Managing Delirium In The Emergency Department: Tools For Targeting Underlying Etiology

Abstract

Delirium represents the complex junction between vulnerable patients, medical conditions, and environmental factors. Given the varied presentations of this disorder and the emergency department clinical environment, recognition and treatment may be challenging. Delirium can be diagnosed using validated standardized screening tools such as the Confusion Assessment Method. Management of delirium is directed towards rapidly treating the underlying medical condition while preventing and managing the behavioral symptoms with nonpharmacological (first-line) and pharmacological (second-line) interventions. In the severely agitated patient, pharmacological treatment tailored to the patient's age and comorbidities may be required as the initial treatment to facilitate evaluation and management of the underlying medical condition. Effective risk stratification and triage tools can positively impact patient and staff safety, as well as patient outcomes.
Opening Cases

It is the beginning of another Saturday night shift, and as you walk in, you see security and the outgoing attending wrestling a large 20-something-year-old man to the bed. He is yelling about a government conspiracy and his right to freedom of speech. A nurse injects medicine into his left deltoid. You are looking forward to the sign-out on this gentleman and wonder what he was injected with and whether there was another way to manage him.

As your colleagues manage the young man, you scan the board and see that the next patient to be seen is a 79-year-old lady who presents for altered mental status. As you approach the bed, you do not see anyone with her. You begin to take her history, and observe that she seems a bit lethargic and is tangential in her thinking. She is able to tell you that she lives with her husband and has a history of high blood pressure and confusion. She then mentions that you look like a friend of hers from work and asks whether you are married. You see your colleagues finishing up with their patient, so you extricate yourself and return to the physician station wondering why this patient is so lethargic and why her attention is so decreased.

Finally, just as rounds are about to begin, you see an intubated patient in the first resuscitation bay starting to buck at his vent. You notice his hands and feet are in 4-point restraints. After inquiring about the reason for his visit, you are informed that he is a chronic alcoholic who had been attempting to detoxify at home and has come in today in delirium tremens, requiring intubation and large doses of benzodiazepines. You are concerned about the 4-point restraints, which you know are not favored, and you wonder if there was a better (and safer) way to manage the patient’s agitation.

Introduction

Delirium is a complex neuropsychiatric disorder that often manifests secondary to a discrete medical condition. The Diagnostic and Statistical Manual of Mental Disorders, Fifth edition (DSM-5) describes delirium as an acute (usually developing over hours or a few days) and/or fluctuating disturbance in attention and cognition due to a medical condition, intoxicating substance, or multiple etiologies.

In the younger population, delirium encompasses common chief complaints such as agitation and altered mental status. Among the elderly population, it is estimated that 7% to 24% of patients presenting to the emergency department (ED) will have delirium, and up to 80% of critically ill intensive care patients will have delirium. A diagnosis of delirium carries with it significant morbidity and mortality, in addition to increased utilization of resources.

Studies have shown that most emergency clinicians do not screen for or document their findings of delirium. Because of this lack of screening and the fluctuating course of the condition, the overall incidence of delirium in the ED is unknown. Some posit that emergency clinicians are aware of the impact of delirium on patient outcomes but are not knowledgeable about its diagnosis and management.

Emergency clinicians are trained to manage the overt signs of delirium while concurrently searching for its underlying etiology. However, gaps in screening, knowledge, and understanding contribute to a missed diagnosis rate in the range of 54% to 89%. Additional complicating factors include the varied presentations of these patients and the inherent time and environmental pressures of the ED clinical environment. Diagnostic accuracy has been poor, and much of the emergency medicine literature on delirium is focused on the issue of recognition. Regarding the prevention and management of delirium in the ED, current guidelines are generalized from inpatient and postoperative studies. This issue of Emergency Medicine Practice focuses on the challenge of evaluating and managing the patient with delirium in the ED using the best available evidence from the literature.

Critical Appraisal Of The Literature

A literature search was performed on PubMed using the search terms delirium OR agitation OR acute confusion AND emergency. Additional references were obtained from the bibliographies of the articles reviewed. A search of the Cochrane Database of Systematic Reviews yielded several reviews regarding the pharmacological management of delirium, as well as 1 review of multicomponent interventions for preventing delirium in hospitalized patients, and 1 study protocol for interventions to prevent delirium in patients in institutional long-term care.

Clinical policies in the National Guidelines Clearinghouse (www.guideline.gov) and the American College of Emergency Physicians (ACEP) were also searched. Emergency medicine societies weighing in on the diagnosis and management of delirium include ACEP, the Society of Academic Emergency Medicine (SAEM), the Emergency Nurses Association (ENA), and the American Association of Emergency Psychiatry (AAEP). In 1999, ACEP published the “Clinical Policy for the Initial Approach to Patients Presenting with Altered Mental Status,” which critically reviewed the literature and provided an evaluation framework; however, it did not address specific pharmacological interventions for delirium. While altered mental status, as a chief complaint, is not sensitive, it has been noted to be specific for delirium, when documented. In 2013, ACEP, the American Geriatrics Society, ENA, and SAEM jointly published “Geriatric Emergency Department Guidelines,” which included recommendations regarding the workup and management of delirium in elderly patients.
patients presenting to the ED.\textsuperscript{15} Various regional and national guidelines for the diagnosis and management of delirium in inpatient settings also exist. Within these guidelines, specific delirium recommendations for the ED are rare, but they can be found in the United Kingdom’s National Institute for Health and Care Excellence (NICE) 2010 guideline, “Delirium: Diagnosis, Prevention and Management,” and in “Delirium: Model of Care,” from the Department of Health of the State of Western Australia.

Overall, the evidence to guide the screening and diagnosis of delirium in the ED is robust, while the literature regarding the subsequent management of delirium in the ED is less exhaustive and more reliant on expert consensus or data extrapolated from inpatient settings. The populations studied in the literature skew heavily towards the elderly patient. The emergency medicine literature reflects the realities of the ED practice environment, with an emphasis on the management of the acutely agitated patient, in contrast to the work done in other specialties that focuses on prevention and management of delirium in the elderly patient. This dichotomy provides unique challenges in the interpretation of the existing evidence.

## Epidemiology
Delirium represents a large burden on healthcare systems, and particularly those that serve the geriatric population. A review of ED delirium in the elderly found that 7\% to 20\% of patients admitted through the ED experience delirium.\textsuperscript{4} The presence of delirium increases the cost of each visit by approximately $2500 per patient, representing a total annual cost of $6.9 billion, or an increase in hospital charges of 27\% for each patient.\textsuperscript{16,17} Contributing to these additional costs are increased hospital length of stay (LOS), increased intensive care unit (ICU) admissions, increased staff support for restraints, as well as a general functional decline of patients.\textsuperscript{5,18,19} Furthermore, patients with delirium require increased social support and have questionable ability to comply with medications as prescribed, leading to difficulties in discharge planning and more frequent nursing home placement.\textsuperscript{5,15,19}

Once patients are discharged from the hospital, they have an increased 30-day readmission rate.\textsuperscript{5,20} Estimates for the total cost to the healthcare system run between $38 billion and $152 billion.\textsuperscript{5,10,21} In addition to the financial costs, there are human costs. Delirium is a predictor of mortality, both independently as well as in various disease states, such as pneumonia and congestive heart failure.\textsuperscript{18,20,22–25} By some estimates, the presence of delirium portends mortality rates comparable to sepsis and myocardial infarction.\textsuperscript{9,17}

## Pathophysiology And Subtypes
Delirium is an acute confusional state on the spectrum of acute brain dysfunction that is suspected to be precipitated by an underlying medical etiology. Current research in delirium suggests 2 distinct, but sometimes coexisting, etiologies: (1) Direct brain insults such as hypotension, hypoxia, trauma, and toxins; or (2) aberrant stress responses induced by physiologic insults such as infections or surgery.\textsuperscript{26} While both categories represent end-organ damage of the brain, there is overlap between the physiologic underpinnings of the 2 groups, and this dichotomy serves as a framework for understanding delirium.\textsuperscript{27} Direct brain insults are defined as entities that affect the energy supply or consumption of the brain or have otherwise disruptive effects on the brain architecture and pathways. Aberrant stress response more closely describes the cellular response to systemic insults. The current belief is that stressors and the ensuing sympathetic surge are associated with a preponderance of inflammatory cytokines, resulting in an imbalance of neurotransmitters. There is an increase in the dopaminergic tone and a decrease in acetylcholine in the central nervous system; however, there is some thought that the different psychomotor subtypes each have a unique mix of neurotransmitter dysregulation, and delirium represents the final common pathway of multiple pathologic neurotransmitter pathways.\textsuperscript{7,28,29}

Physiologically, this description of delirium as both a result of local and systemic etiologies agrees with the current model correlating patient vulnerability factors and both patient and environmental precipitant factors for delirium. (See the “Differential Diagnosis” section, page 4.) Additionally, these cellular changes inform and are consistent with the current understanding of the pharmacological treatment of delirium using antipsychotic agents with antidopaminergic activity.

