpatient-based restraint reduction program, suggested brief interviews with the patient within the first twenty-four hours of admission to develop an individualized crisis management plan that would include any potential triggers, restraint histories, medication preferences, and individualized de-escalation strategies. If restraint was used, a patient-staff debriefing would be held to discuss the event as well

as revise the plan if needed. Bonner and Wellman (2010) gave further guidance on the structure of the post-incident review and summed that it allowed for participants, both staff and patient, to reflect on events leading up to the restraint and their feelings afterward. It was helpful at identifying distress, determining appropriate follow-up interventions, and providing validation for expressed feelings.

Several case reports discussed the impact of utilizing an outside behavioral consultant to either improve reduction programs or on an individual patient basis. For example, the HHC of NYC initiated the "Seclusion and Restraint Reduction Initiative" (Wale, Belkin & Moon 2011) with a series of interventions aimed at reducing overall use of restraint/seclusion and sustained culture change toward a patient-centered and trauma-informed model of care. The program established interdisciplinary change teams at each facility, and held three two-day training sessions that introduced the participants to six core strategies aimed at reducing restraint/seclusion. Each facility subsequently had a consultant visit to individualize a plan based on that site's particular strengths and target areas for improvement. A key element of this initiative was the emphasis on affecting a cultural change, leadership involvement, and flexibility to make site-specific adjustments. Donat (1998) reports on a program in which a method of formal behavioral consultation is established and available to use for difficult-to-manage cases within an inpatient state hospital. A behavioral management committee consisting of an interdisciplinary team of individuals with education and expertise in behavioral emergencies reviews the referred cases and makes recommendations to the treatment plan. This was shown to reduce seclusion/restraint utilization from 18.8 hours per month before the intervention to 7.2 hours per month after the intervention.

Procedure for Use

As outlined by the APA (1985), the policy and procedure for crisis management including the use of restraint and seclusion at each hospital or facility should include written guidelines and be carried out by well-trained staff who have had the opportunity to rehearse the interventions, and should be consistent with the legal and regulatory environment of the institution. The institutional policy should be easy to access, clearly communicated to all disciplines, and routinely reviewed with in-service trainings to both seasoned and new staff.

The first step in the management of a behavioral emergency with an aggressive patient is to recognize the crisis. As stressed throughout this chapter, early recognition and intervention with less restrictive measures is preferable. A team member facing an aggressive patient should always seek help from other staff, which is typically done by either a verbal alert or panic alarm system. If a patient continues to escalate, necessitating the use of restraints/seclusion, then a team leader is necessary to manage the event. This can be any member of the interdisciplinary team, though it is often a nurse, nurse practitioner, or physician.

Once the decision is made to use restraints, a sufficient number of staff is required for application, at least one for each limb in addition to the leader, to ensure safety of the patient and team members. While restraints are being applied, the leader or another designated staff member should stand clear and observe the patient for any adverse effects or incorrect use of technique, and alert the other staff immediately of any concerns or necessary adjustments. As soon as possible, the leader should inform the patient of the rationale behind the intervention. If seclusion is used, staff should take additional precautions such as removal of street clothes, correct positioning of the patient during a coordinated staff exit, and monitoring to ensure that the patient is not escalating to self-injurious behavior that would

require restraints. Patients in restraint or seclusion require continuous observation by staff and frequent intervals of documentation. Meals, fluid intake, and toileting needs should all be attended to regularly. Staff should follow all applicable institutional policies and state and federal laws.

Conclusion

With the success of programs aimed at reducing or eliminating the use of restraint and seclusion, it is clear that their application is limited in scope, and necessity of use may vary by location and available resources. Given the risks involved, this intervention requires a well-trained interdisciplinary clinical team, sufficient oversight, and adequate support for both staff and patient following the event.

Key Points

- Restraint and/or seclusion should only be used when the patient is presenting an imminent danger to self or others, or serious destruction to the environment.
- Restraint and/or seclusion should not be used for punishment or staff convenience.
- Clinical staff should be familiar with the adverse effects associated with restraint use including asphyxiation, suffocation, and blunt chest trauma.
- Staff should be familiar with all applicable institutional policies, local, state, and federal laws and regulations.
- Several core interventions have been identified that have been successful for reducing restraint and seclusion for specific programs and can be modified to suit site-specific needs.

Suggestions for Further Reading

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Chapter

14

Pharmacologic Treatment of Agitation

Leslie Citrome

Introduction

Consider the following case: John is a forty-year-old white male who was diagnosed with schizophrenia during his first hospitalization at age twenty-one. This time, John presented to the emergency department with auditory hallucinations (he heard a female voice commenting on his actions) and the delusion that the police had been keeping him under surveillance; he is well known to the hospital and has been violent in the past. While waiting to be admitted to the psychiatric inpatient unit, John became increasingly agitated, stating that the police were harassing him and that he was feeling restless. Noncompliance with his medication regimen of risperidone was suspected. What intervention would you consider?

John is acutely agitated and has a history of violence – rapid intervention is required. If John is in withdrawal from alcohol, then a benzodiazepine should be considered; otherwise he is clearly psychotic and requires an antipsychotic. In the past, the standard approach was to administer intramuscular haloperidol 5 mg, with or without lorazepam 2 mg. In this chapter, we will review the different options that may be suitable for John, at the same time minimizing the risk for akathisia, acute dystonia, or oversedation. Once the acute episode of agitation is managed, attention will be needed to see what regimens would be helpful to reduce the frequency and intensity of future episodes.

Placing Medication Use in Context

Simultaneous with the use of medication interventions, nonpharmacological techniques are essential. These include verbal de-escalation (Richmond et al., 2012) and appropriate considerations for the use and avoidance of seclusion and restraint (Knox & Holloman, 2012). These are described elsewhere (Chapters 10 and 13). In our case example, hospital staff carefully approached John while respecting his personal space. One staff member, whom John had met before, established verbal contact and engaged John in a discussion about what was going on, and provided clear explanations regarding the admission process and how much time it would take.

Etiology of Disturbed Behavior and Diagnostic Considerations

Agitation, defined as excessive verbal or motor activity, and usually experienced as distressing to the patient, should frequently be considered a medical emergency. Our case patient is restless and irritable, he has heightened responsiveness to internal and external stimuli, and there is concern that this behavior may escalate to aggression (Hankin, Bronstone, & Koran, 2011). Optimal use of psychopharmacological interventions requires at least a rudimentary differential diagnosis. (See Chapters 3 – 9.)

Essentially, for our case example, it will be crucial to determine if John is withdrawing from alcohol or sedatives, as that would make the use of antipsychotics potentially problematic because antipsychotics can reduce the seizure threshold. If there is evidence for a somatic etiology for his disturbed behavior, then immediate medical evaluation would be required. Examples of symptoms and signs that would arouse concern include loss of memory, disorientation, severe headache, extreme muscle stiffness or weakness, difficulty breathing, abnormal vital signs, slurred speech, incoordination, and obvious trauma.

Akathisia can be a confound in persons already receiving antipsychotics or antidepressants (Advokat, 2010); for example, in our case patient, John may also be experiencing akathisia, and giving him an antipsychotic with propensity for this adverse effect will make him feel worse.

A key definition is that for hostility. Hostility can mean many different things; in addition to overt aggression, it may include temper tantrums, irritability, refusal to cooperate, jealousy, suspicion, and many other attitudes and behaviors (Buss & Durkee, 1957). When contemplating longer-term treatment, hostility is a useful concept as a hostile attitude will be an obstacle to the development of a therapeutic alliance. Hostility has been associated with more severe positive symptoms, lower adherence to pharmacological treatment, and more drug or alcohol consumption (Volavka et al., 2015). The Positive and Negative Syndrome Scale (PANSS) includes an item that measures hostility (Kay et al., 1987), and is used as an outcome variable for analyses that will be discussed later in this chapter. Hostility in the PANSS is defined as "verbal and nonverbal expressions of anger and resentment, including sarcasm, passive-aggressive behavior, verbal abuse, and assaultiveness." It is rated on a scale of 1 (absent) to 7 (extreme), with mild hostility (a rating of 3) defined as "indirect or restrained communication of anger, such as sarcasm, disrespect, hostile expressions and occasional irritability." More serious behaviors such as assaultiveness are not captured until the higher end of the scale.

Aggressive behavior in a person with a psychotic disorder can be attributed to a number of causes, some of them potentially coexisting to different degrees at different times. For persons who are persistently aggressive, individuals assault for different reasons at different times (Volavka & Citrome, 2008). When using an assault interview checklist to identify psychotic, psychopathic, and impulsive factors among psychiatric inpatients involved in aggressive incidents, multiple factors were often present in a single event (Nolan et al., 2003).

Overview of Available Medication Approaches for Acute Agitated Behavior

Medication classes: When deciding on different medication strategies to address acute agitation, the main choices include antipsychotics and benzodiazepines, administered orally, sublingually, intranasally, intramuscularly, intravenously, or inhaled. Not all agents are available in all formulations. Project BETA (Best Practices in Evaluation and Treatment of Agitation) recommends that for psychosis-driven agitation in a patient with a known psychiatric disorder (e.g., schizophrenia, schizoaffective disorder, bipolar disorder), antipsychotics are recommended over benzodiazepines, because they address the underlying psychosis, and that second-generation antipsychotics with supportive data for their use in acute agitation are preferred over haloperidol either alone or with an adjunctive medication,

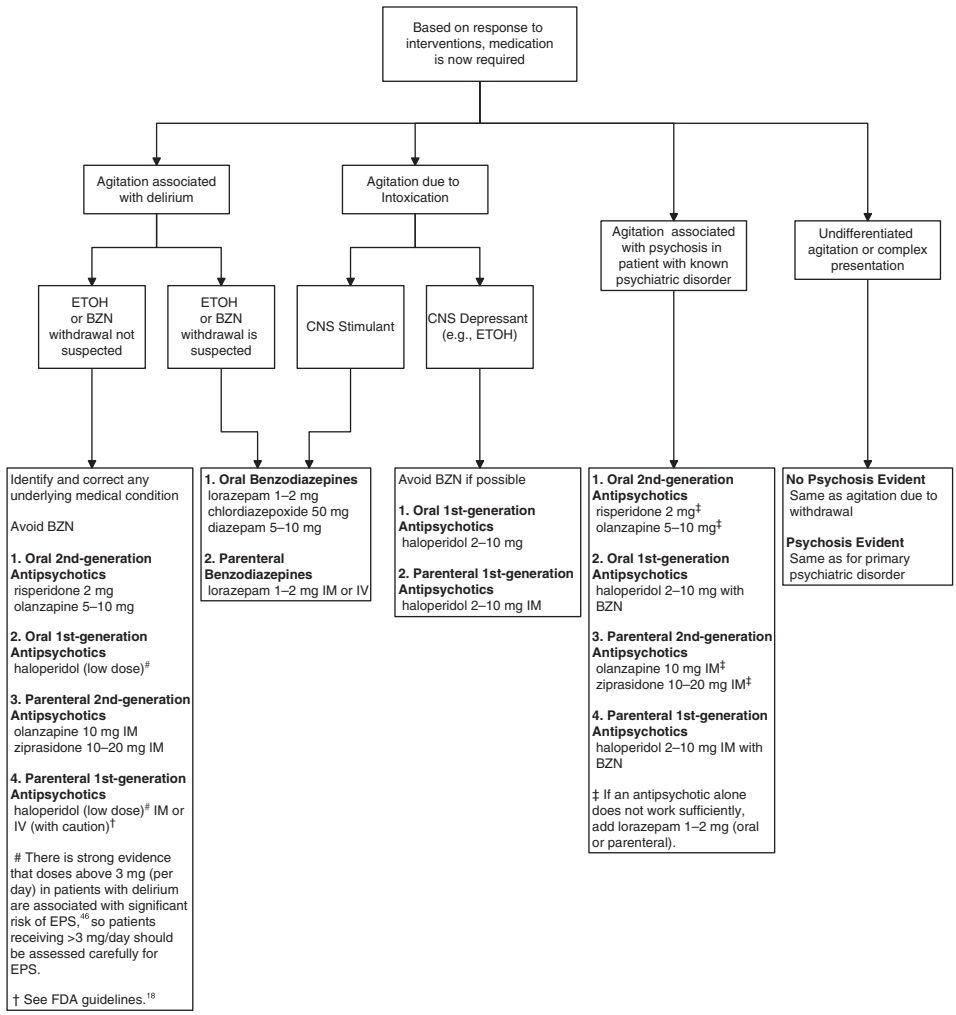

Figure 14.1. Protocol for treatment of agitation.

and that if the patient cannot cooperate with oral medications, intramuscular ziprasidone or intramuscular olanzapine is preferred for acute control of agitation (Figure 14.1) (Wilson et al., 2012).

Formulations and pharmacokinetic considerations: In general, oral administration by swallowing results in the slowest onset of action. Entry to the systemic circulation is via the lower gastrointestinal tract and the portal system; absorption can thus be erratic (Nordstrom & Allen, 2013). Oral therapy for the management of agitation, including liquid formulations (Zeller & Rhoades, 2010), is probably best reserved for mild degrees of agitation where the patient expresses a preference for a specific medication that he or she has confidence in. It is not unusual for patients to calm down readily after receiving medication by mouth, knowing that action has been taken and that their immediate needs are being attended to.

More commonly used for moderate to severe agitation are intramuscular agents. Intramuscular administration enables entry of the active agent into the systemic circulation through the muscle's vasculature, providing the potential for rapid onset of action. Direct intravenous injection can have a more rapid onset of effect; however, obtaining venous access may be a significant obstacle. An alternative route is sublingual, buccal, or intranasal where absorption takes place transmucosally; enteral absorption and first-pass metabolism are bypassed, and thus entry into the systemic circulation can be more rapid than swallowing medication. As a caveat, although several second-generation antipsychotics are available as orally disintegrating tablets (aripiprazole, risperidone, and olanzapine), in general these are not absorbed in the oral mucosa; the tablets disintegrate in the saliva, and after swallowing are absorbed via the gastrointestinal tract. One exception is sublingual asenapine, which if swallowed actually has very low bioavailability (Citrome, 2014).

Administration by inhalation in the deep lung can achieve very rapid entry into the systemic circulation. At present, the only inhaled agent available is loxapine (Citrome, 2013a).

The philosophy of evidence-based medicine: Evidence-based medicine is the careful incorporation of research evidence together with one's own clinical experience, as well as the consideration of a patient's individual values and preferences, when making a medical decision on their behalf (Sackett et al., 1996). Thus, evidence-based medicine is not just about the evidence, but "how we use it" (Citrome, 2011). Evidence-based medicine, therefore, is not "cookbook medicine." With regard to persons who are agitated, aggressive, or violent, evidence-based medical practice requires knowledge of available treatments and methods of considering pros and cons for each alternative. For our case patient, this would be relevant not only for the acute episode of agitation, where John may have had an untoward experience with one of the available choices, and thus would want to avoid that treatment, but also for the next steps, when attempting to identify a medication he would be willing to adhere to in the long run.

The tools of evidence-based medicine: The practice of evidence-based medicine requires knowing about treatment effect sizes. The simplest effect size is the actual change in the measure being observed, whether it is blood pressure or point improvement measured by a rating scale. Standardized effect sizes include the Cohen's *d*, where differences are expressed in standard deviation units. As such, a Cohen's *d* of 0.8 is considered a large effect size and 0.2 is considered a small effect size (Citrome, 2010). However, Cohen's *d* is not a clinically intuitive effect size measure and an alternative concept is number needed to treat (NNT) and its analogue, number needed to harm (NNH) (Citrome & Ketter, 2013). The NNT answers the question "How many patients would you need to treat with Intervention A instead of Intervention B before you would expect to encounter one additional positive outcome of interest?" NNH answers the question "How many patients would you need to treat with Intervention A instead of Intervention B before you would expect to encounter one additional outcome of interest that you would like to avoid?" Low NNT values are desirable so that treatment response is encountered as frequently as possible. An important NNT value is 2–3, which roughly corresponds to a Cohen's *d* of 0.8. In contrast, large values of NNH (≥10 and preferably higher) are desired in order to minimize the potential occurrence of harms. NNT and NNH are treatment effect sizes expressed in "patient units" and these metrics will be used when examining the potential usefulness of anti-agitation agents.

Older Pharmacological Approaches That Remain in Common Use

First-generation antipsychotics: Intramuscular haloperidol has been used for decades for the management of agitation; however, the tolerability burden of haloperidol is substantial, particularly regarding extrapyramidal symptoms and akathisia (Allen et al., 2005; Citrome, 2007). Should dystonic reactions, including laryngospasm, oculogyric crisis, and torticollis become evident (Jhee et al., 2003), these can lead to a general reluctance on the part of the patient to take similar medications in the future. In a Cochrane review that included thirty-two studies comparing haloperidol with eighteen other treatments, the authors concluded that (italics added) "If *no other* alternative exists, sole use of intramuscular haloperidol could be life-saving. Where additional drugs to offset the adverse effects are available, sole use of haloperidol for the extreme emergency, in situations of coercion, could be *considered unethical*" (Powney, Adams, & Jones, 2012). The combination of intramuscular haloperidol and promethazine (an antihistamine with weak neuroleptic properties), not commonly used in the United States but more popular elsewhere, has more favorable supporting data (Huf et al., 2009). The combination of intramuscular haloperidol (5 mg) and lorazepam (2 mg) demonstrates an advantage over haloperidol or lorazepam monotherapy at the one-hour mark post-administration (Battaglia et al., 1997). Although this advantage in speed of onset was also found by Bieniek and colleagues (1998), there is the potential for oversedation (Gillies et al., 2013). In terms of alternatives that have been directly tested against the combination of intramuscular haloperidol and lorazepam, similar therapeutic outcomes have been found with liquid risperidone (2 mg) and lorazepam (2 mg) (Currier & Simpson, 2001; Currier et al., 2004).

The NNT for efficacy of intramuscular haloperidol vs. placebo can be calculated from studies of agitation where haloperidol was used as an active control (Citrome, 2007). In these trials, the primary outcome measure was the PANSS Excited Component (PEC), consisting of the sum of the following five PANSS items: excitement, hostility, tension, uncooperativeness, and poor impulse control. Scores on the PEC range from 5–35, with a score ≥20 denoting severe agitation. The PEC has also been validated in naturalistic treatment settings (Montoya et al., 2011). Treatment response can be defined as a ≥40 percent decrease in the PEC from baseline, and this is commonly calculated at the two-hour mark after medication administration. Using this definition of PEC response, pooled responder rates were 62 percent for haloperidol 6.5 mg or 7.5 mg and 32 percent for placebo, yielding a NNT for haloperidol vs. placebo in agitated patients with schizophrenia of 4 (95% CI 3–5), representing a moderate treatment effect size.

Once popular, droperidol (Shale et al., 2003), a butyrophenone neuroleptic, was withdrawn from the UK market in 2001 and a boxed bolded warning was placed in product labeling in the United States regarding droperidol's lengthening of the QT interval. It is not FDA approved as an antipsychotic; its approved indication is for the reduction of nausea and vomiting associated with surgical and diagnostic procedures. In a position statement from the American Academy of Emergency Medicine, based on literature review, droperidol was judged an effective and safe medication in the treatment of nausea, headache, and agitation. The literature search did not support mandating an electrocardiogram or telemetry monitoring for doses <2.5 mg given either intramuscularly or intravenously. Intramuscular doses of up to 10 mg of droperidol appeared to be as safe and as effective as other medications used for sedation of agitated patients (Perkins et al., 2015).

Benzodiazepines: Lorazepam is a benzodiazepine available in both oral and intramuscular formulations, and has been used to control disruptive behaviors (Salzman, 1988) for almost as long as haloperidol, and is often combined with it. Lorazepam is unique among the benzodiazepines in that it is reliably absorbed intramuscularly (Greenblatt et al., 1979; Greenblatt et al., 1982). Other advantages include a relatively short half-life of ten to twenty hours and its simple route of elimination that produces no active metabolites. Supporting the use of intramuscular lorazepam for the management of agitation are randomized controlled trials comparing lorazepam with haloperidol (Salzman et al., 1991; Foster et al., 1997). Of potential concern is the emergence of respiratory depression in persons with lung disease or sleep apnea. In addition, lorazepam is not useful for control of psychotic symptoms, and the long-term control of aggressive behavior with lorazepam is problematic because of tolerance and dependence, with missed doses potentially leading to rebound anxiety, withdrawal, and grand mal seizures. However, lorazepam is particularly useful to consider in the presence of alcohol or sedative withdrawal. With our case patient, alcohol or sedative withdrawal may explain his agitated behavior, and this can be easily overlooked because of his well-recognized psychotic disorder. Intramuscular lorazepam has been used as an active control in studies of agitation associated with bipolar mania; pooled PEC responder rates at two hours were 67 percent for lorazepam 2 mg and 40 percent for placebo, yielding a NNT for lorazepam vs. placebo in agitated patients with bipolar mania of 4 (95% CI 3–7), (Citrome, 2007), representing essentially the same moderate treatment effect size observed with haloperidol.

Midazolam is a short-acting benzodiazepine and has also been used in the management of agitation, including by the intranasal route in children (Nordstrom & Allen, 2013). However, midazolam is associated with unexpected oversedation when administered intramuscularly (Parker, 2015). Although midazolam's onset of action is rapid, duration of effect is short, requiring repeat dosing.

Newer Pharmacological Approaches with Evidence from Randomized Controlled Studies

Oral second-generation antipsychotics: As noted, liquid risperidone 2 mg combined with lorazepam 2 mg performed similarly to intramuscular haloperidol and lorazepam on a measure similar to the PEC in a convenience sample of willing participants (Currier & Simpson, 2001) and in a prospective randomized clinical trial (Currier et al., 2004).

In a five-day, randomized, double-blind trial of olanzapine 20 mg/d vs. aripiprazole 15–30 mg/d, similar improvements in the PEC were observed in both groups (rate of PEC responders was 57.2 percent in the olanzapine group and 60.4 percent in the aripiprazole group), but a greater proportion of aripiprazole-treated patients received lorazepam at each visit compared with olanzapine-treated patients, significant at visit 5 (41.2% vs. 31.0%, NNT=10) (Kinon et al., 2008). In a comparison of olanzapine up to 40 mg vs. olanzapine 10 mg plus lorazepam up to 4 mg, the high-dose olanzapine group was superior on reduction of the PEC score at twenty-four hours (Baker et al., 2003).

Asenapine is a second-generation antipsychotic indicated for the treatment of schizophrenia, and for the acute treatment of manic or mixed episodes associated with bipolar I disorder (Citrome, 2014). The only available formulation of asenapine is as an orally disintegrating tablet administered sublingually and absorbed in the oral mucosa, with a time to maximum concentration of thirty to ninety minutes.

In a double-blind, placebo-controlled, randomized study of agitated adults presenting for treatment in an emergency department (any diagnosis), sublingual asenapine 10 mg was efficacious in the treatment of agitation (Pratts et al., 2014). The proportion of subjects categorized as PEC responders at two hours for the asenapine-treated group was 78 percent, compared with 33 percent for the placebo-treated group, for a NNT vs. placebo of 3 (95% CI 2–4), representing a large treatment effect size. Rescue interventions were required prior to the study endpoint (two hours) for 32 percent of the subjects in the placebo group vs. 7 percent for subjects in the asenapine group (NNT 4, 95% CI 3–9). Separation from placebo on PEC reduction was noted as early as fifteen minutes after administration. At the present time, asenapine does not have regulatory approval for the indication of agitation, but sublingual asenapine's relative ease of use merits further consideration. Asenapine has been associated with oral hypoesthesia and dysgeusia.

Intramuscular short-acting second-generation antipsychotics: Since 2002, three second-generation antipsychotic have become available in short-acting intramuscular formulations: ziprasidone, olanzapine, and aripiprazole. All three have a lower liability for extrapyramidal side effects than haloperidol (Satterthwaite et al., 2008). In terms of efficacy, ziprasidone and olanzapine have lower NNT values for response vs. placebo (NNT 3) when indirectly compared with haloperidol or lorazepam vs. placebo (NNT 4), but the 95 percent CI values overlap (Citrome, 2007). Table 14.1 provides an overview of the registration trials for ziprasidone (Daniel et al., 2001; Lesem et al., 2001), olanzapine (Meehan et al., 2001; Wright et al., 2001; Breier et al., 2002) and aripiprazole (Andrezina et al., 2006a; Tran-Johnson et al., 2007; Zimbroff et al., 2007), as well as adverse events with incidence ≥5% and ≥2x versus placebo or placebo-equivalent, as noted in product labeling. Each trial was one day in duration, and the primary end point was at two hours after medication administration. The ziprasidone clinical studies did not use a placebo control; instead a subtherapeutic dose of intramuscular ziprasidone 2 mg was used as the comparator. For the olanzapine and aripiprazole clinical trials, in addition to a placebo control, the studies for schizophrenia included an intramuscular haloperidol control and the studies for bipolar mania included an intramuscular lorazepam control. For the olanzapine and aripiprazole clinical trials, the primary outcome measure was the PEC. For the ziprasidone trials, the primary outcome measure was the single-item Behavioral Activity Rating Scale (BARS) (Swift et al., 2002). The BARS is rated from 1 (difficult or unable to rouse) to 7 (violent, requires restraint), with 4 denoting "quiet and awake." A two-point drop in the BARS denotes a clinically relevant effect (i.e., "response"), and is analogous to a ≥40 percent decrease in the PEC (Citrome, 2007). A fourth pivotal trial for intramuscular olanzapine was done in patients age fifty-five or older with agitation associated with dementia; however, olanzapine is not approved for that indication (Meehan et al., 2002). Similarly, a fourth pivotal trial for intramuscular aripiprazole was done in patients with agitation associated with dementia (Rappaport et al., 2009); aripiprazole is not approved for that indication.

Studies have been published that describe the transition from intramuscular to oral administration for ziprasidone (Brook et al., 2000; Daniel et al., 2004; Brook et al., 2005), olanzapine (Wright et al., 2003), and aripiprazole (Daniel et al., 2007), and these studies establish the clinical feasibility of continuing with the same agent orally as administered intramuscularly. Moreover, a post hoc analysis of one of the ziprasidone trials (Brook et al., 2005) also provided evidence that ziprasidone demonstrated specific antihostility effects

Table 14.1. Intramuscular ziprasidone, olanzapine, and aripiprazole for agitation: highlights from the registration trials and U.S. product labeling*

Brand name	Ziprasidone Geodon (Zeldox)	Olanzapine Zyprexa	Aripiprazole Abilify
Year intramuscular approved	2002	2004	2006
Patients enrolled	Schizophrenia, schizoaffective disorder, bipolar disorder with psychotic features, delusional disorder, or psychotic disorder not otherwise specified; approximately 80% of the subjects had schizophrenia or schizoaffective disorder	Schizophrenia, bipolar mania	Schizophrenia, bipolar mania
Approved dose	10 or 20 mg; doses of 10 mg may be administered every two hours; doses of 20 mg may be administered every four hours; maximum of 40 mg/day	10 mg; a lower dose of 5 or 7.5 mg may be considered when clinical factors warrant. Maximal dosing of intramuscular olanzapine (e.g., 3 doses of 10 mg administered 2–4 hours apart) may be associated with a substantial occurrence of significant orthostatic hypotension.	9.75 mg; recommended dosage range is 5.25 to 15 mg. No additional benefit was demonstrated for 15 mg compared to 9.75 mg. A lower dose of 5.25 mg may be considered when clinical factors warrant. If agitation warranting a second dose persists following the initial dose, cumulative doses up to a total of 30 mg/day may be given.
Response rates	Approximately 90% for 20 mg, 60% for 10 mg, and 30% for 2 mg; 70% for pooled 10–20 mg	Approximately 77% for pooled 10 mg and 33% for pooled placebo	Approximately 58% for pooled 9.75 mg and 36% for pooled placebo

Table 14.1. (cont.)

Brand name	Ziprasidone Geodon (Zeldox)	Olanzapine Zyprexa	Aripiprazole Abilify
NNT for response at 2 hours and 95% CI (Citrome, 2007)	10 mg vs. 2 mg: 4 (3–10); 20 mg vs. 2 mg: 2 (2–3); pooled 10–20 mg vs. 2 mg: 3 (2–4)	Pooled 10 mg vs. placebo: 3 (2–3)	Pooled 9.75 mg vs. placebo: 5 (4–8)
When did statistical separation from the non-active control occur on the primary outcome measure?	15–30 minutes	15 minutes (Wright et al., 2001), and superior onset of efficacy for olanzapine vs. haloperidol 7.5 mg (Wright et al., 2001) and lorazepam 2 mg (Meehan et al., 2001). Of note, olanzapine was superior to lorazepam at all time points up to and including 2 hours post-injection (Meehan et al., 2001)	1 hour for aripiprazole, in contrast to 45 minutes for haloperidol 6.5 mg (Andrezina et al., 2006); 45 minutes for aripiprazole 9.75 mg, in contrast to 105 minutes for haloperidol 7.5 mg (Tran-Johnson et al., 2007); 60 minutes for aripiprazole, in contrast to 45 minutes for lorazepam 2 mg (Zimbroff et al., 2007)
Safety concerns of note	Caution in patients with impaired renal function because the cyclodextrin excipient is cleared by renal filtration; potential prolongation of the ECG QT interval (however, the observed QTc prolongation with intramuscular ziprasidone appears similar to that for intramuscular haloperidol (Miceli et al., 2010))	Simultaneous injection of olanzapine intramuscular and parenteral benzodiazepines is not recommended; in a report of safety data from the first 21 months of the availability of short-acting intramuscular olanzapine, among over 500,000 patient exposures, 29 fatalities are documented, with concomitant benzodiazepines or other antipsychotics reported in 66% and 76% of these cases, respectively (Marder et al., 2010)	If parenteral benzodiazepine therapy is deemed necessary in addition to aripiprazole injection treatment, patients should be monitored for excessive sedation and for orthostatic hypotension

Table 14.1. (cont.)

Brand name	Ziprasidone Geodon (Zeldox)	Olanzapine Zyprexa	Aripiprazole Abilify
Adverse events with incidence ≥5% and ≥2x versus non-active control	Somnolence (8, 8, 20%, for 2 mg, 10 mg and 20 mg, respectively), nausea (4, 8, 12%), dizziness (3, 3, 10%), headache (3, 13, 5%), and postural hypotension (0, 0, 5%); somnolence, nausea, and dizziness were more common with 20 mg than with 10 mg or placebo	Somnolence (3 and 6%, for placebo and 10 mg, respectively); of note, no adverse event was significantly more frequent for intramuscular olanzapine compared with intramuscular haloperidol or intramuscular lorazepam	Nausea (3 and 9%, for placebo and 9.75 mg, respectively)
Lowest (more problematic) NNH	Somnolence, 20 mg vs. 2 mg: 9	Somnolence, 10 mg vs. placebo: 34	Nausea, 9.75 mg vs. placebo: 17

NNH – number needed to harm
NNT – number needed to treat
* U.S. product labels obtained from https://www.accessdata.fda.gov/scripts/cder/drugsatfda/index.cfm

over time throughout the forty-two-day study period, with statistically significant superiority to haloperidol on this measure in the first week of treatment (Citrome et al., 2006).

The effectiveness of intramuscular second-generation antipsychotics has been demonstrated in naturalistic studies that enrolled more severely agitated patients than ordinarily encountered in randomized controlled trials (Preval et al., 2005; San et al., 2006; Castle et al., 2009), as well as in children (Khan & Mican, 2006) and in the elderly (Kohen et al., 2005; Suzuki et al., 2013).

Inhaled formulations: Inhaled loxapine received approval in 2013 for the acute treatment of agitation associated with schizophrenia or bipolar mania (Citrome, 2013a). Three double-blind, placebo-controlled, randomized trials are available, two in persons with schizophrenia (Allen et al., 2011; Lesem et al., 2011), and one in persons with bipolar mania (Kwentus et al., 2012). As with the studies of intramuscular olanzapine and intramuscular aripiprazole, the PEC was the primary outcome measure. However, there was no active control and so the only comparison is vs. placebo. See Table 14.2. The treatment effect size is comparable to what was observed for the intramuscular treatment options and for sublingual asenapine. Time to maximum concentration is two minutes (Spyker et al., 2015), and in the clinical trials inhaled loxapine separated from placebo on the PEC at ten minutes, the first time point where this was measured post administration. Because of the risk of bronchospasm, precautions are necessary and in the United States, enrollment is a Risk Evaluation and Mitigation Strategy (REMS) program is mandatory. In the clinical trials, bronchospasm (definition includes wheezing, shortness of breath, and cough) was reported in 2 of the 259 patients (0.8%) receiving 10 mg vs. 0 for placebo (NNH 125). Among all patients treated with inhaled loxapine (5 or 10 mg), 1 of 524 (0.19%) had significant bronchospasm requiring rescue treatment with a usual dose of albuterol bronchodilator and oxygen.

Medication Selection: Back to the Case

Which anti-agitation agent should John receive? Assuming that withdrawal from alcohol or sedatives has been ruled out and that there is no cause for concern about his physical health (vital signs normal, sensorium clear and no evidence of trauma), giving an antipsychotic would be preferred over a benzodiazepine. He has a history of akathisia and extrapyramidal symptoms and thus haloperidol should be avoided; in the registration trials of olanzapine and aripiprazole where haloperidol served as an active control, NNH values for haloperidol vs. placebo were as low (i.e., more problematic) as 6 for parkinsonism or for requiring anticholinergic medication (Citrome, 2007). This is contrast to the relatively high and thus clinically irrelevant NNH values for these adverse effects as observed for olanzapine or aripiprazole vs. placebo in persons with schizophrenia (Citrome, 2007).

The NNH value of concern for ziprasidone, somnolence with a NNH of 9 for 20 mg vs. 2 mg, can be mitigated by using a lower dose if somnolence is an obstacle to use (rates of somnolence were the same for 10 mg vs. 2 mg). For olanzapine and aripiprazole, the most commonly encountered adverse events were somnolence and nausea, respectively, but with relatively reassuring NNH values of 34 and 17, respectively.

If speed of response and the avoidance of an injection are desired, inhaled loxapine is a viable choice. Although loxapine is a first-generation antipsychotic, the clinical trials of inhaled loxapine for agitation did not result in clinically relevant rates of extrapyramidal adverse effects. Sublingual asenapine can also be considered, and has a NNT

Table 14.2. Inhaled loxapine for agitation: highlights from the registration trials and U.S. product labeling*

	Inhaled loxapine
Brand name	Adasuve
Year inhaled formulation approved	2013
Patients enrolled	Schizophrenia, bipolar mania
Approved dose	10 mg; administer only a single dose within any 24-hour period (in the EU a second dose is permitted after 2 hours and a 5 mg dose is also available)
Response rates	Approximately 71% for pooled 10 mg and 33% for pooled placebo
NNT for response at 2 hours and 95% CI (Citrome, 2012)	Pooled 10 mg vs. placebo: 3 (3–4)
When did statistical separation from the non-active control occur on the primary outcome measure?	10 minutes
Safety concerns of note	Contraindicated in patients with a current diagnosis or history of asthma, COPD, or other lung disease associated with bronchospasm, acute respiratory symptoms or signs (e.g., wheezing), current use of medications to treat airways disease, such as asthma or COPD, history of bronchospasm following treatment with inhaled loxapine. Prior to administration, screen for a history of asthma, COPD, or other pulmonary disease, and examine patients (including chest auscultation) for respiratory signs (e.g., wheezing). Monitor patients for symptoms and signs of bronchospasm (i.e., vital signs and chest auscultation) at least every 15 minutes for a minimum of 1 hour following treatment. At the present time in the US, this product is available for use only in a certified health care facility that has immediate access on site to supplies and personnel trained to manage acute bronchospasm, and ready access to emergency response services. Facilities must have a short-acting bronchodilator (e.g., albuterol), including a nebulizer and inhalation solution, for the immediate treatment of bronchospasm.

Table 14.2. (cont.)

	Inhaled loxapine
Adverse events with incidence ≥5% and ≥2x versus non-active control	Dysgeusia (5 and 14%, for placebo and 10 mg, respectively); of note, although loxapine is a first-generation antipsychotic, rates of extrapyramidal adverse events were low (0.4% in patients receiving inhaled loxapine vs. 0 for placebo).
Lowest (more problematic) NNH	Dysgeusia, 10 mg vs. placebo: 12

NNH – number needed to harm
NNT – number needed to treat
* US product label obtained October 22, 2016 from http://www.adasuve.com/PDF/AdasuvePI.pdf

value for response vs. placebo similar to the other choices presented earlier; as a caveat, asenapine is not approved for the indication of agitation and the supporting data are limited to only one study. Both inhaled loxapine and sublingual asenapine can result in rapid stabilization of the acute crisis and potentially avoid coercion, thus fostering a therapeutic alliance.

Of note, John may specifically ask for an injection of a medicine if he has experienced that medicine to be helpful in the past; this is particularly true of the intramuscular second-generation antipsychotics, which are generally more readily tolerated in terms of extrapyramidal effects than haloperidol.

Avoidance of oversedation is a goal shared by clinician and patient alike and this risk may be minimized by using only one agent at a time.

After the Acute Episode

Once the acute episode of agitation is successfully managed, attention is then paid to medication interventions that can reduce the intensity and frequency of future episodes of agitation and/or aggression. Merely receiving foundational medications will reduce violence risk in populations, as evidenced in a Swedish study where compared with periods when participants were not on medication, violent crime fell by 45 percent in patients receiving antipsychotics (HR 0.55, 95% CI 0.47–0.64) (Fazel et al., 2014). This points to the potential usefulness of long-acting injectable antipsychotics where adherence can be guaranteed, provided that the patient returns for his/her injections (Citrome, 2013b). In a fifteen-month study comparing once-monthly paliperidone palmitate with daily oral antipsychotics in patients with schizophrenia with a history of incarceration, paliperidone palmitate was superior in prolonging time to time to first treatment failure, defined as arrest/incarceration; psychiatric hospitalization; suicide; treatment discontinuation or supplementation due to inadequate efficacy, safety, or tolerability; or increased psychiatric services to prevent hospitalization (Alphs et al., 2015).