## Subtypes Of Delirium
There are 3 psychomotor subtypes of delirium: (1) hypoactive, (2) hyperactive, and (3) mixed type. The hypoactive subtype can be correlated to Richmond Agitation and Sedation Scale (RASS) scores of -3 to -1 (moderate sedation to drowsy) while the hyperactive subtype is associated with RASS scores of +1 to +4 (restless to combative).\textsuperscript{7} See Figure 1 (page 4) for a link to a tool useful in determining delirium subtype. The third type is a mixed-type delirium and is associated with a more persistent course.\textsuperscript{30} Older patients are more likely to present with the hypoactive subtype.

Excited delirium syndrome is a newly defined entity representing a special case of hyperactive delirium associated with a metabolic derangement and increased mortality.\textsuperscript{31,32} There is some variabil-
Differential Diagnosis

The differential diagnosis for delirium is divided into the underlying medical condition precipitating the patient’s change in mental status and an alternative diagnosis that can be confused with delirium. It is useful to categorize this first category of conditions into those that are critical, emergent, and iatrogenic. (See Table 1.)

In terms of an alternative diagnosis, dementia is the main entity of concern. Dementia and delirium often coexist, and there are multiple overlapping features and a similar theorized pathophysiology. Without the proper history, it may be difficult to determine the time course and acuity of the symptoms, which are the key differentiating features. Table 2 (page 5) delineates the identifying features of each process. Lewy body dementia can be particularly challenging, as it is characterized by fluctuations in cognition and hallucinations, and its presence potentially redirects management, given the increased extrapyramidal side effects with antipsychotic use.

However, this type of dementia is a diagnosis of exclusion and underlying medical causes should be evaluated first.

Common categories of medical precipitants include: Infection (cited in 16% to 67% of cases, with urinary tract infections and pneumonia predominating; metabolic derangements (including sodium and calcium derangements); intracranial derangements (including cerebrovascular accidents and intracranial hemorrhage); and intoxication and withdrawal syndromes.

One major category of precipitants often under-evaluated, especially in the older population, is prescribed medications. Beers criteria for potentially inappropriate medications describe several drugs.
and classes that are prone to causing delirium in the elderly: tricyclic antidepressants, anticholinergics, benzodiazepines, chlorpromazine, corticosteroids, H₂-receptor antagonists, meperidine, sedative hypnotics, and thioridazine. From the emergency clinician’s perspective, it is difficult to determine whether a single dose of these medications would precipitate delirium. A 2011 systematic review recommended that ED providers avoid meperidine and prescribe oxycodone if opioids are necessary, but otherwise, there was insufficient evidence to make recommendations regarding other classes, such as benzodiazepines, antihistamines, steroids, nonsteroidal anti-inflammatory drugs, antidepressants, cardiac glycosides, and anti-Parkinsonian agents. For these agents, emergency clinicians should continue to use clinical judgment to weigh the risks and benefits of medication administration.

The current understanding of delirium notes an interplay between precipitating factors (as noted in Table 1) and what are commonly identified as vulnerability factors. (See Table 3.) The ACEP Geriatric Emergency Department Guidelines emphasize the presence of the following as significant risk factors for delirium: (1) Vision or hearing impairment, (2) decreased cognitive ability, (3) severe illness, and (4) dehydration. The presence of 1 or 2 factors increases the risk of development of incident delirium by 2.5 times. The presence of 3 or 4 risk factors increases the incidence by > 9 times. Finally, underlying neurodegenerative diseases (such as dementia) have the strongest association with delirium. Two-thirds of geriatric delirium patients who present to the hospital have underlying dementia. In both mouse and human models, it has been shown that there is a direct dose-response curve, with increasing neurodegenerative disease being associated with increased delirium.

Once the patient arrives to the hospital, interventions by medical staff can also precipitate delirium, including physical restraints, malnutrition, the addition of 3 or more medications, introduction of a bladder catheter, or other iatrogenic events. Often, multiple precipitants coexist. However, according to one study, in 13% of cases, no precipitating factor could be found.

### Prehospital Care

The emergency medical services (EMS) system is an important ally in the recognition of delirium. Shah et al prospectively compared the incidence of cognitive impairment in elderly patients arriving to the ED via EMS versus other modes of transport. The study reported that 13% of EMS patients had cognitive impairment compared to 8% arriving via other modes of transport (p < .01). EMS can be particularly helpful in ascertaining from family, caretakers, and environmental clues the patient’s baseline cognitive status and the time course of any changes.

Regarding prehospital detection, we are aware of one study examining a tool for the diagnosis of delirium in elderly patients in the prehospital set-

### Table 2. Delirium Versus Dementia

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Delirium</th>
<th>Dementia</th>
</tr>
</thead>
<tbody>
<tr>
<td>Onset</td>
<td>Abrupt; hours to days</td>
<td>Gradual; months to years</td>
</tr>
<tr>
<td>Course</td>
<td>Fluctuates</td>
<td>Slow decline</td>
</tr>
<tr>
<td>Attention</td>
<td>Impaired</td>
<td>Intact early in course</td>
</tr>
<tr>
<td>Sleep-wake cycle</td>
<td>Disorganized</td>
<td>Usually normal</td>
</tr>
<tr>
<td>Alertness</td>
<td>Impaired</td>
<td>Intact early in course</td>
</tr>
<tr>
<td>Behavior</td>
<td>Agitated, withdrawn, depressed, or a combination of the above</td>
<td>Intact early in course</td>
</tr>
<tr>
<td>Speech</td>
<td>Variable; can be disorganized, rapid, or slowed</td>
<td>Word-finding problems</td>
</tr>
<tr>
<td>Thoughts</td>
<td>Disorganized, with delusions possible</td>
<td>Impoverished</td>
</tr>
<tr>
<td>Perception</td>
<td>Distorted, sometimes with hallucinations</td>
<td>Usually intact early in course</td>
</tr>
<tr>
<td>Level of consciousness</td>
<td>Characterized by altered level of consciousness</td>
<td>Normal</td>
</tr>
<tr>
<td>Disorganization</td>
<td>May be present</td>
<td>Typically absent</td>
</tr>
<tr>
<td>Reversibility</td>
<td>Usually reversible</td>
<td>Rarely reversible</td>
</tr>
</tbody>
</table>

Adapted from Lynn E. J. Gower, DO; Medley O. Gatewood, MD; and Christopher S. Kang, MD. “Emergency Department Management of Delirium in the Elderly.” Western Journal of Emergency Medicine. 2012; Volume 13, Issue 2, pages 194-201. Used with permission of the authors.

### Table 3. Vulnerability Factors In Delirium

<table>
<thead>
<tr>
<th>Not Modifiable</th>
<th>Potentially Modifiable</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dementia*</td>
<td>Visual impairment*</td>
</tr>
<tr>
<td>Cognitive impairment*</td>
<td>Hearing impairment*</td>
</tr>
<tr>
<td>History of delirium*</td>
<td>Depression*</td>
</tr>
<tr>
<td>Functional impairment*</td>
<td>Alcohol misuse*</td>
</tr>
<tr>
<td>Comorbidity or severity of illness*</td>
<td>Immobility</td>
</tr>
<tr>
<td>History of transient ischemic attack or stroke</td>
<td>Low level of activity</td>
</tr>
<tr>
<td>Elder age (&gt; 75 years)*</td>
<td>Decreased oral intake</td>
</tr>
<tr>
<td>Male gender</td>
<td>Dehydration</td>
</tr>
<tr>
<td>Residence in a nursing home*</td>
<td>Malnutrition</td>
</tr>
<tr>
<td>History of falls</td>
<td>Polypharmacy</td>
</tr>
<tr>
<td>Chronic renal or hepatic disease</td>
<td>Treatment with multiple psychoactive drugs</td>
</tr>
<tr>
<td>Neurologic disease</td>
<td>Metabolic derangements</td>
</tr>
<tr>
<td>Terminal illness</td>
<td>Functional impairment</td>
</tr>
<tr>
<td>Infection with human immuno-deficiency virus</td>
<td>Depression</td>
</tr>
</tbody>
</table>

*Studies show an increased relative risk for developing delirium in patients with these factors.
The key to diagnosing delirium is to maintain a high index of suspicion in vulnerable patient populations. Several predictive factors have been identified, including cognitive impairment, severity of illness, age, visual impairment, and elevated ratio of blood urea nitrogen to creatinine (BUN:Cr)\(^{51,52}\).

Crucial to the diagnosis of delirium is the determination of the patient’s baseline mental status and confirmation of any acute change.\(^{53}\) Often, this information will need to be corroborated or provided by a family member or other healthcare professional. Prior documentation of the patient’s cognitive baseline by previous clinicians can be particularly helpful and highlights the importance of subsequent documentation of current findings. While the clinical information provided by the history and physical examination provides a basis for diagnosing and managing delirium, these elements are insufficient by themselves.\(^{54,55}\)

Concurrent with the establishment of the diagnosis of delirium, emergency clinicians must gather information on the possible precipitating medical event as well as stabilize any life-threatening events. The primary survey and scan of the vital signs to determine the severity of the patient’s condition and manage any life-threatening issues (including trauma and infectious signs) is a helpful place to begin. Historical questions and physical examination targeted at patients with suspected delirium emphasize a search for both precipitating and vulnerability factors. (See Table 1, page 4 and Table 3, page 5.) Special attention should be paid to medication, intoxication, and possible trauma, as well as infectious signs, as these represent the most common reversible causes of delirium.

### Emergency Department Evaluation

#### History

The 2010 geriatric competencies for residents include the expectation that residents are able to “assess and document current mental status and any change from baseline in every elder, with special attention to determining if delirium exists or has been superimposed on dementia.”\(^{50}\) This mandate of vigilance applies equally to patients in other age groups.

The ED evaluation of delirium is a parallel process of diagnosis and management that is familiar to providers in the workup of most critical diseases. The first responsibility of the emergency clinician is personal and team safety. Once safety is ascertained, the emergency clinician must simultaneously evaluate the patient and manage emergent conditions. Because delirium can be considered a medical emergency, it is prudent to follow the “airway, breathing, circulation” practice and the primary survey algorithm common in both trauma and medical resuscitations.

The key to diagnosing delirium is to maintain a high index of suspicion in vulnerable patient populations.\(^{51}\) Several predictive factors have been identified, including cognitive impairment, severity of illness, age, visual impairment, and elevated ratio of blood urea nitrogen to creatinine (BUN:Cr)\(^{51,52}\).

### Physical Examination

The neurological examination should focus on the central nervous system, including focal or lateralizing symptoms, the cranial nerves, and examination of cerebellar signs such as gait and truncal ataxia. The mental status examination involves multiple components. The most commonly recommended ED tools, including the mini-mental status examination and the 6-item screener, test areas such as orientation, registration, attention, calculation, and recall as well as language and praxis.\(^{19,36}\) **Table 4 (page 7)** illustrates other commonly cited elements of the history, physical examination, and diagnostic studies as described in delirium guidelines and review articles. The recommendations are based largely on expert consensus.

#### Screening Tools

A challenge unique to the ED is that delirium is often typified by a fluctuating course, and some patients may be diagnosed only on re-evaluation, sometimes by multiple clinicians. If delirium is suspected, multiple screening tools exist and are generally composed of a component of cognitive testing followed by scoring criteria for the diagnosis of delirium. The predominant screening tool described in the emergency medicine literature is the
CAM. The short form of the CAM has become the reference standard for ED evaluation of delirium. The CAM is composed of 4 elements: (1) Acute onset of fluctuating course, (2) inattention, (3) altered level of consciousness, and (4) disorganized thinking. The presence of elements 1 and 2 and either 3 or 4 indicates delirium. 

In 2014, LaMantia et al published a review of the literature and found 29 articles on screening for delirium in the ED setting. The CAM was the only tool validated for ED use. Monette et al evaluated the CAM as administered by trained layperson interviewers compared to geriatrician assessment in 110 elderly patients and found a sensitivity of 86% and a specificity of 100%. These ED study results are comparable to a larger systematic review of the CAM in multiple clinical settings by Wei et al in 2008. This review cited 239 articles and found a sensitivity range of 46% to 100%; an overall sensitivity of 94% (95% CI, 91%-97%); and specificity range of 63% to 100%, with an overall specificity of 89% (CI, 85%-94%). In 2014, Han et al validated the CAM-ICU (intensive care unit) for ED use in a cohort of 406 patients and showed a sensitivity of 72% and specificity of 98.6%.

### Diagnostic Studies

The guidelines for delirium are consistent in the recommendation that diagnostic studies indicated in the workup of delirium are directed by the history, physical examination, and differential diagnosis. These recommendations are based on expert consensus. Clinical training, judgment, and common sense are the common themes in the literature discussing the workup of delirium. More specific to delirium, a search for both precipitating factors and vulnerability factors should be undertaken.

Infection is the most common etiology noted in elderly patients, and it often presents with a hypotensive subtype of delirium. One-third of patients presenting to the ED with delirium will be diagnosed with infection, and a search for infectious etiologies is required. Many of the “basic” laboratory tests (including the complete blood count and basic metabolic panel) are useful not only in the diagnosis of the underlying etiology but also in providing information for predictive models of delirium risk. For example, elevated serum bicarbonate, elevated glucose, elevated BUN:Cr ratios, low hemoglobin, and low chloride levels have all been identified in predictive models for delirium. Given the possibility of contributing liver and abdominal processes, liver function tests, lipase, and ammonia levels are recommended. Blood gases may be useful when hypercarbia is suggested by a patient history of pulmonary disease or when pulse oximetry is unreliable in discerning hypoxia. While the ingestion of many toxins may be evident on history and physical examination, it can be useful to obtain screening for drugs of abuse in the specific setting of co-ingestions or atypical presentations. However, the results of these studies must be interpreted with caution, as false-positive and false-negative results do occur. Additionally, positive results may imply chronic or past use and lead away from alternative acute pathology.

### Table 4. Emergency Department Evaluation Of Delirium

<table>
<thead>
<tr>
<th>Phase</th>
<th>History</th>
<th>Physical Examination</th>
<th>Diagnostic Studies</th>
</tr>
</thead>
<tbody>
<tr>
<td>Initial evaluation</td>
<td>Verification of information via proxy</td>
<td>• Vital signs</td>
<td>• Blood glucose</td>
</tr>
<tr>
<td></td>
<td>Baseline mental status</td>
<td>• Primary survey</td>
<td>• Electrolytes</td>
</tr>
<tr>
<td></td>
<td>Medications: anticholinergics, sedatives/hypnotics</td>
<td>• Mental status</td>
<td>• Urinalysis</td>
</tr>
<tr>
<td></td>
<td>Opioids</td>
<td>• Neurological</td>
<td>• BUN:Cr</td>
</tr>
<tr>
<td></td>
<td>Medication changes</td>
<td></td>
<td>• ECG</td>
</tr>
<tr>
<td></td>
<td>Drug and alcohol use</td>
<td></td>
<td>• Chest x-ray</td>
</tr>
<tr>
<td></td>
<td>Trauma</td>
<td></td>
<td>• Drug levels</td>
</tr>
<tr>
<td>Higher yield</td>
<td>Recent illness</td>
<td></td>
<td>• Blood gas</td>
</tr>
<tr>
<td>(focused by specific history and physical examination features)</td>
<td>Thorough review of systems</td>
<td>• Eye: pupil and funduscopic examination</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Neck: thymomegaly and meningismus</td>
<td>• Liver function</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Lung: signs of pneumonia or pulmonary edema</td>
<td>• Thyroid function tests</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Cardiovascular: new murmurs, fistulas/graffs, pulse deficits</td>
<td>• CT head</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Abdomen: tenderness may indicate inflammatory or infectious process</td>
<td>• PT/PTT; INR</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Genitourinary/rectal: signs of infection or bleeding</td>
<td>• Lumbar puncture</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Skin: rash, cellulitis/abscess, decubitus ulcers; medication patches; hydration status, signs of shock</td>
<td>• Drug/toxicology screen</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• MRI</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• EEG</td>
</tr>
</tbody>
</table>
The electrocardiogram can be especially helpful to search for causes such as arrhythmia and myocardial infarction. Delirium can be the only presenting symptom in up to 5% of elderly patients with ST-segment elevation myocardial infarction. Furthermore, alternative morphologies such as signs of right heart strain suggesting pulmonary embolism, as well as changes suggesting electrolyte imbalance or toxic ingestions (such as tricyclic antidepressant or nodal blocking agent ingestion) can be seen. Finally, special attention to a prolonged QT interval is required, as this finding can represent an underlying etiology such as a genetic predisposition to arrhythmia, electrolyte abnormalities (hypokalemia, hypomagnesemia, hypocalcemia), or drug effects. Additionally, a prolonged QT interval can have direct effects on management, as many of the antipsychotic medications have additional QT prolonging effects.

A study of 106 patients by Hardy and Brennan retrospectively evaluated the results of head computed tomography (CT) scans ordered for acute confusion and recommended that these studies be performed only if a history of fall, trauma, or neurological findings are elicited in the initial workup. This study noted that, of the 14% of head CTs showing acute findings, all of the patients had focal neurological deficits or a history of fall. In a 2013 retrospective study of 291 elderly ED patients (aged ≥ 75 y), 4.9% of patients scanned for delirium without focal neurologic deficits had acute intracranial pathology. While the recommendations of these studies are acknowledged, it is difficult to make final recommendations based on small, retrospective data sets with debatable conclusions on clinically significant yield. Additionally, subacute and chronic findings such as hydrocephalus, atrophy, old infarcts, and subdural hematoma may help direct future care.

The 2013 ACEP consensus geriatric ED guidelines recommend an initial workup specifically targeting the following: Infections (urinary tract infections, pneumonia), medications (anticholinergics, sedatives, hypnotics, opioids, new medications), electrolyte imbalance, alcohol/drug use/withdrawal, and new focal neurologic findings. For admitted patients, it is recommended to screen and provide aids for impaired vision and hearing, cognitive impairment, severe illness, dehydration, and prerenal azotemia. Less-common causes of delirium such as nonconvulsive status epilepticus, herpetic encephalitis, and anti-NMDA (N-methyl-D-aspartate) receptor encephalitis are also routinely found in the literature. While uncommon, these etiologies highlight the need for a lower threshold for lumbar puncture and the involvement of further neurologic testing (ie, electroencephalogram) and consult in undifferentiated cases as next-line diagnostics. The commonality in these causes is that they can be associated with significant morbidity and mortality and are eminently treatable if causes are diagnosed early.