Although not available as a long-acting injectable, clozapine is the antipsychotic with the most robust evidence regarding an anti-aggressive effect. A randomized controlled trial of clozapine in treatment-resistant schizophrenia demonstrated a specific anti-hostility effect (Citrome et al., 2001) and reduction in overt aggression (Volavka et al., 2004).

In a randomized controlled study in non-treatment-resistant patients with a history of physical assaults, clozapine was superior to both olanzapine and haloperidol in reducing the number and severity of subsequent aggressive behavior (Krakowski et al., 2006). In that study, olanzapine was also superior to haloperidol in reducing the number and severity of aggressive incidents. Because there were no significant differences among clozapine, olanzapine, or haloperidol in improvement of psychiatric symptoms as measured by the PANSS total score, the antiaggressive effect appears to be separate from the antipsychotic action of these medications. Both clozapine and olanzapine require ongoing monitoring for weight and metabolic abnormalities. The use of clozapine also requires monitoring for potential untoward effects on the production of neutrophils and on heart muscle function.

Post hoc analyses examining the hostility item of the PANSS have shown that olanzapine is superior to other first-line antipsychotics for specific anti-hostility effect in patients with chronic schizophrenia (Volavka et al., 2014) and those early on in their disease course (Volavka et al., 2011). A specific anti-hostility effect has also been assessed in post hoc analyses of other second-generation antipsychotics, including risperidone, quetiapine, ziprasidone, and aripiprazole (Citrome & Volavka, 2011), with newer analyses recently published for cariprazine (Citrome et al., 2016) and aripiprazole lauroxil (Citrome et al., 2015).

Long-term approaches for the management of persistent aggressive behavior in persons with schizophrenia have also included the use of adjunctive medication such as beta adrenergic blockers (Alpert et al., 1990; Ratey et al., 1992; Caspi et al., 2001) and mood stabilizers (Citrome, 2007), although for the latter, even though utilization is extensive, supporting data is mixed (Citrome, 2009).

Summary

Although several choices are available for the treatment of acute agitation, they can differ markedly in terms of their tolerability profile. Older medications such as haloperidol can lead to troublesome motoric adverse effects. Moreover the use of oral haloperidol for continued treatment is unlikely given the availability of better tolerated second-generation antipsychotics. Intramuscular ziprasidone, olanzapine, and aripiprazole and inhaled loxapine have received regulatory approval for the treatment of agitation associated with schizophrenia and/or bipolar mania, and have favorable tolerability profiles. Although no agents are specifically approved for the indication of persistent aggressive behavior, the best evidence exists for the use of clozapine, followed by olanzapine.

Key Points

- Medication approaches to agitation are implemented in tandem with nonpharmacological techniques, including verbal de-escalation.
- Differential diagnosis is necessary to exclude substance use or a non-psychiatric medical condition as the reason for the altered mental status.
- Differential diagnosis should also consider akathisia, as that will impact medication choice.
- Number needed to treat (NNT) and number needed to harm (NNH) can be used to illustrate benefits and harms for each proposed anti-agitation agent.
- Although haloperidol, with or without lorazepam, has been the most common treatment for addressing agitation, it has been rendered obsolete by the availability of equally

efficacious yet better tolerated second-generation antipsychotic intramuscular alternatives such as ziprasidone and olanzapine.
- Non-injectable alternatives include inhaled loxapine (approved for this purpose) and sublingual asenapine (an "off-label" use).
- The best option to manage persistent aggressive behavior is clozapine, followed by olanzapine. However, long-acting injectable antipsychotics may be ideal in persons whose illness (and aggressive behavior) is worsened due to partial or non-adherence to antipsychotic medication.

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Chapter

15

Understanding the Environmental, Social, Familial, and Cultural Context of Agitation

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Introduction

More than any other acute behavioral presentation, agitation is a profound human experience finding its roots at the intersection of biology, psychology, and social context. One could model agitation as an aberrant reaction presented by a patient whose adaptive capacities are overwhelmed. For the patient, this translates into a feeling of loss of control when dealing with both internal and external stimuli. In that respect, environmental factors almost always play a part, either as a trigger or as a modulator of the person's state of agitation. These environmental factors can be situational or cultural, or they can relate to the person's family or support system.

Managing agitated patients requires a complex skill set that involves quick clinical assessment, formulation of a diagnostic hypothesis, and fast application of guidelines. At the heart of this approach lies verbal de-escalation and the capacity to bond with a patient in crisis (Richmond et al., 2012) Success in using these techniques is achieved through experience, but also by acquiring the necessary flexibility to face each unique situation. To achieve this objective, the clinician must include factors that are purely external to the patient in his or her decisions. This can go from drastically changing protocols and guidelines to simply acknowledging to the patient that these factors exist. By offering an adaptive response to a patient whose own capacities are impaired, the clinician lays the groundwork for a durable therapeutic alliance, not only for him- or herself, but also for mental health care providers to follow.

Environmental Triggers of Agitation

Environmental factors can precipitate a state of agitation, independent of psychiatric symptoms. These environmental factors can be major life events or traumatic experiences, but can also relate to living conditions, bureaucratic issues, or financial problems. Often, others interpret an individual's idiosyncratic reactions to environmental factors as hostile and potentially threatening. This can result in the police or other first-responders being called. This type of response often translates into an escalation of stress and does not reduce the individual's agitation. In fact, it often makes it worse. The presence of the police or other uniformed responders can increase the feeling of injustice that the agitated individual experiences. For this reason, it is preferable – if possible – to limit the presence of police officers in the emergency department to a minimum. Ideally, the patient should be transferred to the care of trained behavioral aides as soon as he or she arrives in the emergency room. Clinicians should then proceed with their evaluation and try to construct a plan that takes into consideration the different factors affecting the patient's situation and mental

state. Research has shown that intervention of the police is likely to influence the decision to hospitalize an individual (Watson et al., 1993) The emergency clinician should be aware of this bias when making decisions.

Clinical Vignette #1

Jackson is a thirty-six-year-old Kenyan-American man from New York. He is unemployed and lives in a shelter in Brooklyn. He is brought to the psychiatric emergency services of a local hospital by EMS after he had an argument with his roommate at the shelter. He has no psychiatric history apart from one visit at the same PES five years ago in similar circumstances.

Jackson is found in the main PES area and shows signs of internal tension such as pacing, clenching his fists, and breathing heavily. When approached, he instantly yells that he has no business being in a mental hospital and that he should not have been brought there in the first place. Despite how intensely aggravated he is, he responds very quickly to verbal de-escalation and agrees to sit down and explain what brought him to the hospital: his roommate had played music all night at the shelter, which kept him from sleeping. But when he got up early in the morning, the roommate yelled at him for making too much noise. An argument ensued, which led shelter staff to call 911.

On psychiatric examination, Jackson appears well groomed and his speech is organized. He denies any psychotic productions such as delusional thought content or hallucinations. He is reluctant to share basic information about his psychosocial history, especially at the beginning of the interview. His personality is marked by a high level of suspicion toward his environment, as well as a very high opinion of himself.

Collaterals at the shelter are contacted and deny any violent behavior in Jackson's history as a resident. In fact, the shelter's manager agrees that the situation could have been de-escalated without calling the police.

By the end of the evaluation, Jackson is calm and even engages with the clinician. He agrees that his current social situation is stressful, and he promises to come back for outpatient treatment. He is discharged shortly thereafter.

This clinical vignette illustrates how a common daily-life situation can trigger an episode of agitation that can escalate and lead to an exaggerated response. In this case, the shelter managers were facing an argument between two residents of the shelter and quickly decided to call 911 without attempting to diffuse the situation with verbal de-escalation techniques. Being transported by the police to the PES proved a distressful experience for the patient and only aggravated him. While the patient met criteria for cluster A personality disorder on initial evaluation, he was nevertheless amenable to therapeutic alliance. This was possible because the clinician showed interest both in his current psychiatric state and in the circumstances that brought him to the hospital. An approach solely focused on the patient's mental state would probably have resulted in an intensification of agitation, followed by use of sedative medications and unnecessary hospitalization.

Clinical Vignette #2

Juan is a forty-four-year-old Hispanic-American man with no psychiatric history. He is married with two teenage children. One Friday morning, he wakes up around 4:00 a.m. noticing that his wife is not in bed. He gets up and finds her dead in the living room, hanging from the ceiling fan. The rest of the household is quickly woken up by Juan's screams, and his oldest son calls 911. When the police arrive, Juan is in a state of shock in the living room. He refuses to speak to the police other than telling them several times that he wants to be dead like his wife. Out of concern for Juan's risk of suicide, he is brought to a local PES for evaluation. As part of the PES's full

evaluation protocol, Juan's property is stored so he does not have access to his cellular phone. While waiting for a clinician to evaluate him, Juan asks staff for his cell phone in order to call his best friend who lives out of state. He is told that this is impossible, and the situation escalates as Juan becomes increasingly agitated.

When approached by the clinician, Juan insists that he wants to talk to his best friend before anybody else. The clinician agrees to retrieve Juan's cell phone and to let him call his friend from a separate office. This immediately and completely resolves Juan's state of agitation. After making several phone calls, Juan agrees to speak to the clinician. He acknowledges experiencing suicidal ideation immediately after finding his deceased wife, but denies those thoughts are still present. In fact, he implores the clinician to discharge him and allow him to be with his children and the rest of his family for whom he feels responsible in these dire circumstances.

Juan's family is contacted, and his parents come to the PES. His support system appears solid, and Juan's parents offer to remain with him at least for the next few days. Juan is discharged with an outpatient appointment.

Exposure to traumatic events can trigger unexpected reactions from people experiencing them. Approaching victims of trauma either on site (where the catastrophe happened) or in their regular environment is an approach that is used more and more (Crocq, 2002) This has the advantage of avoiding unnecessary medicalization of patients suffering from quite terrible life circumstances. Often, however, this is not possible: mobile crisis teams are rarely available, and medical management of the patient is often indeed necessary.

In Juan's case, suicidal ideation precipitated escalation of response. Feelings of guilt and suicidal ideation are extremely common when individuals learn about the death of a loved one, especially by suicide. An onsite response would have allowed resources such as friends and family to be mobilized and used as protective factors against suicide. The patient's desire to contact his best friend for support and his claim that his place was by his children's side under such terrible circumstances were, in fact, factors of good prognosis. Breaking the PES's rules – allowing the patient to use his cell phone, taking him to a separate office, and so forth – was an appropriate strategy for the clinician. This increased the therapeutic alliance, thus further reducing his risk of suicide. Protocols should be adapted when necessary as they cannot envision every possible situation. The clinician should inform his or her team of which rules are being modified and why and insist on the therapeutic interest of those modifications. The patient should also be informed that his specific situation is being taken into consideration and an adaptive response to that situation is being offered.

When evaluating an agitated patient, one should always use clinical judgment and rapidly establish a clinical hypothesis. But the environmental context must also be taken into consideration. Events and circumstances relating to living conditions such as shelter, red tape problems such as benefits eligibility, money problems, major life events, and traumatic events can generate or precipitate intense reactions. This is especially true for patients struggling with diagnoses that are more difficult to establish, such as personality disorders. Even individuals with an otherwise relatively satisfactory level of functioning can find themselves losing control when life circumstances run amok.

When attempting to diffuse the crisis by using de-escalation techniques, the clinician should acknowledge that environmental factors play a part in the patient's state. Subjectively, the patient feels, "There is something wrong with the world," which contrasts with their impression that everyone is telling them, "There is something wrong with you!"

The clinician has the opportunity to try to put an end to the patient's feeling of injustice by conveying a message like "Yes, there is probably something wrong with your environment, and that is making you losing control. Let's help you regain control of yourself and the situation." But while life factors should be integrated into the psychiatric evaluation, the clinician should not turn into a referee that differentiates understandable and non-understandable causes of agitation. Empathy should not turn into compassion for patients who have a "legitimate" reason to get agitated. The clinical evaluation must remain as such and include the appropriate risk assessment. By constructing a plan that includes both stress factors and risk factors, the clinician can build a therapeutic response whose ultimate goal is to help the patient use an appropriate coping strategy. The appropriateness of this response must be reevaluated constantly, and the intervention must be tailored to each patient. This implies, for the clinician, being prepared to alter protocol when necessary. This can include diffusing the crisis by allowing the patient to make a phone call, offering the family to be present during the initial evaluation, or simply telling the patient early on that his or her discharge is the most likely outcome. One must be aware that psychiatric emergency services offer a setting that is not adapted to every patient. This is especially true for victims of trauma, who do not consider themselves psychiatric patients. This is something clinicians must not be afraid to communicate candidly to patients. This usually opens a path toward therapeutic alliance, reduction of risk factors, and ultimately better prognosis.

Recommendations to Evaluate the Environmental Context

- Listen to the patient's story and identify environmental sources of stress and triggers of agitation.
- Acknowledge to patient that environmental circumstances do play a part in the patient's current state.
- Do not stratify states of agitation by understandable causes versus non-understandable causes.
- Use a stress factors/risk factors model to proceed with therapeutic decisions.
- Inform the patient of the model being used and its objectives:
  - Allow the patient to regain control of him/herself and the situation.
  - Evaluate risk presentation and prevent suicide, self-harm, and violence.
  - Restore the patient's level of functioning.
  - Identify stress factors and stimulate formulation of coping strategies.
- Be prepared to alter protocols and guidelines to adapt to a particular situation, especially when managing victims of trauma.

The Immediate Context of the Agitated Patient

The immediate context of the emergency room, whether it be the medical or the psychiatric ED, can have an influence on a patient's mental state. A waiting room or emergency department's dynamic can collide with a patient's mental state, in particular when experiencing internal stimuli or delusions. One should be particularly mindful of the existence of persecutory delusions as they can represent a risk of sudden aggression if the individual feels threatened (van Dongen et al., 2012) By knowing about delusional themes early on,

clinicians and other staff can adapt their management in such a way that results in primary prevention of agitation and aggression.

Patients and health care providers constitute a social group with its own interactions. This unique group dynamic can trigger, worsen, or improve a patient's agitated state through aggravating interactions with other patients, staff, and, last but not least, family members. It can also prevent agitation and aggression through careful planning and early intervention. It is crucial for the clinician to be mindful of these different factors in order to adapt his or her approach. Staff input can be particularly useful in comprehending the dynamic of the waiting room or emergency department. Staff should also be trained to understand when interacting with a particular patient becomes too burdensome. It is not rare for agitated patients to use racial or xenophobic slurs. Despite appropriate training, it can become difficult – even for highly trained health care professionals – to tolerate such outbursts. One should know when to take a break from the situation or even when to pass the torch to another provider.

Clinical Vignette #3

Marylyn is a fifty-three-year-old African American woman with a history of schizophrenia and polysubstance use disorder. She is brought to the emergency department by the police after she verbally assaulted a shopkeeper in her neighborhood. At triage in the ED, she is cooperative, but appears internally preoccupied and shows signs of internal tension. She is placed on a recliner in the hallway of the emergency department's "psych section" and seems to relax. Not far from her, another patient is sitting on a stretcher. She has been in the ED for a few hours already, and her family was allowed to visit her and bring her food. She is wearing a headscarf. Soon, Marylyn asks the other patient and her family if they would share their food with her. They refuse, which aggravates Marylyn, who starts mumbling religiously offensive slurs and complaining about a "rotten food smell." Marylyn starts pacing in front of the other patient and yells louder and louder until staff call a "code orange." Despite attempts to verbally de-escalate the situation, Marylyn remains extremely agitated and ends up assaulting both a staff member and the other patient. She is brought to the isolation room and receives haloperidol 5 mg plus lorazepam 2 mg. When eventually interviewed, Marylyn reveals intense persecutory delusions, mostly revolving around Muslims. In fact, she was cursing and becoming increasingly belligerent toward a Muslim shop owner when the police were called. Her urinary toxicology is positive for phencyclidine, and she admits to not being adherent to her medication.

Usually, police or EMS are laconic when handing off an individual to PES. This means critical information is sometimes missed. In this clinical case, the police omitted to mention the patient had been belligerent toward a Muslim shop owner, using religious slurs. Staff did not ask for details that could have hinted at the patient's current delusional theme. Last, triage staff did not ask the patient why she got so upset in that particular shop. It is impossible to know how much of her thought content she would have shared at that particular moment, but the patient later explained with great detail how she felt threatened by Muslim people. Asking these questions in the context of agitation can help adapt treatment for a particular patient. It can also allow the clinician and other staff to reassure the patient and help establish a therapeutic alliance.

If the team managing the patient had known the content of her delusion earlier, they could have adjusted their management by relocating her to another cubicle, expediting her evaluation by the clinician, and offering her medication earlier.

Recommendations Regarding the Immediate Surroundings

- Establish protocols for efficient information gathering, including from first responders, at triage.
- Include information about delusional themes. Pay special attention to patients with persecutory delusions.
- Adapt immediate management to each situation: fast track patients who deteriorate rapidly when put in contact with other patients, rearrange bed disposition if necessary; don't hesitate to isolate patients who are the most vulnerable to external stimuli.
- Encourage staff to be mindful of the waiting room or emergency department's dynamic and to alert clinicians early about escalating situations.

The Familial Context of the Agitated Patient

Clinical Vignette #4

Tiffany is a twenty-nine-year-old Caucasian-American transgender woman with a history of bipolar disorder. She is brought to the psychiatric emergency services after her sister called EMS. According to the sister who lives out of state, Tiffany is not adherent to her medication and has made several threatening phone calls to various members of the family. At triage, Tiffany appears disheveled, her speech is pressured and disorganized, and her thought content is notable for ideas of grandeur and persecution. Her mood is irritable. She is immediately offered medication (Lorazepam 2 mg PO), which she accepts. Tiffany's agitation seems to settle down, and she is shown to one of the PES's cubicles. Shortly thereafter, Tiffany's mother arrives at the PES. She was alerted by her other daughter that Tiffany was at the PES and came immediately. Tiffany is asked if she wants to receive her mother's visit and gives her consent. Staff leave the two women alone in the cubicle. But, soon after, they hear Tiffany screaming. When the team reaches her bedside, Tiffany is again agitated and logorrheic. While it is hard to make sense of most of what she is saying, she points several times at her mother and accuses her of plotting against her in order to get her admitted. The clinician decides to put an end to the family encounter and has Tiffany's mother walked out of the PES. Tiffany's agitation improves almost immediately, and she accepts more medication (Olanzapine 15 mg). Later, Tiffany explains that she never wanted her mother present and requests that her clinician contact her best friend for collateral, with whom she is in daily contact through Facebook.