Management

The goal of managing delirium in the ED is to rapidly identify and address the underlying medical conditions. Much of the treatment literature is directed towards hyperactive delirium or agitation and involves the balance between optimizing patient safety and minimizing disruptive behaviors and iatrogenic triggers. Emergency clinicians are encouraged to initiate medical management and provide supportive care and nonpharmacological management as the first steps. In the event that a pharmacological intervention is warranted, the ideal agent targets the underlying etiology, has a rapid onset, and has minimal side effects. Algorithms and protocols may assist in the rapid identification, management, and prevention of delirium.

Medical Management

Patients who present with acute delirium should be rapidly evaluated and treated for reversible emergent medical conditions and acute intoxication, with standard emergency care. Common reversible conditions such as hypoglycemia, hypoxia, hyperthermia, hyperthermia, hypotension, pain, or overdose are evident from the initial medical screening and vital signs. Standard treatment such as dextrose, supplemental oxygen, warming, cooling, intravenous fluids, opioids for pain management, or naloxone for opioid overdose often result in rapid resolution of symptoms of delirium or agitation resulting from these conditions. Emergent medical conditions such as severe dehydration; infections; electrolyte abnormalities; metabolic encephalopathy from hepatic, renal, or central nervous system conditions, including central nervous system infections, seizures, hypertensive encephalopathy, acute intracranial hemorrhage, and stroke should also be rapidly identified and treated. Acute intoxication or withdrawal from drugs or chemical agents such as alcohol, tricyclic antidepressants, ethylene glycol, cholinesterase inhibitors, anticholinergic agents, carbon monoxide, and cyanide also require drug screening, rapid treatment, and antidotes. If there is a concern for nonconvulsive status epilepticus, electroencephalography in the ED may be warranted. Initiating rapid workup and treatment of emergent medical conditions (ie, acute intoxication or withdrawal) with standard maximal treatment in the ED should target the suspected underlying etiologies of delirium. Patients with persistent symptoms of delirium and agitation despite administration of standard emergency care may require additional nonpharmacological or pharmacological interventions to control or prevent symptoms of delirium.
Nonpharmacological Management

Nonpharmacological interventions are used to address mild to moderate agitation in cooperative patients. These nonpharmacological interventions may also be used to prevent iatrogenic delirium and agitation. Multicomponent nonpharmacological interventions have been demonstrated to effectively reduce the incidence and duration of delirium and agitation in acute care settings.\textsuperscript{70–72}

Interventions include verbal de-escalation, show of force, one-to-one observation, decreased environmental stimulation, food or drink, limiting tethering and medical procedures (eg, Foley catheters), reorienting and cognitively stimulating patients, facilitating verbal orientation from family members, avoiding medications known to precipitate delirium, and providing visual and hearing assistive devices.\textsuperscript{71–74}

Physical restraints should be reserved for violent and severely agitated patients to facilitate patient and staff safety as well as medical workup.

Verbal De-escalation

Verbal de-escalation is often employed as a first-line treatment, but it is inadequately described in the literature. In 2012, a Consensus Statement of the American Association for Emergency Psychiatry Project BETA (Best Practices in Evaluation and Treatment of Agitation) De-escalation Workgroup provided guidelines in this intervention for emergency clinicians. The workgroup recommends an internationally recognized 3-step approach of: (1) Verbally engaging the agitated patient, (2) establishing a collaborative relationship with the patient, and (3) verbally de-escalating the patient out of agitation.\textsuperscript{73,75,76} This workgroup advises proper training on the 10 elements of verbal de-escalation for maximal effectiveness, which include:\textsuperscript{72,73,77}

1. Respect the patient’s personal space
2. Do not be provocative
3. Establish verbal contact
4. Be concise
5. Identify the patient’s wants and feelings
6. Listen closely to what the patient is saying
7. Agree or agree to disagree
8. Lay down the law and set clear limits
9. Offer choices and optimism
10. Debrief the patient and staff

An initial show of force with security guard activation is a commonly used intervention and was demonstrated in a sample of 223 security activations to be an effective nonpharmacological intervention in 27% of patients who avoided sedation.\textsuperscript{78} Additionally, a survey of emergency departments revealed that one-to-one observation had a perceived efficacy of 48%.\textsuperscript{79} In the event an initial show of force fails or if a severely agitated patient presents violently, physical restraints are often required to facilitate medical and pharmacological management.

Physical Restraints

Physical restraints are to be used as a temporizing measure, as they can increase agitation and the risk of injury. In the literature, physical restraints in agitated patients have been noted to result in significant injuries and death by asphyxiation.\textsuperscript{80,81} The introduction and application of physical restraints should be systematic and performed by an informed, organized, and professional team of staff members. All objects that could be used as weapons should be removed from the patient by security guards and staff. Patients should be placed in the supine position with the head elevated to prevent aspiration. The team leader should control the patient’s head while other team members secure the extremities in extension, with leather restraints, to the bed frame. Frequent monitoring, re-evaluation, repositioning, and anticipation of basic needs are required for patients in physical restraints as well as for patients who have received chemical intervention.\textsuperscript{82}

Multicomponent Protocols

There is growing evidence for instituting a multicomponent nonpharmacological protocol for the treatment of delirium. Traditional strategies rely on isolated interventions such as one-on-one sitters, restraints, or reorientation. A 2011 observational inpatient study supports a promising multicomponent nonpharmacological program consisting of a restraint-free environment maxim of “Tolerate, Anticipate, Don’t Agitate” (TADA). Flaherty and Little describe a strategy of zero tolerance for restraints that emphasizes patient-centered techniques meant to allow for the patient’s natural response to the clinical environment. These tactics return a sense of control to the patient. Instead of immediately restraining patients who have begun to pull at lines and leads, allow the patient leeway, within the bounds of safety, to mobilize and voice his dissent (“tolerate”) and potentially uncover the reason for the discontent (ie, the need to void). Additionally, an example given is in removing unnecessary attachments or camouflaging necessary attachments, as they can be predictably disrupting (“anticipate”). One example of the “don’t agitate” tenet that appears to run contrary to traditional techniques is to stop reorientation when it proves ineffective or is exacerbating to a patient’s condition. This study shows similar LOS, function, mortality rates, and fall rates in hospital for delirious patients in units utilizing the TADA strategy when compared to similar nondelirious patients in other areas of the hospital. While not practical in the current ED setting, with the rise of geriatric and otherwise specialized areas of the department, multicomponent interventions such as these may become more relevant.

Focused interventions have also been shown to be of benefit in reducing delirium in various clinical settings and may be useful for implementation.
in the ED setting. For example, improving sleep hygiene decreases incidences of delirium.\textsuperscript{84} In a 2009 prospective study of 219 patients, Mouzopoulos et al demonstrated that fascia iliaca blocks (as an alternative to systemic opioid medications) decreased delirium from 24\% to 16\% in patients with hip fracture.\textsuperscript{85} By decreasing the rates of delirium in the inpatient setting, studies have shown a decrease in cost per patient as well as overall LOS.\textsuperscript{86}

A single study has evaluated the introduction of medication-specific education and interventions, beginning at their point of entry in the ED. These interventions were continued during the patients’ inpatient stays. By targeting medications known to precipitate delirium, Naughton et al showed a decrease in delirium from 40.9\% at baseline to 22.7\% at 4 months and 19.1\% at 9 months, following the intervention. This study demonstrated decreased delirium and hypothesized decreased hospital costs.\textsuperscript{87} The Care and Respect for Elders with Emergencies (CARE) program in the ED at Mount Sinai Hospital in New York, NY is an example of implementation of multicomponent interventions to reorient, cognitively stimulate, and provide hearing and visual assistive devices in the ED to elders who are at high risk for delirium.\textsuperscript{88} The CARE volunteers were trained to address modifiable risk factors for delirium and other geriatric syndromes. Similar interventions have been built into geriatric ED guidelines.

Pharmacological Management

The mainstay and consensus recommendation for the pharmacological management of delirium is to treat the underlying etiology first, then treat the behavioral symptoms. Pharmacological treatments are considered only when nonpharmacological treatments (such as de-escalation techniques) have proven ineffective and the safety of the patient or staff is at risk.\textsuperscript{89} Pharmacological management is often required for severely agitated and violent patients in order to facilitate rapid medical evaluation and treatment. Pharmacological management should be used cautiously in special populations such as the elderly, patients with Parkinson disease and Lewy body dementia, intoxicated patients, and patients with comorbidities such as cardiac, renal, and hepatic disease. Preferred classes of drugs include antipsychotics and benzodiazepines. Low-dose combinations of these 2 classes are often used to achieve rapid control of agitated behaviors while minimizing risks and side effects.\textsuperscript{89} In the literature, there remains variability in the recommended dose ranges and observed half-life of the classes of drugs used to manage delirium and agitation. Therefore, the dose range and half-life for particular drugs reviewed represent those commonly used in clinical practice and supported by the literature.\textsuperscript{88} Any patient who receives pharmacological management is at risk for cardiac and respiratory adverse effects and should be closely monitored.