This vignette demonstrates the various challenges represented by the presence of family members and other loved ones in the context of psychiatric emergencies. While the presence of this patient's mother seemed like a positive factor at first, it turned out to be a trigger and an aggravating factor of the patient's agitation. There is no universal recipe to handle family and other loved ones in a PES; every situation must be assessed individually (Ampelas et al., 2005). Yet, one clear principle stands out. This consists of approaching the patient first, informing him or her of the family member's presence, and asking if he or she would like to meet with that person. This should be presented in the form of a "Do you think this would help?" question, followed by "How?" and "Why?" in order to better learn of potential family conflicts. In this patient's case, staff did collect her consent before bringing her mother to her bedside, but this was done before the psychiatric evaluation. The examination later revealed that, despite receiving some emotional and material support from her mother, Tiffany felt that her gender identity was not accepted by her mother. Patients going through

acute mania and/or psychosis suffer from altered judgment and cognitive symptoms, including short-term memory impairment. This explains why the patient denied ever giving her consent to meet with her mother despite staff documenting that she did.

This patient's story also highlights recent evolutions of the way people connect and build support systems in Western societies. While it is always ideal to work with family members who are present, one should not dismiss a patient's request to contact someone who is far away or reachable only through social media. Instead, the clinician should acknowledge the reality of the patient's experience (e.g., "I get most of my support from my friends online") but anchor the situation in reality. If a Facebook friend is designated as collateral, can this person talk on the phone? Can she come to the emergency department for a meeting? By showing flexibility and willingness to help while standing by principles of reality and practicality, the clinician creates an alliance with the patient.

Recommendations Regarding the Presence of the Family

- If a family member is present at the PES, always ask the patient if he or she wishes to have that person by his or her side.
- Attempt to identify family conflict by asking questions such as "Do you think this would help and how?"
- Keep in mind that a patient can revoke his or her consent to family presence at any time.
- Enact rules limiting family presence to one or two people at the patient's bedside.
- Be prepared to end the family encounter as loved ones' presence can precipitate a rebound in patient agitation.
- Generally speaking, verbal de-escalation and medication administration should not happen in the presence of the family. Repeatedly reassure the patient that the family is in another room and that the patient will see them again once he or she has regained control.
- Beware of situations of generalized family conflict in which one member is designated as the source of all problems.

Special Situation: When the Entire Family Is the Patient and Comes to the PES as a Group

It is not uncommon to have an entire family collectively asking for the group. In that case, the patient might not be clearly identified or might not be identified at all. These situations can cause confusion among staff who are tempted to dismiss the request as a family argument that has no place in the hospital. Still, a request for intervention must be taken seriously since several individuals can present agitated at the same time. The best approach is likely to register every family member as a patient but respect the wish of a family member who refuses to be registered and prefers to leave. Verbal de-escalation can address the group as a whole; ideally, however, the clinician should try to meet with the group in a quiet environment once the agitation is diffused. If one person presents with a treatable psychiatric diagnosis, this should appear more clearly, and proper care can be offered. If the family is dysfunctional as a group, this type of crisis intervention can allow communication within the family to be reestablished. Family therapy can be offered as aftercare.

Cultural Issues and the Agitated Patient

Cultural background can play an important part in a patient's state of agitation. Just like any other stress factors, dealing with an unfamiliar environmental context can overwhelm an

individual's adaptive capacities and precipitate or aggravate symptoms of agitation. Language barriers, recent immigration, visiting from another country, or acculturation are all situations that present with unique aspects. Generally speaking, principles of ethnopsychiatry, anthropology, and cultural competence do apply to the agitated patient (Kleinman and Benson, 2006) But they must be streamlined in order to craft a rapid and efficient approach to an acute situation.

Clinical Vignette #5

Mamadou is a twenty-two-year-old Frenchman with a history of type 1 bipolar disorder who is brought to the psychiatric emergency services of a large American city by EMS after he was found yelling at the reception desk of an office building. At triage, Mamadou is disheveled: his shirt is untucked from his suit pants, and his jacket is torn in several places. He is logorrheic and inappropriately familiar with staff, smiling and trying to touch their faces. His affect is elevated, and he is pacing in the triage room. He does not speak English and addresses everyone in French. According to the police and EMS report, the patient was trying to meet with an executive of a music label in order to have him listen to rap recordings he made. Numerous CDs are found in his belongings, as well as a French passport and a used boarding pass for a flight arriving from Paris the previous day. Despite this inventory, Mamadou's nationality is mistakenly recorded as Ivorian as the patient's skin tone is black and the clerk thinks he recognizes the patient's family name as a very common name in Côte d'Ivoire. Mamadou's language is correctly identified as French, however, and a French-speaking nurse from another unit is fetched to help as an interpreter. The nurse attempts to bond with the patient by introducing herself as coming from West Africa "just like" the patient. The patient seems to extend his hand to shake the nurse's hand, but instead assaults her by violently slapping her on the face.

Cosmopolitan cities like the one in this example commonly see visitors from all over the world coming through the door of their psychiatric emergency services. Managing such patients requires not only a clinical, but also a cultural and practical approach. Seasoned emergency psychiatrists and supporting staff in big cities have built the necessary adaptive skills to approach patients from all over the world.

In this patient's case, an inclusive and well-intentioned team tried to bond with the patient by trying to connect with him culturally. Yet this approach not only failed, but increased the patient's agitation, ultimately leading to violence. After receiving appropriate medication for agitation, the patient told his clinician that he sometimes encounters difficulties blending into French society because, while French, he is a citizen of sub-Saharan origin. Consequently, when the team suggested he was "African," he felt as though they were denying that he belonged to French culture – a culture he strongly identifies with. Later on, the patient apologized to the nurse he assaulted and reunited with some members of the team who triaged him. Through debriefing and discussion, they could share and understand the cultural misunderstanding that precipitated this highly undesirable outcome. As a behavioral health aide very insightfully summarized: "As an African-American man, how would I feel if, when I was traveling to Europe, people kept asking me which African country I came from?"

This clinical vignette illustrates how subtle and yet critically important the cultural component of agitation can be. When facing an agitated patient speaking a foreign language, clinicians and triage team should try to identify as quickly as possible which language the patient speaks and which language he or she prefers to use. The team should not draw conclusions regarding which culture the patient identifies with.

Table 15.1. Aid to approaching a patient traveling from another city/state/country

Context	Questions to ask or steps to follow
First psychiatric **episode during** a **planned** leisure/business **trip**	– Follow first episode guidelines. – Identify decompensation/stress factors. – Contact family locally or in the patient's country of origin. – Insist on the importance of clinical stabilization as a prerequisite to repatriation despite its being the goal.
Acute episode of a known, usually controlled psychiatric disease **during** a **planned** leisure/business **trip**	– What is the patient's usual medication regimen? – Does the patient have a medication of choice when agitated? – Is the patient adherent to his or her medication? – Are there precipitants (e.g., jet lag, sources of stress)?
Acute episode with psychotic features and thought disturbances that **motivated** an impulsive/**unplanned trip** abroad	– Is this a first episode? – Are there acute symptoms that motivated the trip (e.g., persecutory delusion, ideas of grandeur)? – Is the trip motivated by the patient's or the patient's family's desire to get better care (i.e., is the trip planned after all)? – If recurring episode, what is the patient's usual medication regimen? – Did the patient escape from another mental health institution?
Recent immigrant	– Is the patient's legal status a source of stress? – Was the patient a victim of trauma in his or her country of origin (e.g., acute presentation of PTSD)? – Is family support available locally? – If the patient has no family locally, does another support system exist (friends, community, etc.)?

Recommendations Regarding Patients Who Do Not Speak the Local Language, Recent Immigrants, or Patients Traveling from Abroad

- Identify which language the patient wishes to use by asking him or her directly.
- Do not assume the patient wants to be addressed in his or her native language. If the patient clearly wants to use the local language despite difficulties, adapt your vocabulary and the speed by which you speak.

- Patients sometimes go back and forth between two or more languages, especially when agitated. They might not remain consistent with the choice they expressed and the clinician must adapt.
- Ask where the patient comes from and which nationality or culture he or she identifies with. Do not get confused by complex life itineraries.
- If the patient has past psychiatric history abroad, be mindful that some countries' physicians use classifications other than the DSM when delivering a diagnosis.
- Be aware that retail names of medication vary from country to country, and be prepared to research them to be able to order the same or a similar molecule.
- If the patient is traveling from abroad, try to gather history from the patient and collaterals in order to understand the patient's itinerary and recent history.

Language is far from the only component in approaching a patient coming from a different culture. Patients who are recent immigrants or patients who are traveling from abroad present unique challenges regardless of their ability to speak the local language. While situations of "foreign patients" might at first blush appear similar to clinicians and other staff, they can be incredibly different from one case to another. For example, the questions a clinician would pose to an individual who is a recent immigrant from a less-developed country are likely to be very different from the questions the clinician would put to a business traveler from the developed world. And, of course, the plot thickens when "tourists" become settlers or when undocumented immigrants are afraid to explain their situation to hospital staff because they fear potential legal consequences (Perez-Rodriguez et al., 2006). Because of these different layers of complexity, it is imperative to have in mind a classification of the most common situations. Failure to capture and summarize a patient's precise circumstances exposes a team of clinicians to misunderstanding and has the potential to trigger or increase patient agitation.

A first step when facing a patient traveling from abroad is to introduce oneself and remind the patient of the principles of safety, care, and confidentiality. This should be done in simple words, and one should not hesitate to reiterate these core principles. Only then should the clinician ask where the individual comes from and which culture he or she identifies with. This should not be done in an interrogational way, and a patient's refusal to share such information should be respected. The clinician has other opportunities to understand the patient's life story – by asking collateral, for example, or simply by asking the patient in subsequent interviews. Information about recent events in the individual's life should be gathered in an attempt to paint a picture of the patient's current situation and stress factors. Showing interest in the patient's life circumstances may help the agitated patient put his or her feelings and frustrations into words and may constitute a first step toward successful verbal de-escalation.

Special Situation: Agitation during Transportation

All types of transportation can precipitate states of agitation. By far the most anxiety-triggering means of transportation is air travel. In a study compiling causes of in-flight emergencies, acute anxiety was found to be a very common situation aboard planes (Nable et al., 2015) Clinicians familiar with behavioral emergencies probably find themselves facing this type of situation while traveling themselves. While crews are trained to use protocols for handling disruptive passengers, the seasoned clinician should not hesitate to offer help in the form of verbal de-escalation or medical care. In offering to assist, he or she should keep in mind that all

passengers – including, of course the clinician – must by law obey the crew. When facing an individual getting agitated in the context of transportation, it is important to set safety (the patient's and other travelers') as the number-one priority. The enclosed space of a plane or a train, the likely very limited medical equipment, and the absence of trained support staff might lead the clinician to take a more aggressive approach to managing the agitated patient, including the use of manual or mechanical restraints. Coercive methods may be in the interest of the "patient" as erratic behaviors in the highly secure context of, for example, an airport, can lead to tragic outcomes (Nordqvist, 2005). The Good Samaritan clinician should also keep in mind that agitation can be triggered by substance abuse. Acute alcoholic intoxication is a common in-flight situation. This prospect should lead the clinician to use medication prudently, should it be available. Finally, once the situation is stabilized, it is important for the clinician to advocate for the individual who became his or her patient and insist that he or she is treated as such and not as a troublemaker. This implies insisting for the highest level of care in the air just as on the ground.

Conclusion

Agitation is the clinical end point of a complex itinerary that entails biological, psychological, and social components. External factors such as the circumstances of the crisis, the immediate environment, relations with the family and other loved ones, as well as cultural factors, can play a major role either as triggers or modulators of a patient's state of agitation. These factors are by definition highly subjective and are too complex to be included in guidelines and protocols. They are nevertheless highly relevant and must be part of every clinical assessment. By approaching agitated patients with a genuine desire to comprehend the unique nature of their experience in all its constituents, the clinician gains an opportunity to address them as people and to build a lasting therapeutic alliance.

General Recommendations Regarding the Environmental, Social, Familial, and Cultural Context

- Look for environmental triggers or modulators of agitation and include them in your assessment.
- Be prepared to adapt protocols to manage special situations, especially when dealing with victims of recent trauma.
- Ultimately, therapeutic decisions should be based on clinical factors such as intensity of agitation and risk assessment. Clinicians and other staff should not pass judgments on environmental causes of agitation.
- Optimize information gathering from first responders about the circumstances of their intervention in the community. Optimize triage to detect the presence of persecutory delusions.
- Be mindful of psychosocial interactions in the waiting room or emergency department. Train staff to observe signs of tension between patients.
- If family is present, ask the patient if he or she wants family to be there and how the patient thinks the family will help (or not). Be prepared to end the family encounter if it aggravates the patient.

- Family members should not be present when the team attempts verbal de-escalation and/or administers medication.
- If the patient speaks a different language or belongs to a different culture, identify the patient's language of choice first and attempt to accommodate that choice.
- If the patient is a recent immigrant or is traveling from abroad, be prepared to spend time establishing a complex life itinerary. Showing interest and understanding for complex life paths can help de-escalate the patient's agitation and lays the groundwork for future therapeutic alliance.

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Chapter 16

The Ethics of Agitation: When Is an Agitated Patient Decisionally Capable?

David Pepper and Michael Wilson

Introduction: A common scenario faced in many emergency departments and emergency psychiatric units is an agitated patient who wishes to leave. The ethics of allowing a patient to leave are complex, but involve basic ethical principles about the ability of a patient to understand the consequences of his or her own actions. This chapter explores the basic principles of medical ethics that sometimes come into conflict when managing an agitated patient.

Case Example

JT is a forty-nine-year-old divorced white male who presents to the emergency department asking for "help." The patient is well known to the emergency department due to his frequent visits and episodes of extreme agitation. He has a history of bipolar disorder, alcohol-use disorder, and cocaine-use disorder, as well as a history of diabetes, chronic kidney injury, and coronary artery disease. During this visit, he is irritable but compliant with nursing care until he is approached by the emergency provider for an examination. At this point he becomes irate, refuses all physical and laboratory examination, and demands, "either let me sleep or let me out!"

Why a Discussion about Ethics?

The study of ethics concerns the classification and systematization of moral behavior (Derse 2006). The field itself has a long history, dating back to ancient Greece. Modern bioethics has evolved, however, because both ethics and federal and state law have either largely ignored the application of ethics to the medical setting or deferred such complicated decisions to medical providers (Derse 2006). This means that emergency providers are often expected to make weighty decisions about the correct care of their patients. Typically, these decisions are made quickly under enormous time pressure, sometimes even with incomplete information. The consequences of these decisions can have a profound impact on the future care. In one landmark case, *Shine v. Vega*, a twenty-nine-year-old female was intubated against her will for a severe asthma attack because she was considered in an "extreme emergency." Two years later during another severe attack, she refused to seek medical help and subsequently died (Annas 1999).

Basic Principles of Medical Ethics

There are many moments in medical care providers' careers when they are presented with the choice between allowing a patient to leave or to keep the patient involuntarily. These choices are often difficult because fundamental elements of medical ethics, in this case the

desire to help the patient but also to protect from the harm of an unwise decision, sometimes conflict (Gillon 1994). Medical ethics that have been adopted by many medical societies, including the American College of Emergency Physicians, include four main principles: beneficence (the maximization of good for an individual patient), non-maleficence ("first, do no harm"), respect for patient autonomy (allowing each patient to make his or her own decisions), and justice (the equitable distribution of scarce emergency department resources). Although patients may not know each of these terms by name, they nonetheless enter the medical setting expecting the care to follow these principles. However, what do providers do when two of these principles conflict? More practically, can providers simply let an agitated patient walk out? Is there ever a justification to hold an agitated patient against his or her will?

Decision-Making Capacity

Decision-making capacity refers to the patient's ability to exercise autonomy, that is, to make his or her own healthcare decisions (Iserson 2006). Decision-making capacity is both a question and time-specific evaluation. It answers the question: "Can this patient make this decision at this time?" In contrast, *competency* is a legal term reflecting a more general view of a patient's ability to make such decisions. Decisions about competency are generally made by courts, who then appoint a decision maker if the patient is found incompetent.

Decision-making capacity, on the other hand, is often decided by medical care providers. In order to establish this, patients must be able to: communicate a choice; understand the relevant information about their current condition and recommended treatments; understand the consequence of their decision; and manipulate information in a rational manner. Note that patients' ability to do this crucially depends on how much information has already been shared by their provider (i.e., it is impossible to understand recommended treatments that haven't yet been mentioned). The cornerstone of evaluating decision-making capacity is therefore a discussion about available options. At a minimum, patients should be informed of their current condition, the treatments recommended for this condition, and any risks/benefits of either treatment or no treatment. Patients who cannot participate in this conversation because of intoxicating substances, disease, dementia, or injury are presumed not to have decision-making capacity.

The question of how much information should be shared in order to allow patients to participate in their own care can sometimes be difficult. Some conditions and treatments will require a more detailed explanation, while others can be quite simple. Explaining why a urine sample is needed, for instance, may often be a brief conversation, but consenting to an invasive procedure such as a central line or open heart surgery likely warrants a longer conversation. In general, providers should err on the side of providing more information rather than less. Patient caregivers or family, if present, should also be given the opportunity to ask questions if desired.

Decisional Capacity in Agitation

When evaluating an agitated patient, the evaluation of decisional capacity becomes even more difficult. Most patient encounters are based on a patient's reported problem, but often an agitated patient's primary complaint is that he or she is being detained in the emergency department. Like every patient, agitated patients should be given the opportunity for self-direction unless their behavior is placing themselves or others in danger (CMS 2016). This

means that patients should be informed of impending treatments, and restrained patients should be informed about what actions are necessary to get out of restraints. Note that crucially, the evaluation of decisional capacity does not depend on any particular level of agitation. Some agitated patients can both comprehend and manipulate information rationally. Grossly psychotic patients, however, may not be able to participate in decision making even if they are not agitated.

Emergency Exception to Informed Consent

Once a patient has demonstrated either that they are not in control of their own behavior or present a risk to themselves or others, urgent action is needed. The choice of action can have a profound effect on the course of events. If the approach is too passive, there is a risk that patient and staff may be injured, but if the approach is too stern, both patients and staff may be injured during unnecessary restraint or medication. The appropriate but judicious use of medication and restraints can have a huge impact on both the ED visit and subsequent visits, and is covered in detail elsewhere in this text (see, for instance, Chapters 13–14).

Emergency exceptions to the routine process of informed consent allow medical care providers to care for patients who lack capacity to make health care decisions. Many emergency care providers are aware of these exceptions, as they are routinely used with patients who are altered or in cardiac arrest. Important, however, such emergency exceptions do not allow providers to force medical treatment on patients who are in an emergent situation, but capable of refusal. In *Shine v. Vega*, a twenty-nine-year-old female patient named Catherine Shine with severe asthma was intubated against her will by an emergency department physician, Dr. Vega (Annas 1999). Evidence presented at trial indicated Catherine was so traumatized by this experience she refused to go to the hospital. She died during another attack two years later.

Shine v Vega is a reminder that the right to control one's own body is fundamental in both ethics and law, and when a provider performs an emergent procedure, the failure to obtain informed consent must be justified. Given that Shine was capable of refusing treatment, a higher court overturned the original verdict for the defendant, and the case – later settled out of court – has now become a stark example of the risks of ignoring the wishes of decisionally capable patients. If performing a procedure or intervention, it is critical at a minimum to identify why the procedure had to be performed without consent, what treatments were performed, and why the patient was unable to provide consent. Although the discussion may be brief, the clinical assessment and medical decision-making process should be documented in the record. Once a provider has assessed the patient both to lack decisional capacity and require emergency treatment, providers are of course obligated to provide that treatment.

Further case details:
JT is informed that the emergency medicine care provider would like to perform a physical to ensure that he is not acutely medically ill. He agrees to an assessment of his vital signs, but refuses a physical exam until "later." Emergency medicine staff attempt to verbally deescalate JT, but he continues to escalate. He begins to verbally threaten staff and attempts to assault the provider. Security officers are called. After a short time in restraints, JT falls asleep and passively consents to physical assessment and the drawing of labs. He is taken out of restraints, and sleeps another hour. His labs show mild dehydration and a slight worsening of his renal function. He agrees to IV hydration with the promise of a sandwich and access to a phone.

The Ethics of Involuntary Medication and Restraint

Despite expert appeals to the contrary, the use of restraint is frequent in emergency settings, although there are no precise rates internationally regarding this practice (Wilson & Sloane 2012; Marx & Rosen 2006; Simpson et al. 2014). Regulatory institutions have generally distinguished between behavioral restraints for control of dangerous or violent behavior and medical restraint, in which are restraints are placed to allow medical care. There is little difference between these two types from an ethical perspective, as both require a determination that the patient is incapable of making decisions on his or her own behalf. In addition, involuntary medication given to restrict movement is ethically no different than four-point restraints, which are administered for the same purpose.

Given that no randomized studies exist on the benefits of restraint, but there are several studies on restraint-related harm, the use of restraints is fraught with ethical complications. Restraints likely deprive patients of autonomy, do not provide beneficence, and may violate the principle of non-maleficence. The use of restraints, particularly for behavioral control, is now discouraged by most professional societies. When used, they are appropriate only as a last resort in which the individual is effectively incarcerated but without access to a judge or jury. Despite the negative consequences of restraints, restraint use for behavioral reasons is generally viewed more positively by staff (Fisher 1994; Stewart et al. 2009), which may in part be because ED staff encounter frequent verbal and physical abuse (ENA 2011).

Restraint use may also remain frequent because the benefit of restraints seems intuitively obvious: a restrained violent patient cannot attack staff, thus keeping staff safer. In addition, at least one study has shown increasing levels of violence against staff in institutions that have minimized restraints (Fisher 1994; Khadivi et al. 2004). This argument, based on the principle of justice for other staff and patients, has been often been presumed to outweigh the ethical problems with restraints. However, this argument also ignores many of the harmful aspects of restraints. Most injuries to staff, for instance, occur during the application of restraints. Although the risks of restraints to patients are low in prospective studies in the ED, restraint-related injuries still ranked seventh among the types of events reported to the Joint Commission from 1995 to 2005 (Zun 2003; Ednie 2009). The American College of Emergency Physicians, unique among professional organizations in that it did not appeal for an outright ban on the procedure, nonetheless states that restraints should be used "only after" other methods, such as verbal de-escalation, have been attempted (see Table 16.1).

Staff should always attempt verbal de-escalation with an agitated patient as a first-line intervention (Richmond et al. 2012). There is a major misconception that some patients are "too agitated" to attempt verbal de-escalation, when it can be the loud and boisterous patients who benefit the most from an empathic provider. Restraints or involuntary medication should never be used with patients who are decisionally capable and not a danger to themselves or others.

Further case details:
As JT has no evidence of trauma, he is allowed to rest for several minutes before disposition is attempted. After JT has taken a brief nap, the emergency medical care provider notes erratic behavior, loud rambling speech, and paranoia about "government agencies" trying to find him. The provider attempts to discuss his concerns about his current mental state, and his desire to have a formal psychiatric evaluation performed. At this point, JT shoves the provider out of his way and attempts to leave, stating, "F&^ that, I'm out of here!"*

Table 16.1. ACEP policy on restraints

ACEP endorses the following principles regarding patient restraints:
Restraints should be instituted only after verbal de-escalation has been attempted.
Protocols to ensure patient safety should be developed to address observation and treatment during the period of restraint and periodic assessment as to the need and means of continuing or discontinuing restraint.
The use of restraints should be carefully documented, including the reasons for and means of restraint, alternatives to restraint, and the periodic assessment of the restrained patient.
ACEP opposes any requirement by hospital representatives or medical staff that emergency physicians provide inpatient restraint or seclusion orders. Patient restraint or seclusion requires comprehensive patient assessment, and the emergency physician's principal legal and ethical responsibility is to patients who present to be seen and treated in the emergency department.
The use of restraints should conform to applicable laws, rules, regulations, and accreditation standards.
Restraint of patients should be individualized and employed in a manner that makes all reasonable attempts to maintain the patients' privacy and dignity.
The method of restraint should be the least restrictive necessary for the protection of the patient and others.
Staff should be properly trained in the appropriate use and application of restraints and in the monitoring of patients in restraint and seclusion.

The Ethics of Disposition: When Is a Patient Able to Leave?

Many ethicists have argued that decision-making capacity exists on a sliding scale. That is, the more serious an option the patient is considering, the higher the bar should be for proving decisional capacity. In essence, although all four elements of informed consent still apply (i.e., communicating a choice; understanding relevant information about the current condition; understanding the consequences of a particular decision; and manipulating information in a rational manner), the patient in our vignette must meet a higher threshold for leaving than would be necessary to simply refuse a blood draw.

Typically, patients who are safe for discharge are not grossly psychotic, not grossly impaired by alcohol or drugs, not severely demented, and have a logical reason for leaving the emergency department. Their reasoning may be medically suboptimal (i.e., checking on a pet or a loved one), but must make some logical sense within the context of the patient's expressed wishes. For instance, leaving the emergency department for home would be logical and consistent if the patient is caring for others at home, but would not make sense at all if the patient is single and homeless. Much useful information about a patient's values and decision-making capacity can be gathered from the simple question: "You must have a good reason to put your health at risk by wishing to leave. Do you mind telling me what it is?" Patients who are highly irritable may not initially respond to this question, complicating the evaluation of their decisional capacity. However, a useful follow-up statement often is, "I know you may not want to tell me everything about why you want to leave. However, the hospital (the state, or other institution) requires me to list a reason why you wish to leave, especially since you might get a lot sicker or even die after you leave.

Can you tell me why you wish to leave so badly?" The answer to this brief series of questions often provides a useful start for determining decisional capacity in the emergency setting.

Physicians often face an additional dilemma with decisionally capable patients who are somewhat agitated, in that they may begin to "pick and choose" or dictate the terms of their own care in the emergency department. Although the practice of patient-centered decision making should be encouraged, physicians should not allow patients to refuse elements of care that would be detrimental to effective diagnosis (for instance, vital signs or a physical exam). In these instances, if the patient is not convinced of the necessity of a particular procedure or intervention after discussion, it may be a wise choice simply to discharge the patient prematurely against medical advice. This allows patients the option of seeking care from a different physician or returning if their symptoms worsen.

The Ethics of Using Others to Decide: The Role of Surrogates

When a patient is deemed to not have decision-making capacity, physicians should if at all possible substitute the decision making of another individual that has ethical or legal responsibility for the patient (AMA 2016). This scenario is obvious and quite familiar to emergency providers in cases of patients with severe dementia, for instance, in which family members are often called upon to help make decisions. However, these same principles apply to patients with agitation. If a patient can participate even slightly in his or her medical care, deference should be given to any stated wishes. If a patient cannot participate in his or her own care, emergency care providers should make an attempt to obtain evidence of the patient's values and preferences from an available proxy such as a family member or close friend.

If the patient is completely unable to make decisions, informed consent for non-emergent procedures must be obtained from proxies (Legal Guidelines 2016). State law may vary, and providers are urged to look up the applicable laws in their area of practice. Generally, however, preference is given first to any individual the patient has designated as a health care decision maker, including individuals with a power of attorney or individuals who have been appointed as legal guardians. If the patient has not appointed such an individual, spouses or domestic partners are generally considered the next responsible decision makers, followed by siblings. Of note, groups of clinicians are never considered appropriate surrogate decision makers, and should not attempt to substitute their judgment for the patient's wishes.

Conclusions

Case conclusion:
As JT wishes to leave, the providers initially face a difficult choice: either restrain and sedate him or elicit his reasons for leaving. After a few minutes of verbal de-escalation, JT can express that he is worried about making the last bus that serves his home on the other side of town. Given that he has a logical although medically suboptimal reason to leave, he is deemed to have decision-making capacity. He is counseled about his diagnosis and the treatments administered in the emergency department, and urged to make appropriate follow-up appointments with his primary physician. He is then discharged without need for involuntary medication or restraints.

The ethics of managing an agitated patient start first with an evaluation of decision-making capacity. A decisionally capable adult can understand relevant medical

information; communicate a choice; understand the consequence of his or her decisions; and think critically about the information presented (i.e., manipulate information in a rational manner). Decisionally capable patients should never be restrained or involuntarily medicated unless they are a danger to themselves or others, and should be allowed a choice in their own care. If these decisions prevent the physician from delivering quality care, decisionally capable patients may be discharged and allowed to seek care elsewhere.

Key Points

- All adults are presumed to have decision-making capacity; that is, the ability to make decisions about their own care in an autonomous manner.
- Involuntary medication and restraint should never be used with decisionally capable adults who are not a danger to themselves or others.
- If patients do not have decisional capacity, information about their wishes and consent for procedures should be gathered from surrogate decision makers.

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Chapter

17

Patient Rights, Patient and Family Perspectives on Agitation

Phyllis Foxworth

Patient and family considerations are an important component for treating agitation symptoms when an individual presents at the emergency department (ED). The literature demonstrates that this involvement not only decreases the likelihood of an extended patient stay in the ED, it also increases patient satisfaction.

What preconceived notions do patients and family members have when arriving at the ED? How do these compare with the actual treatment delivered? This chapter will examine these questions, as well as patient and family rights, which, when fully understood and acted on, can help clinicians treat acute episodes in the most compassionate and resource-effective manner. Throughout this chapter, we will provide implementable recommendations on how clinicians and the ED can narrow the gap between patient/family expectations and the services actually received, with the goal of improving the quality of care delivered.

Patient-Centered Care: Why It Matters

The U.S. National Institute of Mental Health (NIMH) defines patient-centered care as "health care that establishes a partnership among practitioners, patients and their families (when appropriate) to ensure that decisions respect patients' wants, needs and preferences, and solicit patients' input on the education and support they need to make decisions and participate in their own care" (AHRQ, 2001). When care is focused on the patient's needs, irrespective of what may be most expedient or convenient for the facility or staff, better outcomes are achieved.

To better understand the patient and family experience in the ED, the Depression and Bipolar Support Alliance (DBSA) distributed a survey titled *Agitation and Emergency Care* through DBSA social media properties and by reaching out to DBSA chapter affiliates (DBSA, 2015). Two different surveys were developed: one for patients and one for family members. The intent of the survey was to provide a forum for patients and their families to share their experience with the ED and illuminate what works and areas of care that can be improved. Responses to survey questions included in this chapter, while not constituting scientific research, are presented with the hope that readers will gain a better understanding of the ED experience as viewed by patients and family members. The quotes included in this chapter were taken from survey respondents to open ended questions about their experience.

Patient and Family Expectations

"Treat us like we're human beings who really are in need of serious help. Just because we're not bleeding, it doesn't mean we're not hurting."
—DBSA survey respondent

In the DBSA *Agitation and Emergency Care* survey, respondents were first asked what medical attention or symptom relief they hoped to receive at the ED. Of the patients responding to this open-ended question, 58 percent responded with answers that suggested they were seeking medical attention. Forty-two percent indicated they were seeking social services or therapy – services not traditionally provided by an ED (Figure 17.1).

Family members had even higher expectations that they would receive non-ED services. Sixty-one percent of family members answering this question indicated they were seeking some type of social service, a psychiatric diagnosis, or therapy for their loved ones. Note that, among both patients and family members, respondents anticipated that the function of the ED was to make a medication change. One family member responded: "He needed to talk to someone and probably needed to be put back on his antipsychotics." Comments from patients included, "I thought the ER could make a medication change" and "I expected to be able to get the medication I needed and discharged."

Emergency departments have different institutional goals and objectives for handling psychiatric emergencies. Some facilities are focused on triage, while others are better equipped to provide more extensive psychiatric treatment, including psychiatric admission. Approximately one quarter of all survey respondents indicated they had hoped that they or their loved one would be admitted. It is not clear if they understood whether the ED was associated with a hospital that even offered psychiatric inpatient services. Unfortunately, the public is usually unaware of these nuances and, in a time of crisis, these distinctions are not front-of-mind. One way the ED can narrow the gap between public perception and actual services rendered is through community mental health care outreach.

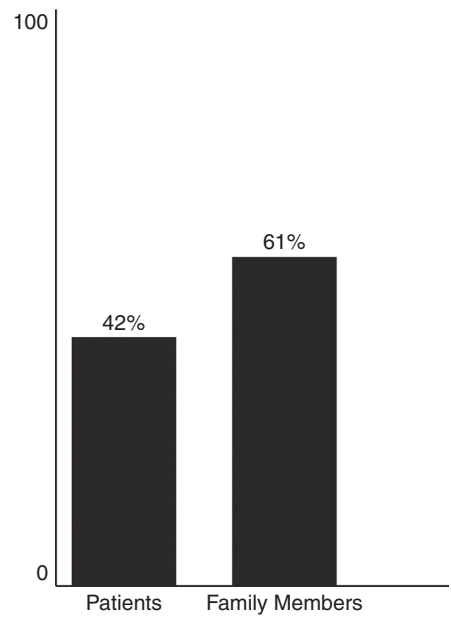

Figure 17.1. Indicated they were seeking social services, therapy, a diagnosis, referral, or medication change when presenting at the ED.

Connection to Community Resources

With most medical emergencies, once the acute condition has been resolved, the patient is released with a list of referrals for long-term treatment or follow-up of the condition that brought them to the ED in the first place. Yet the DBSA *Agitation and Emergency Care* survey revealed that overwhelmingly patients and family members are not generally provided with information about community behavioral health care centers or a list of psychiatrists. Community behavioral health care centers are the mainstay of mental health care services in many communities. These organizations receive federal funding and are authorized by the U.S. government to provide coordinated and continued mental health care services to qualifying individuals and their families. Building a bridge between the ED and these facilities can narrow the referral gap identified by survey respondents.

Community outreach should not end with a connection to community behavioral health care centers and local psychiatrists, however. One way to ease the ED staff's burden of educating patients and loved ones in the United States is to ask the hospital's community liaison staff to develop relationships with local DBSA chapters. These local organizations provide support group meetings for both individuals living with mood disorders and their family members. More than 85 percent of individuals who attend a DBSA support group meeting state that they are more willing to take medications, cope with side effects, and follow their doctors' instructions. Even more encouraging, those who attended support group meetings for more than a year were less likely to be hospitalized within the past year.

Another such resource in the United States is the local chapter affiliate of the National Alliance on Mental Illness (NAMI). This organization offers an intensive family education course on mental health conditions through its chapter affiliates. Gaining knowledge can reduce fear, and the less fear family members have about their loved ones' mental health condition and symptoms, the more likely they are to have realistic expectations about the role of the ED in treating agitation symptoms.

It Gets Brighter (2015) provides a wealth of information to individuals and families throughout the world. This multinational organization currently provides information about mental health care resources in six different countries: Australia, Canada, Germany, Lebanon, the United Kingdom, and the United States.

Affiliated with the Department of Psychiatry at the American University of Beirut Medical Center (AUBMC), Embrace (Embrace Fund, 2015) works to eliminate stigma that can keep so many people from seeking help before it becomes a crisis. Supporting the Middle East region, this nonprofit also provides financial assistance to individuals who cannot access care due to financial constraints.

Developing relationships with community resources not only creates the opportunity to better serve patients, it may also play a significant role in reducing return ED visits. Sixty percent of all respondents indicated that they or their loved one returned to the ED within a year, and 34 percent within sixty days. Perhaps this high rate of return ED visits could be reduced if referral information were routinely provided.

Staff Training

"Be sure that ED staff has training in COMMUNICATION with sensitive patients as well as in calming so that serious mistakes are not made and civil rights are not violated."
—DBSA survey respondent

In addition to providing information about mental health care resources, the hospital can train staff to better understand the stress patients and family members are experiencing. Training should include awareness that the public may have a different perception of services offered by the ED than that of the staff. By understanding this service gap perception upfront, staff is in a position to better assist both patients and family members navigate what for them is a complex medical system.

It is important to also include non-medical staff in a sensitivity training program. Ancillary personnel such as intake clerks, security guards, and custodial staff often have quite meaningful interactions with patients and family members. Sensitivity training to help staff understand that they are seeing people on what is often their "worst day" can provide the empathy that patients and family members need, and can actually assist them in hearing that the extended services they are seeking are not provided at the ED.

What Does Quality Care Look Like?

"I hoped to get a calm place, where I could relax, feel safe, and receive compassion, understanding, and encouragement. . . . Look at us as individuals that matter and having a mental illness doesn't make us less intelligent. . . . I think TALK is a powerful tool when someone comes into the ERD in such a low, hopeless place. Also wait time for someone in such a desperate place is, in my mind, a dangerous thing."
—DBSA survey respondents

One criteria of patient-centered care is to engage patients in their own treatment. There are several reasons this is good practice, especially for an individual experiencing agitation symptoms. The goals of the ED staff include stabilizing the patient's acute symptoms and referring the patient for the appropriate follow-up care. A therapeutic alliance not only helps achieve these goals, but lessens the trauma that can be produced by physically restraining a patient through force or medication. ***Having a positive first experience can go a long way in creating the desire and motivation for the patient to pursue long-term treatment once discharged from the ED.***

As other chapters in this book have detailed, one best practice for treating agitation symptoms is verbal de-escalation. Unfortunately, the DBSA *Agitation and Emergency Care* survey revealed that this protocol was not provided at many of the EDs where respondents were presenting. When asked to rate efforts by ED staff in verbal de-escalation, 60 percent of patients rated this effort 1–3 (very low) on a 1–10 scale (10 being high).

Clinicians are encouraged to review the literature that demonstrates the effectiveness of this protocol as the DBSA survey identified encouraging outcomes. Of the patient respondents giving high marks (8–10) for verbal de-escalation efforts by the ED staff, the overwhelming majority of respondents in this subgroup shared that they have either never returned to the ED or that it has been within one year (on a scale of 30 days, 60, days, 120 days, within 1 year, or never). More research is required, but it is promising that a therapeutic alliance has the transformational potential to carry through to positive engagement with long-term mental health care for the individual.