Typical Antipsychotics

Haloperidol (Haldol\textsuperscript{®} in the United States), a first-generation typical antipsychotic is considered an agent of choice due to extensive clinical experience with the drug. Haloperidol is given in doses of 2.5 mg to 10 mg and has a 5-minute to 60-minute onset of action.\textsuperscript{90} Haloperidol dosing should be reduced by half in the elderly patient. Haloperidol may be administered via multiple routes: intravenous, intramuscular, and oral. Droperidol (Inapsine\textsuperscript{®}), an analog of haloperidol, is another first-generation typical antipsychotic given in doses of 2.5 mg to 5 mg. Droperidol has the added advantage of a shorter onset of action, and shorter half life; however, it is more likely to cause orthostatic hypotension. These first-generation antipsychotics have been noted, on postmarketing surveillance, to potentially cause QT prolongation, cardiac dysrhythmias (such as torsades de pointes), and increased mortality in dementia patients, and they received a controversial black box warning from the United States Food and Drug Administration (FDA) in 2008.\textsuperscript{89} However, a retrospective study of 2468 patients aged 20 months to 98 years who received droperidol in the ED identified 6 serious adverse events and concluded that there was no evidence of a causal relationship between droperidol and the adverse events.\textsuperscript{91} Therefore, it is recommended that caution be used in patients at risk for QT prolongation, hypokalemia, hypomagnesemia, and other electrolyte disorders. In addition, caution should be used in patients with drug withdrawal syndromes, seizures, or those at risk for anticholinergic toxicity. Furthermore, first-generation typical antipsychotics are not indicated in the treatment of dementia-related psychosis due to increased mortality risk and they are contraindicated in Parkinson disease or Lewy body dementia due to the risk of neuroleptic sensitivity reactions.\textsuperscript{92,93} Certain patient populations may benefit from second-generation atypical antipsychotics or benzodiazepines for management of delirium and agitation.

Table 5 (page 11) summarizes the recommended pharmacological management of delirium and acute agitation. These recommendations are based on both ED and inpatient studies and illustrate the fundamental principal to “start low and go slow.”

Atypical Antipsychotics

Atypical antipsychotics are commonly used for acute agitation in the psychiatric population, but their use in the ED for delirium and agitation is not well characterized. The atypical antipsychotics may be useful in delirium and acute agitation in patients with a contraindication to the use of typical antipsychotics or patients with acute agitation secondary
to an underlying psychiatric disorder. Risperidone (Risperdal®) and quetiapine (Seroquel®) are only available for oral administration, limiting their use in the ED to cooperative patients. Olanzapine (Zyprexa®), ziprasidone, and aripiprazole (Abilify®) are available for intramuscular (IM) and oral administration. The atypical antipsychotics with intramuscular formulations may be useful for uncooperative, severely agitated patients in the acute ED setting. Olanzapine 10 mg IM has a rapid onset of action. Ziprasidone (Geodon®) 10 to 20 mg IM also has a rapid onset of action; however, it may be more likely to cause QT prolongation. Additionally, due to the limited dopamine antagonism effect, the atypical antipsychotics, at low doses, are preferred over the typical antipsychotics in patients with Parkinson disease or Lewy body dementia.94,95

Recent studies compared the use of atypical antipsychotics to the current standard ED management for delirium and acute agitation. In one study, oral risperidone plus lorazepam demonstrated similar efficacy to the standard and common ED use of intramuscular haloperidol plus lorazepam for rapid control of psychotic agitation, but the study did not assess efficacy in undifferentiated delirium or acute agitation in an ED setting.96 A 2013 multicenter randomized double-blind placebo-controlled clinical trial of 336 patients was performed in an ED setting using olanzapine in 1 arm for management of acutely agitated patients. In this trial, patient ICD-10 categories included intoxication, mental illness, and organic illness. Intravenous droperidol or intramuscular olanzapine as an adjunct to midazolam was, similarly, found to result in effective and more-rapid sedation than midazolam alone.97

**Benzodiazepines**

Benzodiazepines are an additional class of medication preferentially used and effective in the treatment of patients in the ED with undifferentiated severe agitation, intoxication or withdrawal syndromes, younger patients, and in Parkinson disease or Lewy body dementia patients with acute agitation.98 Lorazepam is given in doses of 0.5 to 2 mg IV or IM, has a rapid onset of action and half-life of 10 to 20 hours. Midazolam is given in doses of 2.5 to 5 mg intravenously (IV) or IM and has an even more rapid onset and shorter half-life of 2 to 7 hours. Benzodiazepines place patients at risk for respiratory depression and hypotension; therefore, all patients, especially those with underlying pulmonary disease and/or those with concurrent use of central nervous system depressants, require close monitoring after administration.98 Use of benzodiazepines is an independent risk factor for delirium, and adverse effects include sedation and falls in the elderly in the acute ED setting.99 Additionally, doses should be reduced by 20% to 50% in elderly patients, patients with chronic illnesses such as liver and renal disease, and in combination with opioids or other central nervous system depressants.

A 2010 systematic review of 31 clinical trials found benzodiazepines to be effective and well-

### Table 5. Medications For Management Of Delirium And Acute Agitation

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dose</th>
<th>Adverse Effects</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Typical Antipsychotics</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Haloperidol</td>
<td>2.5 mg-10 mg oral, IM, IV</td>
<td>QT prolongation, Extrapyramidal symptoms, Orthostatic hypotension</td>
<td>Preferred in acute psychosis, Initial and serial ECGs recommended, Reduce dose in elderly patients, Avoid in QT prolongation, Parkinson disease, Lewy body dementia, withdrawal syndromes, seizures, hypokalemia, hypomagnesemia, congestive heart failure, bradycardia</td>
</tr>
<tr>
<td>Droperidol</td>
<td>2.5 mg-5 mg IM, IV</td>
<td>Orthostatic hypotension</td>
<td></td>
</tr>
<tr>
<td><strong>Atypical Antipsychotics</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Olanzapine</td>
<td>5-10 mg IM</td>
<td>QT prolongation</td>
<td>Preferred over typical antipsychotics, at reduced doses, in Parkinson disease or Lewy body dementia, Reduce dose in elderly patients, Avoid in QT prolongation or intoxication with CNS depressants</td>
</tr>
<tr>
<td>Ziprasidone</td>
<td>10-20 mg IM</td>
<td>Orthostatic hypotension, Extrapyramidal symptoms</td>
<td></td>
</tr>
<tr>
<td><strong>Benzodiazepines</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Midazolam</td>
<td>2.5-5 mg IM, IV</td>
<td>Respiratory depression, Hypotension</td>
<td>Preferred in intoxication and withdrawal syndromes, Midazolam is preferred for IM administration; when compared to lorazepam, it results in rapid onset and rapid time to arousal, Reduce dose in elderly patients, Reduce dose in chronic liver and renal disease, in combination with opioids or other CNS depressants</td>
</tr>
<tr>
<td>Lorazepam</td>
<td>0.5-2 mg IM, IV</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Recommended doses are consolidated from those cited in the literature and confirmed by pharmacological reference manuals. Abbreviations: CNS, central nervous system; ECG, electrocardiogram; IM, intramuscular; IV, intravenous.
tolerated pharmacological therapies for agitation. In a prospective randomized double-blind trial of agitation in the ED in a population aged 19 to 68 years with a majority of patients diagnosed with intoxication on initial assessment, midazolam resulted in a more rapid and adequate sedation when compared to droperidol and ziprasidone. Additionally, a randomized prospective double-blind study of violent and severely agitated patients in the ED noted that midazolam (5 mg IM) resulted in a significantly more-rapid onset of action and rapid time to arousal when compared to lorazepam (2 mg IM) and haloperidol (5 mg IM). A Cochrane review of benzodiazepines for alcohol withdrawal reemphasizes benzodiazepines’ protective benefit against alcohol withdrawal symptoms when compared to placebo. For more information on management of alcohol withdrawal syndrome in the ED, see the June 2015 issue of Emergency Medicine Practice, “Alcohol Withdrawal Syndrome: Improving Outcomes Through Early Identification And Aggressive Treatment Strategies,” at www.ebmedicine.net/alcoholwithdrawal.

Ketamine
Ketamine is often used for procedural sedation in the ED and has also been used in the prehospital and hospital settings to manage severe undifferentiated agitation. Ketamine dosed at 1 to 2 mg/kg IV or 4 to 5 mg/kg IM may be used for acute agitation after traditional management has failed. The studies on ketamine use are limited to small samples, and neither dosing for acute agitation nor its use in delirium has been established in the literature to date. Adverse effects include hypertension, tachycardia, laryngospasm, emergence reactions, and intubation. Ketamine use should be avoided in elderly patients and in patients with heart disease or schizophrenia. A 2015 study of ketamine given for pharmacologic management of agitation in 51 patients demonstrated increasing dose-related rates of hospital admission and intubation (29%) in patients receiving prehospital intramuscular ketamine. Additionally, patients treated with ketamine for acute agitation in the ED were noted to require additional doses of sedatives due to ketamine’s short half-life. These studies highlight the need for further research.

Combination Therapy
Combination therapy is often used in the management of acute agitation in emergency settings. A multicenter randomized double-blind placebo-controlled clinical trial of 336 patients aged 18 to 65 years was published in 2013 on undifferentiated acutely agitated ED patients. The patients’ ICD-10 categories included intoxication, mental illness, and organic illness. In this study, intravenous droperidol or intramuscular olanzapine as an adjunct to midazolam was found to similarly result in effective and more-rapid sedation than midazolam alone. Extrapolating from studies performed in patients with psychotic agitation, a prospective randomized double-blind multicenter ED trial compared haloperidol (5 mg), lorazepam (2 mg), or both in combination for acute psychotic agitation. Effective symptom reduction was achieved in all treatment groups. Rapid symptom resolution was achieved in the patients receiving the combination treatment of haloperidol and lorazepam.