Conversely, it is possible that staff attitude, sometimes resulting from stigma toward individuals with a mental health condition, permeates across the entire spectrum of care for the agitation event. Sixty-four percent of patient respondents who provided a low ranking for staff use of verbal de-escalation (1–3) also indicated they were not asked for their consent

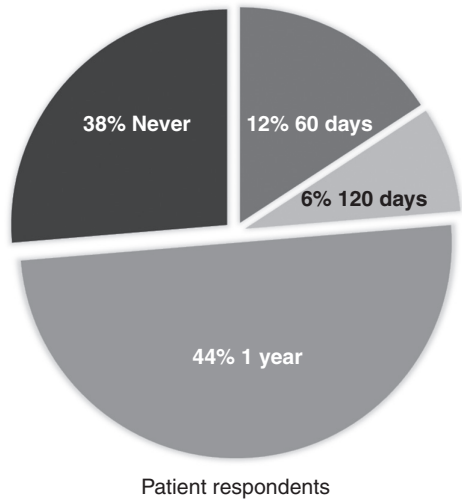

Figure 17.2. Return rate to ED from patients reporting high marks for staff attempts to help calm them.

prior to medication being administered. If any further evidence that quality care means engaging patients in their own treatment, one only need consider the average ranking for overall experience at the ED for patients in this subgroup. Sixty-nine percent rated their overall experience 1–3 and 26 percent rated it 4–6.

Recommendations for Achieving Patient-Centered Care

Key factors for improving the quality of care for agitation symptoms include:

- understand and educate about the patient/family expectation around the ED service gap
- develop close relationships with community resources for non-crisis triage redirection and/or post-release follow-up
- provide sensitivity and verbal de-escalation training to all levels of staff
- engage in de-escalation protocols as the first line of treatment whenever possible

These recommendations can provide long-term benefits for not only the patient, but the ED as well.

Patient and Family Legal Rights

As previously discussed, when individuals and family members present at the ED with agitation symptoms, they arrive with a preconceived set of ideas on just what medical treatment they will receive. Regardless of whether it is the individual experiencing the agitation symptoms or the family member, both arrive with varying degrees of knowledge about their rights. This knowledge ranges from very limited to well-researched, but can also include incorrect assumptions about their rights as a patient or as a family member. It is extremely helpful for clinicians to understand the rights of the people they serve, as there may be misconceptions among all the participants: clinical staff, patient, and family member. This is useful on two fronts: first, it enables clinicians to provide empathetic

care by recognizing that people may not have an accurate understanding of their legal rights and, second, this is one more tool to support overall de-escalation of the agitation situation.

Honoring patients' rights can also save lives. "Deadly Restraint," a historic 1998 investigative series by the Hartford, Connecticut newspaper *Hartford Courant*, was the catalyst for the U.S. Department of Health and Human Services' review of patients' rights. The investigation revealed that at least 142 patients had died over a ten-year period after being restrained or secluded while being treated in facilities across the United States (Weiss et al. 1998). While the *Hartford Courant* investigation focused on mental health care and mental retardation facilities and group homes, the alarming findings prompted the U.S. Congress to commission a survey by the Health Care Financing Administration (HFCA), now known as the Centers for Medicare and Medicaid Services (CMS).

More alarmingly, this statistic (142 deaths) is believed by many to be grossly inaccurate for two reasons: first, there was at that time no requirement to report such deaths and, second, many deaths may have been attributed to other medical causes. Fortunately, this tragic exposé resulted in a final rule, issued on December 8, 2006, by the Department of Health and Human Services' CMS, titled "Medicare and Medicaid Programs; Hospital Conditions of Participation: Patients' Rights" (CMS, 2006). The final rule refers to federal statute in making some of its determinations and encourages de-escalation best practices.

It provides clear direction on Patients' Rights of Participation (CoP) for U.S. hospitals taking part in Medicare and Medicaid reimbursement programs. First and foremost, the rule stipulates that all patients have the right to

- receive care in a safe setting
- be free from all forms of abuse or harassment

Further, the Patients' Rights CoP promotes patients' right to be involved in and to make decisions about their own care. This includes being involved in care planning and treatment, and being able to request or refuse treatment (CMS, 2006).

Use of Restraints or Seclusion

"Medication and restraint should never be the first treatment. . . . Physical restraints should be the last resort."
—DBSA survey respondent

As the *Hartford Courant* reported, use of restraints and seclusion can result in a patient's death, which prompted the rule issued by CMS. All ED clinicians should be familiar with the policies included in the document regarding restraints and seclusion.

CMS defines *restraint* as:

- any manual method, physical or mechanical device, material, or equipment that immobilizes or reduces the ability of a patient to move his or her arms, legs, body, or head freely;
- a drug or medication, used as a restriction to manage the patient's behavior or to restrict the patient's freedom of movement, which is not a standard treatment or dosage for the patient's condition (CMS, 2006).

Seclusion is defined by CMS as:

- the involuntary confinement of a patient alone in a room or area from which the patient is physically prevented from leaving (CME, 2006).

The CMS final rule is very clear as to when and how clinical use of restraint and seclusion can be applied: the patient has the right to be free from restraints of any form that are not medically necessary.

- They may only be used to ensure the immediate physical safety of the patient, staff or others.
- They must be used only if needed to improve a patient's well-being, and if less restrictive interventions have been determined to be less effective.
- They cannot be used as a form of coercion, discipline, convenience, or retaliation by staff.
- Holding a patient down to conduct a physical exam without his/her permission is considered a restraint.
- The patient must be informed of the medical risks associated with refusing the use of a restraint (CMS, 2006).

The conditions do not prohibit the use of restraints or seclusion. CMS provides very clear guidance on patients' rights if restraints or seclusion are used:

- The patient has the right to the safe application of restraint or seclusion by trained and competent staff.
- The patient should be monitored for vital signs, circulation checks, hydration needs, elimination needs, level of distress and agitation, and mental status.
- Face-to-face evaluation by a licensed independent practitioner must be conducted within one hour.
- Restraint or seclusion is only permitted while the unsafe condition persists and must be discontinued at the earliest possible time.
- There are time limits on use:
  - four hours for adults
  - two hours for children aged nine to seventeen years
  - one hour for children aged under nine years (CMS, 2009)

Keeping in mind that developing a therapeutic alliance can produce better outcomes, the best protocol is for the patient to engage in administering medication to themselves through an oral medication or an inhalant.

In developing the final rule, CMS demonstrated that the patient's dignity and self-esteem need to be addressed when treating an individual experiencing agitation, especially when the symptoms of agitation are brought on by an underlying mental health condition. Recommendations include taking steps to protect the privacy of the patient while adhering to monitoring requirements.

Family Rights

"I would love to see a policy change that ER staff can release certain information if the patient is deemed 'disabled' under the wellness act so that family members can be helpful." *—DBSA survey respondent*

Sharing a medical emergency with a loved one can be a frightening and stressful experience, and not knowing what is happening to their loved one once they have been admitted to the emergency department only adds to the stress and anxiety. In DBSA's *Agitation and*

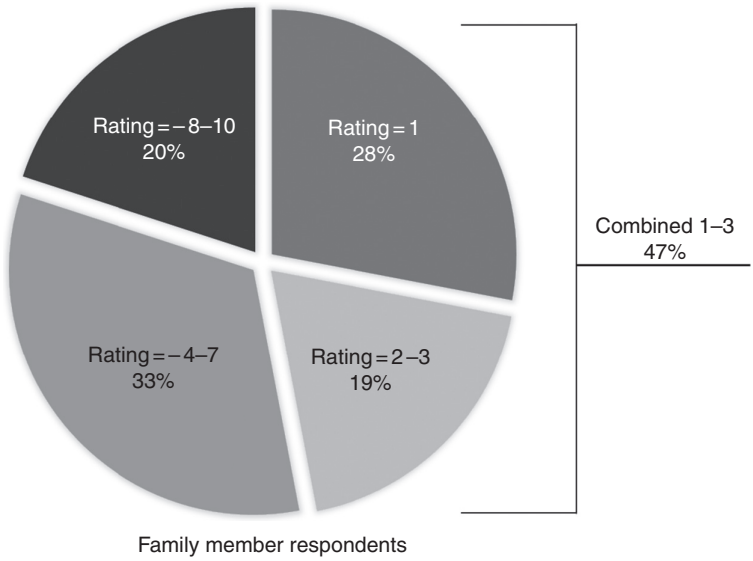

Figure 17.3. ED kept me informed about loved one's care 1–10 with 10 high.

Emergency Care survey, only 20 percent of family member respondents gave the hospital good marks for keeping them informed about the protocol of treatment their loved one was receiving (Figure 17.3). Ranked on scale from 1–10 (10 being the highest), 47 percent of family members ranked the hospital with a score of 3 or less. Twenty-eight percent gave the hospital a score of 1 – the lowest score possible.

The DBSA survey did not ask family members about knowledge of their rights as a family member. However, understanding current U.S. patient privacy laws may provide some insights.

Health Care Insurance Portability and Accountability Act (HIPAA)

Patients in the United States have protections and an expectation of privacy of their medical records due to this federal statute enacted in 1996. While HIPAA gives patients the right to access their medical records, it is more commonly known for restricting access. Many clinicians and health care systems take a limiting approach to sharing a person's medical information with family members. This is particularly true when the clinician believes that sharing this information with a family member would be harmful to the efficacy of the patient's treatment, or cause the patient to inflict harm on him/herself or others.

This restriction can be acutely troubling to family members who feel that their loved one (1) is not capable of making medical decisions due to their mental health or (2) is experiencing agitation. Yet, according to the U.S. Department of Health and Human Services, "the HIPAA Privacy Rule at 45 CFR 164.5.10(b) specifically permits covered entities to share information that is directly relevant to the involvement of a spouse, family members, friends or persons identified by a patient, in the patient's care or payment for health care. The covered entity may also share relevant information with the family and these others when the patient does not object" (GPO, 2002). Therein lies the quandary. Many clinicians prefer to err on the side of caution rather than risk violating the letter of the law.

While clinicians may be reluctant to share information with family members, it may be their misunderstanding of the law that inhibits them from soliciting information from those same family members. Nowhere in the law is *obtaining information from others* about the patient's medical condition prohibited, yet less than half of family members in the DBSA survey indicated that the medical staff at the hospital asked them for the contact information of their loved one's psychiatrist, therapist, or counselor. Also concerning, 73 percent responded "more than two hours" or "never" when asked how long their loved one waited to see a psychiatrist. Clearly, input from a clinician familiar with the patient has the potential to ensure the best treatment in the ED, especially if a psychiatrist is not available onsite at the ED. However, it is very encouraging that more than two-thirds responded that they were asked to provide information about medications their loved ones were taking and more than half indicated they were given the opportunity to share additional medical history information about their loved one.

Psychiatric Advance Directives

One predominant hospital policy experienced by family members taking the survey was lack of access to information about a loved one's care. Admittedly, there could be legitimate reasons why the individual receiving the care does not wish to share medical information with his or her family. It is interesting to note, however, that 40 percent of patients shared that they were given the opportunity to complete a HIPAA form indicating with whom they wanted their medical information shared.

Given that 71 percent of family members indicated that their loved ones returned to the ED, there is an opportunity for clinicians to better educate the public on legal steps that patients can take to safeguard that treatment is in accordance with what they want and family members have the opportunity to be full participants.

A Psychiatric Advance Directive (PAD) can ensure that the patient receives the care he/she envisioned as most appropriate; it also ensures that family members are not put in the position of having to "guess" what was wanted. Half of all states allow patients to specify, in advance, what kind of care they will receive should they be unable to request it themselves. Thus, filing a PAD can be a relief for both the patient and the family members "stepping up" to oversee ongoing care.

States either have approved PAD forms or statutes that list the criteria for making a valid form. Generally, it must be witnessed and formally signed (and perhaps notarized). The form must be given to the patient's primary care physician or mental health treatment provider, who must be able to access the PAD during any future crises.

According to the National Resource Center on Psychiatric Advance Directives (NRC PAD), additional information that can be contained in the PAD includes:

- a person to contact in case of a mental health crisis
- possible causes of your mental health crisis
- ways to help you avoid hospitalization
- how you generally react to hospitalization
- other relevant instructions (NRC PAD, 2015)

The website of the NRC PAD (www.nrc-pad.org) provides a comprehensive suite of tools and information to help patients create their own PDAs:

- first-person testimonials from people who have created PADs

- advice on how to be certain physicians access them when needed
- guidance for complying with state laws
- suggestions on making a PAD as comprehensive as possible
- tips for communicating the expectation that it will be implemented during medical care

Individuals living with a mental health condition would be wise to engage with a family member and explore this option together. ED clinicians have a unique opportunity to educate patients and family members about this option and prevent in advance some of the more serious challenges that arise in the ED when the patient is unable to articulate their preferences for care.

Recommendations for Honoring Patient and Family Rights

Key factors in honoring patient and family rights in EDs include:

- ensure all levels of clinical staff have a thorough understanding of patient and family rights
- utilize restraints and seclusion as a last-choice option and if used, following all guidelines by the CMS ruling
- exercise HIPAA regulations in a way that protects patients' rights to privacy but allows for family members to provide critical background information that contributes toward a fully informed treatment decision
- seek out and encourage the use of Psychiatric Advance Directives (PADs) in preparation for any future visits to the ED

When implemented, these recommendations can have a great impact on not only the quality care for the immediate event, but can increase likelihood that a patient will seek ongoing treatment.

Creating the Patient-Centered ED

It is generally recognized that the role of the ED is transitory: its function is to mitigate acute symptoms and either admit for further medical treatment or discharge for outpatient follow-up. However, the evolving role of the ED as perceived by the public is changing: many people view the ED as the gateway to the health care system. Lack of societal commitment to sufficient mental health care resources makes this no less true for patients experiencing a psychiatric emergency. As a result, many patients and family members turn to the ED because they don't know where else to go during a crisis.

Hospitals that accept this reality have an opportunity to be innovators in their field by creating patient-centered environments that emulate best practices and improve the quality of care. They can, at the same time, address the economic realities that reduced resources and ever-increasing demands make on the ED.

Several recommendations presented in this chapter, if implemented, have the potential to decrease the stress on current resources by lessening the demand for future services.

1. Staff training has the potential to make lasting, transformative impressions on both patients and family members by focusing on whole health and wellness and, in addition, incorporating cultural complexities. Training should include skills to assist staff in looking beyond the agitation symptoms that brought the patient to the ED: it should enable staff to provide a supportive environment that seeks out the root cause of the symptoms.

The CMS Final Rule on Patients' Rights outlines very specific staff training regarding the correct application of restraints and seclusion and, in addition,

- the use of nonphysical intervention skills (de-escalation)
- how to choose the least restrictive intervention based on an individualized assessment of the patient's medical and behavioral status or condition (CMS, 2006)

2. Just as important is training on how to partner with community resources. These partnerships help the ED move beyond just mitigating today's emergency, and into the role of preventing future psychiatric emergencies from happening in the first place. They do so by lining up patients and family members with appropriate mental health care services.
   - At a minimum, the ED should establish relationships with local community behavioral health care centers. In the United States, the National Council for Behavioral Health's 2,500 member organizations can be accessed at http://www.thenationalcouncil.org. The site includes listings with a hyperlink to each center where one can find information on services provided and contacts.
   - The Depression and Bipolar Support Alliance (DBSA) has a similar listing of more than 350 chapters offering more than 800 support group meetings around the United States. Contacts for chapter leaders who can provide information on the times and locations of meetings can be accessed at www.dbsaliance.org.

3. Psychiatric Advance Directives (PADs) can reduce stress on family members who feel they must act as proxies for loved ones unable to articulate their treatment preferences as well as ensure that the patient establishes a therapeutic alliance with the ED staff. Creating community awareness of this tool can be a valued public health education initiative that reduces stress on ED resources and creates a partnership with the patient and family member. The National Resource Center on Psychiatric Advance Directives (www.nrc-pad.org) contains a wealth of information on how to complete the directive as well as state-by-state FAQs.

In addition to the strategies explored earlier in this chapter, next are highlighted two emerging initiatives for achieving patient-centered care in EDs that are gaining momentum, as well as a call for additional research.

Designing a Therapeutic Environment

"Create trauma-informed spaces. . . . Add peer specialists to your EDs."
—DBSA survey respondent

More and more hospitals are renovating the sterile treatment and procedure rooms of the past, updating them to spa-like environments with the goal of providing a less stressful experience for their patients. Who is in more need of a less stressful experience than an individual experiencing agitation? As a result, many hospitals are looking at the success of mental health respite centers as models.

These centers are often referred to as "living rooms" because the intent is to create a safe, secure environment just like the welcoming environment of a home. The difference between this experience and the typical ED intervention can be felt from the moment the patient enters the facility. Individuals are usually referred to as "guests" and are greeted by a trained

peer support specialist, someone who lives in wellness with a mental health condition and can relate to the individual.

Respite centers are prepared to handle a wide variety of psychiatric emergencies and are staffed by clinical supervisors, a psychiatrist, a registered nurse, and peer support specialists. The staff, all of whom have been trained in de-escalation techniques, work together as a team to ensure that the guest receives mental health care tailored to his or her immediate needs.

A major goal of the team is to empower the guest to identify the outcomes they wish to achieve to move forward from the immediate crises. The team then works with the guest through intervention techniques and assists in developing coping skills and a wellness plan. The plan includes connecting the guest with mental health care resources and embraces the idea that wellness does not end with the mitigation of the current episode; instead, the hope is to influence the guest to embark on long-term treatment.

Many mental health respite centers have beds that can accommodate short-term stays. Many are associated with hospitals or are even part of the hospital facility. The cost-efficiency of this model cannot be ignored. According to U.S. government reports, an estimated 17 percent of adults in Medicaid expansion states live with a mental health condition. When viewed alongside the fact that an estimated 20 to 50 percent of psychiatric emergencies involve patients at risk for agitation (Marco and Vaughan, 2005), there is strong financial motivation to develop protocols that not only reduce lengthy ED stays, but create a therapeutic experience that encourages follow-up treatment – and keeps patients from returning to the ED.

One mental health respite center, The Living Room associated with Turning Point Behavioral Health Care Center in Skokie, Illinois, reports a 97 percent deflection rate from hospitals in the surrounding area (Haggard, 2015). For EDs that seek to lower their mental health patients' lengths of stay, this model is worth investigating either through implementation or partnering with other facilities.

Utilizing Peer Support Specialists

Central to the success of mental health respite centers is the utilization of peer support specialists as an integral member of the professional care team. These professionals act as trusted and motivating role models and they help their guests

- navigate the often confusing health care system
- obtain needed services
- get the most out of treatment
- develop recovery plans
- build skills in daily living
- identify community resources

Peer support services do not take the place of clinical services; rather, they supplement and improve the effectiveness of mental health care. This evidence-based model of care has been shown to:

- reduce expensive inpatient service use
- reduce recurrent psychiatric hospitalizations for patients at risk of readmission (Solomon et al. 1995; Davidson et al. 2000; Wexler et al. 2008)

- improve individuals' relationships with their health care provider (Solomon et al. 1995; Davidson et al. 2000; Wexler et al. 2008)
- better engage individuals in care (Solomon et al. 1995; Davidson et al. 2000; Wexler et al. 2008)

Many of the challenges that have been identified in delivering patient-centered care and achieving patient-centered ED outcomes could be resolved with the addition of peer support specialists on-staff. For example, a peer support specialist trained in de-escalation techniques could assist patients in identifying their preferred courses of treatment and communicating the requests to the medical staff. They could stay with the patient throughout treatment, assisting them in staying calm and working with them on a discharge plan and follow-up care—freeing the medical staff to attend to other medical emergencies and reducing costly boarding.