Additionally, a 2013 Cochrane review of 21 studies involving 1968 patients found insufficient evidence to support or refute the emergency management of acute agitation with benzodiazepines alone or in combination with antipsychotics. Given the insufficient evidence and risk of adverse effects with high doses of either class, a combination of benzodiazepines with antipsychotics, which has been found to be superior to either class alone, remains a recommended clinical practice. Therefore combination treatment with antipsychotics and benzodiazepines remains the recommended treatment of choice for acute agitation for rapid resolution of symptoms. This combination treatment approach has the added benefit of reducing doses to minimize the adverse effects of both classes of drugs.

Controversies And Cutting Edge
The National Institutes of Health Task Force on Research in Emergency Medicine has identified specific areas of delirium requiring further research, including the following: assessment of delirium and thresholds for involuntary treatment; better definition of outcomes, including calming and sedation; development and efficacy of nonpharmacological interventions; the study of the safety and efficacy of pharmacological interventions, physical restraints, and other interventions; and new treatments for delirium. Regarding prophylaxis in the ED with pharmacological agents, a Dutch randomized controlled multicenter study evaluating the efficacy of haloperidol for the prevention of delirium in patients admitted through the ED (HARPOON Trial) has been proposed. Identified in the literature review of pharmacological management, further research is needed to delineate the optimal management of delirium and undifferentiated agitation in ED settings and in the elderly; the safety of droperidol for use in the ED setting; the utility, safety, and efficacy of atypical antipsychotics in the ED setting; and the minimum effective dose for ketamine use in the prehospital and ED setting. Further research is also necessary to identify the combinations of therapy that are optimal for particular subpopulations. Finally, due to the controversy over the FDA black box warnings issued for the typical and atypical antipsychotics, the FDA plans to revisit this issue.
**Risk Stratification Tools**

Regarding improved ED diagnosis of delirium, several proposals have been published in recent years. Risk stratification tools have been derived to identify high-risk patients. In a 2009 study, Han et al studied 303 older patients presenting to the ED and derived a prediction rule identifying the presence of delirium, functional impairment (a Katz Activities of Daily Living Score ≤ 4), and hearing impairment. The test characteristics demonstrated an area under the curve (AUC) value of 0.82, and a score of ≥ 1 had a sensitivity of 96% and a specificity of 49.3%. If the score had been applied to the study population, 165 patients (54.5%) would have been screened and 1 patient with delirium would have been missed; 141 of these patients would not have had delirium.

In 2014, Kennedy et al evaluated 700 older patients in the ED and developed a risk stratification tool that included: older age, prior stroke or transient ischemic attack, dementia, suspected infection, tachypnea, and acute intracranial hemorrhage (AUC, 0.77). Additional findings associated with delirium included a serum bicarbonate level > 30 mmol/L, a serum glucose level > 300 mg/dL, history of anxiety, and APACHE II score > 15. Finally, in 2014, Hare et al developed a screening tool for nurses to use with the following elements: cognitive impairment, arrhythmia, and depression. A score of ≥ 2 yielded a reported sensitivity of 87% and a specificity of 70%. These risk stratification tools have yet to be validated in the ED setting and, as such, are not recommended for current use. However, they may be used in the future to inform triage protocols targeted at both screening for and preventing delirium.

**Triage Tools**

One recently published triage protocol is gaining traction in the ED literature. Despite the prevalence of the CAM over the past 2 decades as a brief, validated tool in the ED, the number of missed delirium cases has not improved. Low overall recognition has been attributed to lack of education and the heavy workflow found in the typical ED. The recent geriatric ED guidelines now recommend a 2-tiered approach to diagnosis. A sensitive delirium triage screen (DTS) incorporated into the initial screening of elderly patients has been proposed. Patients who screen positive will be followed with a more specific delirium screening. This approach is akin to the recent developments in sepsis screening and is also consistent with the clinical approach to human immunodeficiency virus (HIV) screening and the workup of pulmonary embolism. Figure 2 is an algorithm based on a 2013 study by Han et al of 406 elderly patients. When compared to a psychiatrist reference standard, physicians completing the 2-part screening process (the DTS followed by a brief form of the CAM [bCAM]) showed a sensitivity of 82%.

---

**Figure 2. Delirium Triage Screen And bCAM 2-Step Algorithm**

**Step 1: Delirium Triage Screen (DTS)**

**Rule-Out Screen: Highly Sensitive**

- **Feature 1: Altered mental status or fluctuating course**
  - NO
  - YES

**Feature 2: Inattention**

- ("Can you spell the word "lunch" backwards?")
- > 1 ERROR
- 0 OR 1 ERROR

**Feature 3: Altered level of consciousness (RASS)**

- NO
- YES

**Figure 2**

**Step 2: Brief Confusion Assessment Method (bCAM)**

**Confirmation: Highly Specific**

- **Feature 4: Disorganized thinking**
  1. Will a stone float on water?
  2. Are there fish in the sea?
  3. Does 1 pound weigh more than 2 pounds?
  4. Can you use a hammer to pound a nail?
  Command: “Hold up this many fingers” (Hold up 2 fingers.) “Now do the same thing with the other hand.” (Do not demonstrate.)

**Step 1 (DTS) can be integrated into the nurses’ triage assessment. If the DTS result is negative, then delirium is ruled out and no additional testing is needed. If the DTS result is positive, then a confirmatory delirium assessment such as the bCAM should be performed. Both assessments use the RASS, which assesses for arousal and ranges from -5 (coma) to +4 (comatose). A score of 0 indicates normal level of consciousness.**

Abbreviations: bCAM, Brief Confusion Assessment Method; DTS, delirium triage screen; RASS, Richmond Agitation-Sedation Scale.

Clinical Pathway For Diagnosing And Managing Delirium In The Emergency Department

Patient presents with suspected delirium or risk for delirium; glucose and oxygenation normal

Are patient and staff safety a concern?

Ensure safety:
- Attempt de-escalation
- Consider pharmacological intervention over physical restraint
  - Haloperidol (Class II)
  - Atypical antipsychotic (Class II)
  - Benzodiazepines (Class III)

Perform history and physical examination including:
- Verification of information via proxy
- Baseline mental status
- Administer mental status examination
- Administer neurological examination
- Address any life-threatening concerns and stabilize patient
- Assess medications:
  - Anticholinergics
  - Sedatives/hypnotics
  - Opioids
  - Medication changes
  - Drug and alcohol use

Screen for delirium using:
- CAM (Class II)
- DTS, followed by the mCAM (Class III)

Delirium present?

Undifferentiated delirium without psychosis:
- Correct underlying medical etiology
- Nonpharmacological management
- Pharmacological management:
  - Benzodiazepine or antipsychotic alone or low-dose combination of benzodiazepine and typical antipsychotic
    - Midazolam IV, IM or lorazepam IV, IM (Class II)
  and/or
    - Typical antipsychotic: haloperidol IM, IV or droperidol IM, IV (Class I)
    - Atypical antipsychotic: olanzapine IM or ziprasidone IM (Class I)

Delirium with psychosis:
- Pharmacological management:
  - Atypical antipsychotic: olanzapine IM or ziprasidone IM (Class II)
  or
    - Typical antipsychotic: haloperidol IM, IV or droperidol IM, IV (Class II)

Delirium with intoxication:
- CNS stimulant: benzodiazepine
  - Midazolam IV, IM or lorazepam IV, IM (low dose) (Class II)
- CNS depressant: typical antipsychotic
  - Haloperidol IM, IV (low dose) (Class II)

Delirium with intoxication:
- CNS stimulant: benzodiazepine
  - Midazolam IV, IM or lorazepam IV, IM (low dose) (Class II)
- CNS depressant: typical antipsychotic
  - Haloperidol IM, IV (low dose) (Class II)

Abbreviations: CAM, Confusion Assessment Method; CNS, central nervous system; DTS, delirium triage screen; IM, intramuscular; IV, intravenous; mCAM, modified Confusion Assessment Method. For Class of Evidence definitions, see page 15.
Disposition

Consistent with general ED care, the disposition of patients with delirium hinges on the severity of disease, the underlying etiology, medical comorbidities, and functional status, as well as factors relating to social support and appropriate follow-up. It is difficult to make broad generalizations regarding the disposition of ED patients with delirium, but emergency clinicians should recognize that delirium is an independent risk factor for increased morbidity and mortality. It should be stressed that delirious patients represent a vulnerable population with demonstrated poorer outcomes. Studies have shown that up to 37% of delirious ED patients are discharged home. Mortality for discharged delirium is increased 2 to 3 times in the 3- to 6-month period, when adjusted for comorbidity, age, and severity of illness. Two large ED studies with 653 elderly ED patients combined demonstrated a 31% to 37% mortality rate at 6 months post-ED-discharge compared to 14.3% for nondelirious patients.

Observation units may not be the solution for disposition for delirious patients in the ED. A single study of delirious patients managed in an ED observation unit demonstrated similar mortality rates of 30%, versus 10% for patients with and without delirium, respectively.