Making the Case for Research

Patient-centered care is a medical trend that is becoming deeply entrenched and is supported by the U.S. National Institute of Mental Health. This public health policy received a big boost from U.S. federal mandates in the 2010 Patient Protection and Affordable Care Act (ACA), which established funding for a nongovernment agency to administer research contracts that promote patient-centered outcomes. The Patient Centered Research Outcomes Institute (PCORI) was founded out of this mandate and has a rolling deadline for accepting proposals. One major objective is to ensure that research is "inclusive of an individual's preferences, autonomy, and needs, focusing on outcomes that people notice and care about such as survival, function, symptoms, and health related quality of life" (PCORI, 2012).

Central to the PCORI mission is securing patient input in the development of the research aims. Many large research institutions have been successful in securing PCORI grants by partnering with patient advocacy organizations such as DBSA. The inclusion of patient advocacy organizations as co-investigators on research projects provides PCORI with reassurance that research is being driven from the bottom up (from the people) rather than top down (from the researchers).

There are different protocols for treating agitation in the ED. Understanding the effects of patient-centered care as it relates to the ED experience has the potential to shift health care policies. Recommended areas of study include the following:

- Does engaging patients in their own treatment decisions (as opposed to coercive treatment) lead to a therapeutic alliance that decreases the risks of returning to the ED?
- Can utilizing peer support specialists as part of the ED treatment team increase patient engagement with medical staff and support self-determined care?
- What cost benefit does the ED derive from investing in appropriate staff and staff training to better support patient-centered care and outcomes?

Recommendations for Creating Patient-Centered EDs

Implementation of extensive training across all levels of staff; operationalizing a systemic connection to critical community resources; gaining better understanding and exercising of patient and family rights; and proactively implementing strategies such as encouraging the use of PADs, would significantly enhance patient-centered care in EDs. However, additional

research and implementation of emerging and innovative strategies like redesign of EDs to create physical environments and utilization of peer support specialists offer the potential for monumental change in the ways we address agitation and/or mental health crises in the future.

Patient-centered care is an idea whose time has come. Government reimbursement agencies are influencing this movement through performance-based financial incentives based on improving patient care experiences. Just as important, a great deal of research has already concluded that patient-centered care leads to better patient outcomes (AHRQ, 2001). Understanding and managing patient and family treatment expectations, supporting agitation treatment protocols that increase patients' engagement in their own care, and recognizing the rights of both patients and family members maximizes value for all actors in the health care theater. That is a benefit that is truly positive for all involved.

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Chapter

18

Diagnosis and Management of Agitation in Children and Adolescents

John S. Rozel, Keith R. Stowell, and Gregory D. Thorkelson

Introduction

Management of pediatric behavioral emergencies can be extremely challenging, especially as they may often be encountered in suboptimal settings such as general emergency departments or psychiatric emergency services focused on adults. Obtaining a thorough history including triggers and effective interventions for agitation can be critical with children. As with adults, comprehensive evaluation and interventions tailored to the specific patient are essential. Adverse effects of medication and unclear efficacy of PRN agents make blind selection of medications precarious. Attention to the traumatic impact of agitation management on patients, bystanders, and staff is important.

Case 1: Eddy is a nine-year-old with irritable depression and ADHD who has been waiting in the medical ED for a bed search for sixteen hours. As it is a medical ED staffed by adult emergency medicine physicians, they defer to the child psychiatry consultant to write appropriate orders; the consultant has been unavailable and the patient has not had any medications in more than twenty-four hours. After staying up late watching TV, he was awoken early for a blood draw. He is now jumping up and down on the bed shouting obscenities at staff.

Case 2: Molly is a fifteen-year-old who arrives with police after group home staff called for assistance. She is screaming, crying, and still struggling in handcuffs in the back of the squad car. She appears intellectually disabled and is difficult to engage. Any time the officer or the nurse approach (both male) she screams "Not again!" and escalates, kicking at anybody getting close to her. The officer says, "Staff said they were following right behind me, all I know is she is on an involuntary hold. Didn't they call the charge nurse with her history?" The charge nurse reports no call on file.

Case 3: Marco, an eighteen-year-old who is well known from prior admissions with a history of Bipolar I and heavy use of hallucinogens and designer drugs. He is brought in by police in full cardiopulmonary arrest. Shouting from the ambulance bay for help, the officer states that the patient collapsed during a struggle after they tried to restrain him for running down a street naked and psychotic. He was so aggressive that several officers were involved in the takedown and he was held prone, threw up, and stopped breathing at some point.

It seems obvious: children and adolescent should not be hurt, let alone killed, by health care professionals trying to manage acute agitation. While data can be hard to come by, one of the original landmark reports on restraint-related death identified that children were twice as likely to die (Weiss, 1998). Consistent use of scaled interventions favoring verbal

and less-restrictive interventions as initial responses has begun to take hold in psychiatry (Harris & Morrison, 1995; Holloman & Zeller, 2012). It has, however, been slow progress. This chapter will explore the special challenges of managing pediatric agitation in emergency and inpatient settings.

Why Children Are Different

Most clinicians are familiar with the aphorism that children – and adolescents – are not just small adults. From etiology to intervention, numerous differences require different approaches by clinicians to assess and manage agitation in children and adolescents. Major differences include psychopathology, development, psychopharmacology, and legal issues.

Childhood and adolescence are active and dynamic phases in neurodevelopment. As a result, syndromes that are ultimately continuous with adult diagnoses may have significantly different symptom profiles during early stages. In part due to the evolving psychopathology of the illness itself, but also due to the changing substrate of the brain and related symptoms. For example, the threshold for compulsive traumatic reenactment may be different in a young child than in a young adult with PTSD.

Numerous aspects of medication use in children are different from adults, including absorption, distribution, pharmacokinetics, and variability in neuroreceptor expression (Klassen et al., 2008). Additionally, significant differences in lean body mass and body fat distribution can impact medication distribution and half-life. FDA-approved medications are limited and off-label use is normative. Neither approved nor off-label use is assuredly free of side effects, both mild and severe.

Finally, practitioners need to be mindful of specific legal and regulatory differences for children and adolescents. Federal standards for use of restraint and seclusion for children and adolescents require significantly shorter intervals for reviewing or reordering and notification of parents or legal guardians (Centers for Medicare & Medicaid Services, Department of Health and Human Services, 2006). Some states may have specific additional qualifications on the use of restraint and seclusion for youth as well. Many states' chapters of the American Civil Liberties Union provide guidance on this, and the Center for Adolescent Health and the Law has significant resources available by state (English et al., 2010). Additional legal issues that may be of concern to the management of agitation in minors may include:

- Age of consent for psychiatric care, particularly inpatient or emergent psychiatric care
- Processes for involuntary psychiatric hospitalization and treatment of minors, with or without the consent or assent of parents or legal guardians
- Legal standards for and rights resulting from emancipation
- Legal standards for emergency exception to informed consent as it applies to minors
- Legal standards for reporting of child abuse occurring in institutional settings, including injuries occurring during management of acute agitation
- Legal standards for reporting agitation management-related injuries of children occurring at other facilities that are discovered during care at your facility

Finally, the social and ethical framework of emergency child psychiatry poses a specific challenge. Research in emergency settings, with acutely psychiatrically ill patients, and in minors are each restricted by additional ethical safeguards in research design. Put the three of them together, and research is exquisitely difficult and this leaves even the most savvy

clinician to extrapolate data from other fields. The resulting dearth in high-quality research in pediatric psychiatric emergencies has been noted for some time, and has only begun to yield to scientific progress (Goldstein & Horwitz, 2006; Rozel, 2015).

Medical Evaluation of Acute Agitation

Medical etiologies must always be considered and excluded a priori. Initial assessment of the agitated youth should include vital signs and a brief history, if possible. As the acutely agitated patient is often unable or unwilling to provide additional information, history must often be obtained from family members or other care providers.

If possible, a brief and focused physical exam including a neurologic exam should be completed, as well as indicated studies. Consider whether there is a known underlying medical condition that may be playing a role in the patient's current presentation. Medically caused agitation in youth with no prior significant medical history or current abnormalities on exam is very unusual. Particular caution must be used in patients who are nonverbal or unable to communicate due to other barriers.

Acute medical evaluation: Symptoms that suggest a need for emergent medical evaluation include severe headache, abnormal vital signs, dyspnea, disorientation, and changes in memory, incoordination, and focal neurological findings (Nordstrom et al., 2012). As in adults, medical evaluation of the pediatric psychiatric patient should be problem focused and should not use nonspecific screening laboratory or imaging studies (Santillanes et al., 2014).

Agitation may be a component of the initial or subsequent presentation of a variety of medical illnesses. Exploration of such etiologies is based on a balancing of factors, including the patient's prior personal and family history of relevant psychiatric and medical problems. Possible etiologies to consider are shown in Table 18.1.

Drugs of abuse: Drugs of abuse should be considered as a matter of routine, including both intoxication and withdrawal syndromes. Adolescents may be especially likely to use experimental or designer drugs that providers may be unaware of and toxicology screens may not detect. Additional testing may be available, but results are not readily available at the point of care in the emergency setting. Table 18.2 lists substances of abuse to consider. Unlike adults, children and adolescents may have less money to spend on drugs or ability to travel to areas where they may be acquired. As a result, clinicians should be particularly vigilant for illicit use of substances of convenience: cough medicines, alcohol, marijuana, and prescription drugs acquired from homes or peers.

Note that states with increased availability of legal medical or recreational marijuana for adults often see increased abuse of marijuana – and other substances – in adolescents (Hopfer, 2014). Adolescents may be more susceptible to psychotogenic adverse effects of the higher potency cannabis preparations used by medical dispensaries or in edibles, with both acute and chronic exposure (Stone, 2015).

Unintentional exposure to environmental toxins – including drugs of abuse used by parents or siblings and discovered by the child – is also a possible etiology of agitation, especially in younger children. The nature of the presentation will depend on the substance ingested. Symptoms may include alteration in mental status, seizure activity, abnormal vital signs, disturbance in heart rhythm, and metabolic abnormalities. Finally, while once a historical footnote in child psychiatry, lead exposure has reemerged as a concern and

Table 18.1. Possible medical etiologies of agitation (Adapted from Chapman, Katz, & Chun, 2010)

• Brain tumor
• Cerebral hemorrhage
• Meningitis
• Seizure disorder
• Head injury
• Pulmonary insufficiency
• Severe anemia
• Carbon monoxide poisoning
• Electrolyte imbalances
• Hypoglycemia
• Hypocalcemia
• Thyroid disease
• Adrenal disease
• Hepatic failure
• Diabetes mellitus
• Porphyria
• Reye's syndrome
• Wilson's disease
• HIV
• Pain

potential cause for acute and chronic behavioral issues, including agitation and irritability and may need to be considered (Flora, Gupta, & Tiwari, 2012).

Prescription medications: Prescribed medications can be a significant contributor to acute and chronic agitation in children and adolescents. Children – especially younger children or those with comorbid neurologic and neurodevelopmental issues – seem especially sensitive to side effects in general and neurobehavioral side effects in particular (Aagaard & Hansen, 2010). Off-label prescribing of psychiatric medications in children and adolescents is common practice and commonly associated with behavioral adverse effects (Zito et al., 2008). Many child practitioners have known intuitively for years that younger patients seem more likely to develop agitation and other adverse effects from medications; new research supporting this shows young patients to be twice as likely as adults to develop agitation from SSRIs (Sharma et al., 2016).

Chronic medical illnesses: Agitation in medically hospitalized children and adolescents may stem from a number of sources, including boredom, irritability associated with depression or an adjustment disorder, alterations in the sleep/wake cycle, physical discomfort and pain, or other factors. Medical illness itself, polypharmacy, or side effects can lead to agitation

Table 18.2. Substances of abuse that may play a role in agitation

• Alcohol
• Cannabis
• Opioids (i.e., heroin, OxyContin)
• Amphetamine compounds (i.e., Adderall)
• Methamphetamine and methamphetamine-based compounds (i.e., MDMA/ecstasy/Molly)
• Cocaine
• Jimson Weed Tea
• Anticholinergics, diphenhydramine abuse
• Dextromethorphan
• Barbiturates
• PCP
• Hallucinogens
• Anabolic steroids
• Synthetic cannabinoids (i.e., K2)
• Synthetic cathinones (i.e., bath salts)

through various mechanisms, including delirium (Zavodnick & Sternlicht, 1997). Burn injuries, sepsis, transplants, and multiple organ failures are more common causes of delirium in hospitalized youth and may be associated with agitation (Paddick, Kalaria, & Mukaetova-Ladinska, 2015). For the chronically medically ill, pain is associated with agitation, particularly in the intellectually limited population (Ageranioti-Bélanger et al., 2012). Even once pain is well managed, risk continues: analgesic and anesthesia withdrawal is widely associated with increasing agitation (Anand et al., 2010; Cole et al., 2002). Patients with underlying chronic neurologic, metabolic, or metastatic illnesses may require an especially thorough evaluation to exclude or manage medical contributors to agitation.

Aside from the challenges of determining etiology for acute agitation in chronically medically ill or hospitalized children and adolescents, drug interactions are particularly important with the frequent use of polypharmacy in this population. Indeed, according to one retrospective cohort, after seven days in the hospital, the average child received up to thirty-five distinct medications (Feudtner et al., 2012). Multiple pharmacodynamic considerations are important to note and monitor in chronically medically ill individuals receiving antipsychotic medication, especially if in multiple doses. Anticholinergic side effects are particularly salient as antipsychotic dose escalation in the setting of anticholinergic toxicity is associated with increasing behavioral derangement (Gee, Lin, & Tobias, 2015). Furthermore, constipation is already problematic in many chronically ill and hospitalized children and adolescents, and worsening constipation can be associated with increases in discomfort and agitation. Finally, conditions involving renal or hepatic impairment can increase the likelihood of adverse effects from the use of pharmacologic agents for agitation management.

Psychiatric Evaluation of Acute Agitation

Assessment of the acutely agitated patient can be quite challenging. In emergency settings, clinicians will often be unable to complete the full psychiatric evaluation until after the patient calms. Therefore, the psychiatric evaluation in the setting of acute agitation often involves an initial brief evaluation to guide the initial treatment approach. De-escalation strategies should occur concurrently with the initial assessment and mental status exam. After further intervention and improvement in the patient's agitation, a more thorough psychiatric evaluation can be undertaken.

Initial screening should involve assessment for delirium. Like adults, it is not uncommon for pediatric patients to have under-recognized delirium, especially in medical settings such as emergency departments and intensive care (Schieveld et al., 2009; Turkel & Tavaré, 2003). As with adults, an altered or wavering level of awareness, new-onset difficulty sustaining attention, and known or suspected medical issues or toxin exposure should be considered risk factors and prompt further evaluation.

The examiner should next consider whether the patient has a chronic cognitive issue, such as intellectual disability or history of brain injury. The next question is whether there is substance intoxication or a withdrawal syndrome. Subsequently, the clinician should consider whether the agitation is due to a known psychiatric disorder. If there is no known history of a psychiatric disorder, further assessment should be undertaken to ascertain the underlying cause (Stowell et al., 2012). See Table 18.3 for issues to consider in the differential diagnosis of acute agitation.

When the patient has calmed, further assessment can continue. History from parents or other caregivers can be critical in evaluating causes of agitation. Monitoring interactions between the child and caregiver may also illuminate the role of interpersonal interactions

Table 18.3. Differential diagnosis of acute agitation

• General medical condition
• Delirium
• Substance intoxication or withdrawal
• Pervasive developmental disorder
• Bipolar disorder
• Depression
• PTSD with or without dissociation
• Anxiety
• Psychotic disorder
• Conduct disorder or oppositional defiant disorder, including instrumental behavior to intimidate or manipulate health care providers
• Attention deficit hyperactivity disorder
• Sensory deficits (i.e., blindness, deafness)
• Severe communication disorder (childhood aphasia)

with major attachment figures in mitigating or exacerbating agitation. Note that not all agitation requires a psychiatric of medical diagnosis; a person is entitled to be angry, upset, or mad because of their circumstances without becoming encumbered with a diagnosis. Not every irritable child or adolescent is necessarily medically or psychiatrically ill.

That said, severe agitation is often associated with high levels of distress and impulsivity. These in turn are highly associated with risk for suicide and aggression. Any meaningful evaluation of agitation should also attend to these potential concerns.

Environmental, Behavioral, and Verbal Interventions

Our least restrictive interventions include combinations of environmental, behavioral, and verbal interventions short of physical intervention. Effective use of these interventions can be difficult to achieve with untrained or unskilled staff or in inappropriate physical environments. Prevention, as always, can be critical. Short of physical interventions and medication (i.e., highly restrictive interventions), several other less restrictive and intermediate restrictions may be considered in inpatient, residential and some emergency settings as in Table 18.4.

Assessment prior to acute agitation: A description of agitation obtained during assessment should be as specific as possible. A chief complaint or reason for referral of "agitation" or "aggression" is all but useless. Often, the instruction to "describe it like you are directing a movie" can be helpful. Understanding behaviors of caregivers that may contribute to agitation or fail to de-escalate the patient can be illuminating.

Less informative: "He gets upset and angry when he has to do schoolwork."

More helpful: "He avoids doing his reading. When I put the book in front of him, he bats it away so I hold him in my lap. Now when I do that he bites my arms and runs away and that's when he gets a paddling."

Or: "He does his math homework just fine, but when it comes to reading, he just won't do it. As long as we don't force the issue, he's fine, but he will yell and then hit me rather than do

Table 18.4. Spectrum of interventions

Less restrictive	Intermediate	More restrictive
• Distraction, redirection, and interruption • Reflective time in room • Wing assignment/limits • 1 on 1 support • Increased observation levels • Unit and off-unit privilege restrictions • Sensory room	• Reflective time in room • Wing assignment/limits • 1 on 1 support • Increased observation levels • Unit and off-unit privilege restrictions • Sensory room • Voluntary medication	• Escorts • Seclusion • Manual restraints • Mechanical restraints • Seclusion • Involuntary medication

Table 18.5. A good agitation history guides psychosocial interventions

• Typical agitation episode description (i.e., how long does it last, what does the patient do, and how often do they recur)
• Common triggers for agitation and aggression – including events, language, or behaviors that may provoke or worsen agitation
• Major events that may be linked to acute increases in agitation
• Warning signs of increasing agitation or imminent aggression
• Preferred calming and distracting interventions
• Preferred staff / staff gender (with the understanding that they may not always be available)
• Preferred positive reinforcements for maintaining good behavioral control
• Known effective and ineffective PRN medications in the patient or first degree family members

his reading. He's been like this since his teacher had him read in front of class and the other kids teased him because of his speech impediment."

Or: "He was moody and sullen for so long I didn't think he had the fight in him but for the past two weeks, he has been angry and shouting all the time. The doctor said that his medication might cause irritability, but he started that fluoxetine a month ago."

Luckily, not all patients with agitation present in acute distress. Often the first clinical episode of agitation in a child or adolescent in the health care setting has occurred after assessment has already begun. When possible, discussion with a patient or parent prior to an episode of agitation can provide valuable information as outlined in Table 18.5.

Sometimes this information can be obtained as part of the assessment in the emergency department or during the intake to the inpatient unit. It may make sense to prioritize gathering this specific information early in the assessment, especially if there is concern for future agitation. In an emergency department with a significant wait time, prepared self-report forms can be used to gather this information from the patient and family while aiding to keep them distracted during their wait. Often, this detailed history of effective and ineffective interventions is gathered painstakingly through the course of multiple presentations or admissions – to wit, through clinical trial and error.

While oft neglected, debriefing of staff and patient after restraint, seclusion, or aggressive episodes provides invaluable data about triggers and effective and ineffective interventions to guide future interventions. Sharing this information with current and future treatment providers can be an invaluable tool to prevent or mitigate agitation. Discussion of these factors under explicit headings in documentation – especially initial evaluations and discharge summaries – is critical in conveying these lessons learned to future providers. Discussion of these factors with the patient, done properly, can also be highly therapeutic.

Staff, positioning, and body language: When the situation permits, getting physically on the level of an agitated child or adolescent can be helpful; it is all too easy for adult staff to loom over children, intentionally or accidentally. Being on the same level supports engagement and is experienced as a sign of respect by the child. Children, like adults, may not take well to directives from a person standing above or over them.

Similarly, considerations of the number and gender of staff are worth attention. While physical presence of additional staff can be reassuring to staff trying to de-escalate a child or adolescent, too many staff may be experienced as provocative to the youth, signaling that a physical intervention is a foregone conclusion. When possible, an excessive "show of force" should be avoided. Finally, and especially if physical intervention seems likely, male staff restraining female patients should be avoided both due to the potential distress of the patient and the unnecessary risk accusations of impropriety that may ensue.

Of note, agitation in emergency and inpatient settings may be provoked by interactions with parents, guardians, or group home/residential staff who may be visiting or communicating with the patient by phone. Care must be taken to balance the potential triggering effects of such contacts with the putative goal of reintegration into the natural or original environment (e.g., successfully returning home). It is difficult to make progress in an inpatient setting when caustic interactions with a parent continue to escalate a child – but it is impossible to successfully discharge that child home without family work.

Environmental adaptation and facility design: A psychiatric emergency service (PES) or ED lacking specific areas for children and adolescents may be unavoidable, but is also an invitation to adverse outcomes. Specialized and separated areas that provide privacy and age-appropriate distractions while protecting children from seeing or hearing care of other children or adults can be essential. Seeing other psychiatric patients agitated (and restrained, secluded, or medicated) or the management of medical or surgical emergencies in the general ED can be extremely upsetting and can be a source of unneeded trauma for young psychiatric patients.

Additionally, many traditional ED settings often have limited structural resources to safely contain children and adolescents. What results can be a de facto seclusion where they are kept in a confined area such as an isolation room, stripped of the potentially dangerous accouterments of the ED (e.g., otoscopes, oxygen lines, IV poles, and television controls) with a sitter restricting their ability to leave.

Removing children and adolescents, especially those who may have autism spectrum or sensory integration issues, from areas where they may become overstimulated can be extremely important. Letting the youth rest in a waiting area may seem like a good idea until an ambulance pulls up next to the window with lights and sirens running. Media choices in patient care and waiting areas should be age appropriate or, at least, not excessively inappropriate. Police procedurals with graphic depictions of physical and sexual violence fill the airwaves and few children will benefit from their influence. Put bluntly: *Law and Order SVU* is a perennially poor choice for a waiting room filled with children, psychiatrically ill or otherwise, with often endemic rates of past trauma. Even ostensibly benign media choices can be unnecessarily distressing to many: violent and traumatic deaths of parents can be seen in a startling number of Disney and Pixar films, for example. Upsetting media choices can be a trigger for trauma reactions and agitation that can be easily avoided.

Distracting, interrupting, and redirecting: Skillful staff can often effectively distract, interrupt, or redirect a child or adolescent as they begin to escalate. Distracting is more passive, often done without even acknowledging that the youth is escalating. A passing question – "Are you thirsty? Would you like a juice?" or "Hey, what's that comic book you have there?" – can be enough to change the child's focus and help them regain self-control. Interrupting may

explicitly reference the escalating behavior – "Before you get too upset, let's change directions and talk about something different." Redirecting involves actively assigning a new task, such as "Okay, I see you are upset with your mom, why don't you come over to this room and tell me why while she stays in the waiting area for a little bit?" Such interventions may be paired with gentle touch – a hand on a shoulder or upper arm.

Depending on staff training and availability, relaxation and calming exercises can be employed. Such interventions help in a variety of ways, including distracting the youth and providing active calming. Additionally, this training helps the youth attain some degree of self-control over their own agitation, which can be therapeutic. Simple interventions including square breathing and other mindfulness techniques may be helpful both acutely and prophylactically (Bögels et al., 2008; Schonert-Reichl & Lawlor, 2010; Singh et al., 2011).

Verbal de-escalation: Verbal de-escalation is a preferred intervention in essentially all settings and populations when time and circumstances permit (Richmond et al., 2012). Verbal de-escalation in children and adolescents does not differ significantly from adults. The guidance of calm tone, simple language, and clear statements and directions work equally well with children as with adults, although extra care must be taken to use age-appropriate language. Staff are advised that lapsing into their "home role" of mother or father, manifest in the tone or content of their voice, may be no more effective with the adolescent in their treatment setting than with the adolescent in their home; such lapses can be surprisingly easy and may be perceived more quickly by the youth than by the staff.

Pharmacologic Interventions

Medication management of pediatric agitation is risky. There is no medication with FDA approval for management of acute agitation in children and adolescents. The authors are aware of no published controlled trials of medications for acute agitation in children and adolescents. Chronic agitation in children with autism spectrum disorder may be benefitted by aripiprazole or risperidone, although both also have significant side effects (Young & Findling, 2015). A retrospective study found few differences and general efficacy for both IM ziprasidone and IM olanzapine in aggressive children and adolescents (Khan & Mican, 2006).

Added to the dearth of data is the concern that children may be more prone to paradoxical agitation from benzodiazepines and sedating antihistamines diphenhydramine and hydroxyzine than adults (Mancuso, Tanzi, & Gabay, 2004; Vlajkovic & Sindjelic, 2007). So, what is a practitioner to do in the management of acute agitation? Optimally, good clinical history may aid in the selection of a medication that is more likely to be beneficial than others. Considerations may include:

- What PRN medications or classes of medications have been helpful (or ineffective, or harmful) before for this patient? (e.g., during triage, when asked about allergies, the patient reports past severe dystonia with haloperidol)
- What medications is the child on currently that are believed to be helpful or harmful (e.g., a patient believed to have shown improvement on PO ziprasidone may benefit from IM ziprasidone if acutely agitated)
- Is there a known family history of therapeutic or adverse response to medications especially for agitation (e.g., mother reports the patient's older sibling does very well with hydroxyzine but had dystonia with aripiprazole)

If there is inadequate history, clinicians may wish to consider optimal medications for empirical management of pediatric agitation to be those which:

- Have good evidence or FDA approval for management of agitation in adults
- Have some evidence of tolerability or an FDA indication for something else in children and adolescents
- Have ready availability in both PO and IM formulations
- Have dosings that are easily calculable for weight and PO vs. IM administration

This is a short list but does include hydroxyzine, diphenhydramine, lorazepam, chlorpromazine, and aripiprazole. A few general considerations, however: sedating antihistamines and benzodiazepines may lead to paradoxical agitation. Aripiprazole is prone to causing akathisia. Chlorpromazine has many adverse effects and is difficult to use IM given the low concentration of injectable solution.

Front-line clinicians widely use second-generation antipsychotics for management of agitation, but these are prone to some risks, as will be discussed later.

Second-generation antipsychotics and extrapyramidal side effects: The pharmacologic mainstays of pediatric agitation management are atypical antipsychotics. Numerous potential side effects need to be considered and may limit their efficacy and safety in this population.

Dystonic reactions and akathisia are particularly relevant to acute administration as rates are higher with first-generation antipsychotics, with the highest rates of dystonia occurring in young males (Addonizio & Alexopoulos, 1988; Kumar & Sachdev, 2009). As akathisia often presents several hours after dosing with a neuroleptic, the anxiety, restlessness, or agitation that develops may be misperceived as further agitation, leading to dose escalation, especially in children, who may lack the communication skills or vocabulary to describe the experience (Van Putten, 1975). Youth are at greater risk for dystonias than adults, including potentially life-threatening involvement of pharynx and larynx (Mathews et al., 2005).

Neuroleptic malignant syndrome (NMS), an uncommon but potentially lethal complication of antipsychotic treatment, involves severe hyperthermia and muscle rigidity associated with a number of other possible symptoms. Less common with atypical antipsychotics, the presentation in children and adolescents taking atypical antipsychotics who develop NMS differs from that of adults in important ways. In one case review, roughly half of pediatric patients with NMS from atypical antipsychotics did not present with both rigidity and fever, two symptoms required for DSM-IV diagnostic criteria. Indeed, only two out of five patients met full criteria for NMS. Importantly, CPK was elevated in all cases reviewed (Neuhut, Lindenmayer, & Silva, 2009). Conversely, there was no difference in presentation between adults and children who developed NMS while primarily taking typical antipsychotics (Silva et al., 1999).

Drug interactions: In general, pharmacokinetic interactions with antipsychotic medications are primarily mediated by alterations in cytochrome P450 enzyme activity, particularly CYP 1A2, 3A4, and 2D6 (Murray, 2006). Diphenhydramine is commonly used because its over-the-counter status lends it the impression of safety. Anticholinergic risks notwithstanding, it is also a potent 2D6 inhibitor; drug interactions can be significant and easily missed.

Cardiac risks: Additional notable potential side effects with second-generation antipsychotics include sedation, QTc prolongation, anti-cholinergic side effects, including constipation, decreases in blood pressure leading to increase in fall risk, and increased risk of seizure

(Bleakley, 2012). Providers should be equally vigilant in monitoring these side effects in children and adolescents as they are in adults, especially in the context of polypharmacy or repeated dosing. QTc prolongation is seen with antipsychotics in children and adolescents (Blair et al., 2005). If repeated medication doses are required and a strong family history of sudden deaths or other factors are identified, including a history of syncope in the patient, electrocardiographic monitoring may be warranted. Guidelines suggest altering therapy if sustained resting heart rate is >130 beats per minute, the QRS is >120 milliseconds, the PR interval is >200 milliseconds, or the QTc is >460 milliseconds (Gutgesell et al., 1999).

Sedation: Sedation in the psychiatric setting is not the desired outcome of agitation pharmacotherapy, but is often a consequence of medicating aggressive patients. Optimally, medication relieves distress and mitigates agitation to support the processes of assessment and therapeutic engagement. It is difficult to engage or assess a child who is asleep or drowsy. In a comparative study of long-term use of antipsychotics in children and adolescents, sedation was more likely to occur at higher doses of medication, with more sedating medication such as olanzapine, and with concurrent illicit drug, over-the-counter medication, or certain prescription drug use (Sikich et al., 2003).

Given the broad and significant risks of pharmacotherapy – especially in youth with unknown clinical histories – the value of early evaluation of triggers and management strategies becomes self-evident. Clinicians may also wish to consider delaying pharmacologic interventions until history can be appropriately reviewed or collateral obtained – especially if the behavior can be contained with seclusion or restraint and such information can be available in a timely manner. Spending ten minutes to review history can seem like an ordeal when there is a screaming adolescent in the background, but the time will be more than saved if a medication known to trigger paradoxical agitation is avoided.

Seclusion and Restraint

In the setting of acute agitation, seclusion and restraint may be considered. Seclusion is defined as the involuntary confinement of a patient alone in a room or area from which the patient is physically prevented from leaving. A restraint is defined as any manual method, physical or mechanical device, material, or equipment that immobilizes or reduces the ability of a patient to freely move arms, legs, head, or body (Centers for Medicare & Medicaid Services, Department of Health and Human Services, 2006). General considerations for children and adolescents and the use of seclusion and restraint are much like adults (Knox & Holloman, 2012). Less restrictive options including open seclusion are universally preferable; time out and sensory rooms are increasingly common in child and adolescent treatment settings and can be invaluable.

Restraints: Restraints can include tape, cuffs, straps, or hands, applied in any manner on the body to restrict movement. These more restrictive interventions should be used only when other less restrictive means have failed to control the agitation. It is also important to note that seclusion and restraint should not be used for coercion, discipline, or staff convenience, and only for the immediate safety of the patient or others. The benefits of restraint or seclusion in controlling agitation may include mitigating the risk of harm to self or others and allowing for assessment and treatment of a potentially emergent injury or medical condition. Risks of the intervention include potential injury to the patient during the process up to and including death (Nunno, Holden, & Tollar, 2006).

Children and adolescents are anatomically different from adults in critical ways that impact restraint use. Joints may have more laxity than adults and relative hand or foot size may present challenges in physical restraints. When a buckling restraint is used, continuously variable adjustment is preferred over devices with holes or slots. The latter device creates a risk of a restraint that is either too loose and easy to escape or too tight and risks distal pain or injury. Additionally, many emergency departments that have a bed set up at all times with restraint devices to rapidly deploy on the arrival of an agitated patient; when used with a child, their shorter stature may require uncomfortable or dangerous positioning of the limbs. Restraint devices for hospital beds for children should always be modified for the height and size of the child. Different physical techniques may also be needed for escorts and manual restraints with children and adolescents.

Seclusion: As with adults, children who are prone to escalate or self-injure may be poor choices for seclusion. Small structural gaps in a seclusion room (e.g., a gap between the door and the floor) can pose greater risk for a child than an adult because the child may be able to get their fingers into such crevices more easily. Children who have been abused by being locked in a room or closet by a caregiver may show a trauma response when placed in seclusion. Finally, since observation windows in most seclusion rooms are placed at eye level for the adult staff observers, smaller children may not see the staff. Unless the staff is verbally communicating with the child, the child may fear they have been abandoned, which is unlikely to help them calm.

Monitoring: During the course of restraint, monitoring of the patient's airway, vital signs, and assessment of extremities for neurovascular functioning should be undertaken. As children whose condition is deteriorating will often show evidence of respiratory compromise first, there should be a low threshold for use of continuous pulse oximetry monitoring (Masters & Wandless, 2005). Use of a prone position should be avoided during restraint due to risk of respiratory compromise. Basket holds, once quite common in child and adolescent treatment settings, should be categorically avoided.

Intellectual and Developmental Disabilities

It is beyond the scope of this chapter to delve deeply into this issue. It is worth noting that prevalence of autism spectrum disorders are increasing in younger cohorts and their patterns of agitation can be significantly different. Additionally, while physical interventions may be more commonly used in this population, they are not necessarily more effective (Gaskin, McVilly, & McGillivray, 2013). Receptive and expressive language issues are common and a significant risk factor for aggression (Brownlie et al., 2004). Interventions adapted to the specific needs of autism spectrum youth include heightened awareness to sensory stimuli, including tactile experiences (e.g., adhesive tape, IV placement "done routinely," but not specifically needed in a psychiatric patient in the ED), use of visual cues or pictograms along with verbal cues, and somatosensory supports (e.g., stim toys) may be beneficial (McGonigle et al., 2014).

Trauma and Agitation

Psychological trauma can play a role in many aspects of childhood agitation. Trauma can be a cause of agitation or a result of clinical interventions. Experiencing restraint or seclusion

can be traumatic for the child. Witnessing or participating in the intervention can be traumatic for other patients, family, and even staff.

Agitation – both in response to trauma-specific triggers and as a form of general psychomotor activation – is a common symptom in posttraumatic stress disorder, and trauma history itself is a common finding in children and adolescents presenting for emergency or inpatient care. Additionally, given the nature of trauma, it is often not the type of history that a child (or adult) will willingly or quickly disclose to strangers or in new environments (Fallot & Harris, 2001). While history obtained through interview or review of available records may be useful, the general use of trauma-informed care as a universal precaution may be a more efficient approach. Trauma-informed adaptations in assessment and care of children and adolescents can include expressly providing children permission not to discuss trauma, availability of same-gender staff, especially during searches and physical interventions, providing for privacy without making a child feel isolated with the adult interviewer, respect for personal space and modesty, and limiting exposure to triggering peripheral events (ranging from seeing other patients agitated or restrained to inappropriate content on televisions in waiting and patient care areas) (Harris & Fallot, 2001).

Certain behaviors of agitated youth may suggest past trauma. Youth who stop talking, moving, or interacting once a physical intervention is initiated in response to agitation may be seen as compliant but may actually be dissociating. A youth may start to use specific but incorrect names while trying to interact with staff if they are dissociating or having a flashback to a prior restraint. Some youth with a history of sexual assault may respond to perceived threats (e.g., staff responding to a behavioral emergency) by stripping or engaging in sexualized behavior (e.g., masturbation or trying to touch staff's genitals or breasts during restraint) as a form of re-enactment or flashback. Notably, some youth with a history of institutionalization may also have learned that this can be an effective strategy to keep staff away or delay a restraint or seclusion. As such, while such behavior may prompt exploration of possible prior trauma history, it should not be considered conclusive evidence thereof. Any experience of being restrained or secluded may, in and of itself, become a traumatic experience for the child going forward, sabotaging his or her engagement with providers and clinical progress (Mohr, Mahon, & Noone, 1998).

Witnessing the restraint or seclusion of an agitated child or adolescent can be extremely distressing to others. Other patients witnessing the agitation and intervention may become concerned for their own safety, worry about whether they could become that agitated or what would happen to them if they did, or experience the event as a triggering of their own past trauma. Trauma responses in parents hearing about the restraint of their children – especially in parents who have a history of being restrained themselves – may be significant and require clinical attention when they are informed of the event. Finally, the impact on staff themselves should not be discarded and part of the debriefing after an event should include assessment of staff response; few staff would say that restraining an agitated child is a high point in their day. A good clinical leader will be attentive to all staff after such an event; the staff member who is nonchalant and overly comfortable, even enthusiastic, about the restraint of a child may be as concerning as the staff who appears upset or distraught.

Conclusions

Agitation is a common challenge in a variety of pediatric settings. Careful evaluation needs to explore all possible etiologies in a manner that is sensitive to the diagnostic and

epidemiologic issues specific to children and adolescents. Blind use of adult interventions including adult-dosed medications or adult sized restraints can be ineffective or even dangerous. Finally, attention should always be paid to the role of trauma as an etiologic factor, iatrogenic effect, or nidus of staff burnout when working with agitated children.

Take Home Points

- Pediatric agitation is multifactorial and requires assessment and management tailored specifically to the age and history of the patient.
- Pharmacotherapy of acute agitation, especially in the absence of adequate history, should be undertaken with caution.
- Trauma can play a number of roles in the etiology and outcome of agitation for patients, bystanders, and staff.

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