While some delirious patients may otherwise warrant discharge, the emergency clinician should be mindful of potentially complicating factors. There is a markedly decreased understanding of the current illness and discharge instructions in this patient population. Furthermore, discharge plans require cohesive planning, possibly including geriatric assessment in the ED, telephone follow-up, home-based rapid referral, integration into community centers, in-home assessments, and staff education programs. As hospitals see an increase in the number of acute delirium units or specialized elder-care floors and teams, disposition decisions may best be made in the team setting.

Summary

Delirium represents a difficult diagnosis of acute brain dysfunction and/or geriatric syndrome in the ED population. The emergency clinician is well trained to evaluate the patient’s condition, treat emergent conditions, and search for underlying etiologies. Special emphasis should be given to obtaining history verifying the patient’s baseline cognitive status as well as medication history. However, the recognition and diagnosis of delirium in the ED remains elusive. While the CAM has been available and validated for ED use for over 2 decades, the inherently pressured characteristics of the ED environment persist, leading to a gap in diagnosis. The current guidelines recommend a systematic and team-based approach to the diagnosis of delirium. At-risk individuals are initially screened at triage, with a subsequent confirmatory test performed if screened positive. Finally, the management and treatment of delirium in the ED population, both with pharmacological and nonpharmacological means, is an area of particular interest and requires further study.

Case Conclusions

You noted that your 20-something-year-old patient with apparent excited delirium syndrome had received haloperidol and lorazepam, so you continued to monitor him via telemetry monitoring, pulse oximetry, and end-tidal

Class Of Evidence Definitions

Each action in the clinical pathways section of Emergency Medicine Practice receives a score based on the following definitions.

Class I
- Always acceptable, safe
- Definitely useful
- Proven in both efficacy and effectiveness

Level of Evidence:
- One or more large prospective studies are present (with rare exceptions)
- High-quality meta-analyses
- Study results consistently positive and compelling

Class II
- Safe, acceptable
- Probably useful
- Possibly useful
- Considered optional or alternative treatments

Level of Evidence:
- Generally higher levels of evidence
- Nonrandomized or retrospective studies: historic, cohort, or case control studies
- Less robust randomized controlled trials
- Results consistently positive

Class III
- May be acceptable
- Possibly useful
- Evidence not compelling
- Indeterminate

Level of Evidence:
- Evidence not available
- Higher studies in progress
- Results inconsistent, contradictory
- Results not compelling

This clinical pathway is intended to supplement, rather than substitute for, professional judgment and may be changed depending upon a patient’s individual needs. Failure to comply with this pathway does not represent a breach of the standard of care.

Copyright © 2015 EB Medicine. 1-800-249-5770. No part of this publication may be reproduced in any format without written consent of EB Medicine.
1. “I thought that this was the patient’s baseline dementia.”
   Dementia is a common confounder for delirium, but it is also a major risk factor for the development of delirium, as the neurologic pathology follows similar pathways. Demented patients are a higher-yield group for delirium screening and they benefit from additional attention and specialized care.

2. “I didn’t have time to do a delirium screen on this patient.”
   While the time pressures of the ED environment are uniquely challenging, brief tools have been developed for ED use; specifically, the short version of the CAM takes about 2 minutes to administer.

3. “The patient was agitated, so we sedated and restrained him and put him in the corner.”
   Agitated patients often have underlying metabolic disturbances. Once sedated, they are at risk for respiratory depression and, if placed on supplemental oxygen, would benefit from additional ventilatory monitoring in the form of end-tidal CO₂ monitoring. Furthermore, if the patient meets criteria for excited delirium syndrome, there is an increased chance of arrhythmia.

4. “We did not find anything wrong with the patient, so we sent him home with our usual discharge instructions.”
   While a certain subset of delirious patients are appropriate for discharge, overall, there is an increased risk of recidivism, morbidity, and mortality, especially in the elderly patient. At the very least, many of these patients have an increased need for coordination of care and may benefit from team-based services such as medication reconciliation, geriatric consultation, home-based assessment, and establishment of support networks.

5. “Our elderly patient had a urinary tract infection, so we admitted her to the floor with a urinary catheter.”
   While often indicated, urinary catheters are a known precipitant for delirium and should be avoided, when possible. Admitted patients may benefit from a team-based approach to prevent delirium and other geriatric syndromes. Many hospitals currently have specialized geriatric wards or delirium units that may be more appropriate for elderly patients at risk for delirium.

6. “Our elderly patient had mild pneumonia and confusion, so I discharged her.”
   While pneumonia severity scoring systems do not supersede clinical judgment, they include factors such as age and mental status changes that indicate poorer outcomes and warrant increased consideration for admission.

7. “He was agitated, so we restrained him right away.”
   Providing visual and hearing assistive devices should be attempted first. Alternative nonpharmacological techniques include verbal de-escalation, show of force, one-to-one observation, decreased environmental stimulation, food or drink, limiting tethering and medical procedures, reorienting and cognitively stimulating patients, verbal orientation from family members, and avoiding medications known to precipitate delirium. If patient or staff safety is a concern, restraints and pharmacological agents may be indicated as first-line treatment.

8. “The patient had a psychiatric history, so we assumed this was his usual psychosis.”
   Patients with an episode of acute psychosis may be difficult to distinguish from patients with delirium due to a medical etiology, and they are easy to dismiss as having a strictly functional diagnosis. However, these patients are also at increased risk for delirium, and, specifically, excited delirium syndrome is associated with baseline psychiatric comorbidity. Pay particular attention to the patient’s baseline, usual episodes, changes in attention, cognition, and the time course of these changes, as well as any signs or symptoms pointing to a medical diagnosis.

9. “The patient said he was fine and did not know why he was even in the hospital.”
   Patients with delirium often have baseline confusion, and it is vital to the workup to obtain corroborating information via proxy. A specific timeline of cognitive change is high-yield, as acute alterations or fluctuation are a hallmark of delirium.

10. “The patient said she was not prescribed any new medications.”
    Medications are a particularly prevalent cause of delirium, especially in older patients. Even without new prescriptions, it is important to obtain a detailed medication history as changes in dosages and interactions with over-the-counter medications can lead to unintended delirium.
CO₂. Intermittently, his breathing slowed, his end-tidal CO₂ rose, and the patient required stimulation and airway repositioning. His lab results showed rhabdomyolysis and an elevated lactate. You initiated fluid and monitored his renal function and urine output.

You returned to your 79-year-old patient who presented for altered mental status. Although her husband returned and stated that he was not sure why she was in the hospital, as she had baseline dementia, she screened positive for delirium. Preliminary laboratory and diagnostic testing was significant only for a positive urinalysis, which you treated promptly. You placed her in the newly designed geriatric ED and initiated a geriatric team consult, inquiring about further admission to the inpatient delirium ward.

Finally, for your struggling mechanically ventilated patient, you initiated an analgesic agent and you were able to gradually titrate down the sedative dose and change the patient over to soft restraints.

References

Evidence-based medicine requires a critical appraisal of the literature based upon study methodology and number of subjects. Not all references are equally robust. The findings of a large, prospective, randomized, and blinded trial should carry more weight than a case report.

To help the reader judge the strength of each reference, pertinent information about the study will be included in bold type following the reference, where available. In addition, the most informative references cited in this paper, as determined by the authors, will be noted by an asterisk (*) next to the number of the reference.


Time- And Cost-Effective Strategies

- While delirium is widely prevalent in the ED population, screening can be directed toward patients with specific risk factors, including increased age, underlying cognitive impairment, visual or hearing impairment, and multiple comorbidities.
- After the identification of at-risk individuals, the current recommendation is for a 2-tier assessment. The initial delirium triage screen has similar performance characteristics when performed by trained lay interviewers, as compared to clinicians.
- While a comprehensive testing program for altered patients is reasonable, directed testing for high-yield etiologies based on the initial history and physical examination can be cost-effective. For example, head CT scan in undifferentiated delirium has a diagnostic yield of only roughly 5%, and those patients will usually manifest signs of trauma or neurologic deficits. However, the caveat here is the need for a reliable history and physical examination.


67. Douglas VC, Josephson SA. Delirium. *Continuum (Minneap Minn).* 2010;16(2 Dementia):120-134. doi:10.1212/01.NCN.0000368215.71588.22. (Review)


5. Delirium and dementia are most reliably differentiated by their:
   a. Abrupt onset
   b. Memory loss
   c. Alterations in perception
   d. Thought content

6. According the The Confusion Assessment Method (CAM), which of the following features are required for the diagnosis of delirium?
   a. Acute onset or fluctuating course
   b. Inattention
   c. Altered level of consciousness
   d. A and B

7. Which of the following tests has the highest yield in ED patients presenting with delirium?
   a. Head CT
   b. Electrocardiogram
   c. Urinalysis
   d. Electroencephalogram

8. The primary pharmacological aim in the treatment of delirium is to:
   a. Treat the underlying cause
   b. Reverse the neurotransmitter imbalance
   c. Sedate the hyperactive psychomotor subtype
   d. Prevent further precipitants

9. Which of the following interventions has been shown to be effective in the prevention of delirium in the ED population?
   a. Fascia iliaca block
   b. Geriatric consultation
   c. Improved sleep hygiene
   d. Medication interventions to decrease polypharmacy and the use of psychoactive agents

10. The estimated mortality for delirious elderly patients discharged from the ED is approximately how many times greater when compared to matched nondelirious patients?
    a. 1 time
    b. 2 times
    c. 5 times
    d. 10 times
Are you headed to the 2015 ACEP Scientific Assembly in Boston October 26-28?

Make sure that you plan to stop by the EB Medicine booth (#576)!

Dear *Emergency Medicine Practice* subscriber,

If you are going to be in Boston for the 2015 ACEP conference Oct. 26-28, we would love to meet you in person! Our Publisher and CEO will be in attendance, so you’ll have the chance to tell us first-hand what your experience has been with *Emergency Medicine Practice*.

When you stop by our booth, we have a special gift for you, and you can enter our drawing to win a free Tiffany pen (valued at $190).

Don’t miss out! We are at **booth #576** and will look forward to your visit.

— The EB Medicine Team

P.S. Have you tried out the mobile app yet? Stop by our booth to get a demo and we will even help you install it on your phone!
SPECIAL SAVINGS:
The 2013-2016 Lifelong Learning And Self-Assessment Study Guides

Receive FREE article reprints,* CME, and more when you order yours today!

<table>
<thead>
<tr>
<th>DESCRIPTION</th>
<th>AMOUNT</th>
</tr>
</thead>
<tbody>
<tr>
<td>The 2016 Lifelong Learning And Self-Assessment Study Guide</td>
<td>$199</td>
</tr>
<tr>
<td></td>
<td>$159</td>
</tr>
<tr>
<td>The 2015 Lifelong Learning And Self-Assessment Study Guide</td>
<td>$199</td>
</tr>
<tr>
<td></td>
<td>$159</td>
</tr>
<tr>
<td>The 2014 Lifelong Learning and Self-Assessment Study Guide</td>
<td>$199</td>
</tr>
<tr>
<td></td>
<td>$159</td>
</tr>
<tr>
<td>The 2013 Lifelong Learning And Self-Assessment Study Guide</td>
<td>$199</td>
</tr>
<tr>
<td></td>
<td>$159</td>
</tr>
<tr>
<td>• Full reprints of the original articles*</td>
<td>FREE</td>
</tr>
<tr>
<td>• 35 AMA PRA Category 1 Credits™ or 35 ACEP Category I CME Credits.</td>
<td>FREE</td>
</tr>
<tr>
<td>• A handy summary of key points so you get the “must know” information for each article.</td>
<td>INCLUDED</td>
</tr>
<tr>
<td>• An in-depth discussion of each article to clarify and elaborate on the key points.</td>
<td>INCLUDED</td>
</tr>
<tr>
<td>• Sample questions to help you quiz yourself on your knowledge of the material.</td>
<td>INCLUDED</td>
</tr>
<tr>
<td>• Answers and explanations to the sample questions that drive home the main points.</td>
<td>INCLUDED</td>
</tr>
<tr>
<td>• A critical discussion and critique of the article that answers the question, “What does this article really tell us?”</td>
<td>INCLUDED</td>
</tr>
<tr>
<td>• 100% money-back guarantee: If, for any reason, you are not completely satisfied, simply call us to receive a full and immediate refund. No questions asked.</td>
<td>INCLUDED</td>
</tr>
</tbody>
</table>

*Due to copyright restrictions, 1 article from the 2016 LLSA, the tables from 1 article in the 2014 LLSA and 2 articles in the 2013 LLSA are not included.

2 EASY WAYS TO ORDER

1. Go online to: www.ebmedicine.net/NHLJC
2. Call 1-800-249-5770 or 678-366-7933

Use Promotion Code: NHLJC at checkout to secure your discount
Emergency Medicine Practice

SPECIAL ANNOUNCEMENT

The New FREE Emergency Medicine Practice Mobile App—Available Now!

Mobile-optimized content from Emergency Medicine Practice, powered by AgileMD, will enable you to instantaneously search our entire publication library—so you have access to hundreds of topics on your mobile device at the point of care.

Content will be updated in real-time so that new clinical topics are available as soon as they are released. The new app also features easy-to-use reference tools, such as bookmarking and note-taking, that enable you to easily follow up on cases and finish research.

We are excited to bring you this new subscription benefit—at no charge to you. To download the app, go to www.ebmedicine.net/app on your smart phone, tablet, or computer.

Powered by AgileMD

Physician CME Information


Accreditation: EB Medicine is accredited by the Accreditation Council for Continuing Medical Education (ACCME) to provide continuing medical education for physicians. This activity has been planned and implemented in accordance with the Essential Areas and Policies of the ACCME.

Credit Designation: EB Medicine designates this enduring material for a maximum of 4 AMA PRA Category 1 Credits™. Physicians should claim only the credit commensurate with the extent of their participation in the activity.

ACEP Accreditation: Emergency Medicine Practice is approved by the American College of Emergency Physicians for 48 hours of ACEP Category I credit per annual subscription.

AAFP Accreditation: This Medical Journal activity, Emergency Medicine Practice, has been reviewed and is acceptable for up to 48 Prescribed credits by the American Academy of Family Physicians per year. AAFP accreditation begins July 1, 2015. Term of approval is for one year from this date. Each issue is approved for 4 Prescribed credits. Credit may be claimed for one year from the date of each issue. Physicians should claim only the credit commensurate with the extent of their participation in the activity.

AOA Accreditation: Emergency Medicine Practice is eligible for up to 48 American Osteopathic Association Category 2-A or 2-B credit hours per year.

Needs Assessment: The need for this educational activity was determined by a survey of medical staff, including the editorial board of this publication; review of morbidity and mortality data from the CDC, AHA, NCHS, and ACEP; and evaluation of prior activities for emergency physicians.

Target Audience: This enduring material is designed for emergency medicine physicians, physician assistants, nurse practitioners, and residents.

Goals: Upon completion of this activity, you should be able to: (1) demonstrate medical decision-making based on the strongest clinical evidence; (2) cost-effectively diagnose and treat the most critical presentations; and (3) describe the most common medicolegal pitfalls for each topic covered.

Discussion of Investigational Information: As part of the journal, faculty may be presenting investigational information about pharmaceutical products that is outside Food and Drug Administration-approved labeling. Information presented as part of this activity is intended solely as continuing medical education and is not intended to promote off-label use of any pharmaceutical product.

Faculty Disclosure: It is the policy of EB Medicine to ensure objectivity, balance, independence, transparency, and scientific rigor in all CME-sponsored educational activities. All faculty participating in the planning or implementation of a sponsored activity are expected to disclose to the audience any relevant financial relationships and to assist in resolving any conflict of interest that may arise from the relationship. In compliance with all ACCME Essentials, Standards, and Guidelines, all faculty for this CME activity were asked to complete a full disclosure statement. The information received is as follows: Dr. Wong, Dr. Abraham, Dr. Dienstag, Dr. Schwartz, Dr. Damilini, Dr. Toscano, Dr. Jagoda and their related parties report no significant financial interest or other relationship with the manufacturer(s) of any commercial product(s) discussed in this educational presentation. Dr. Zun reported honoraria for teaching/papers and consulting services for Teva Pharmaceutical Industries, Ltd.

Commercial Support: This issue of Emergency Medicine Practice did not receive any commercial support.

Earning Credit: Two Convenient Methods: (1) Go online to www.ebmedicine.net/CME and click on the title of the article. (2) Mail or fax the CME Answer And Evaluation Form (included with your June and December issues) to EB Medicine.

Hardware/Software Requirements: You will need a Macintosh or PC to access the online archived articles and CME testing.

Additional Policies: For additional policies, including our statement of conflict of interest, source of funding, statement of informed consent, and statement of human and animal rights, visit www.ebmedicine.net/policies.

CEO & Publisher: Stephanie Williford Senior Business Analyst: Robin Wilkinson Director of Editorial: Dorothy Whisenhunt Senior Content Editor & CME Director: Erica Scott Content Editor: Cheryl Belton Editorial Content Coordinator: Angie Wallace Director of Operations: Robin Salet Office Manager: Kiama Collier Client Data Associate: Paige Banks Director of Business Development: Susan Woodard Product Marketing & Communications Manager: Kelly Smith Online Marketing Manager: Marcus Snow Client Services Associate: Cory Shrider

Direct all inquiries to:
EB Medicine
Phone: 1-800-249-5770 or 1-678-366-7933
Fax: 1-770-500-1316
5550 Triangle Parkway, Suite 150
Norcross, GA 30092
E-mail: ebm@ebmedicine.net
Website: www.ebmedicine.net
To write a letter to the editor, please email: jagodamd@ebmedicine.net

Subscription Information

Full annual subscription: $349 (includes 12 monthly evidence-based print issues; 48 AMA PRA Category 1 Credits™, 48 ACEP Category I credits, 48 AAFP Prescribed credits, and 48 AOA Category 2A or 2B CME credits; and full online and mobile app access to searchable archives and additional CME). Call 1-800-249-5770 or go to www.ebmedicine.net/subscribe to subscribe.

Individual issues: $39 (includes 4 CME credits). Call 1-800-249-5770 or go to www.ebmedicine.net/EMPissues to order.

Group subscriptions at discounted rates are also available. Contact Cory Shrider, Account Manager, at 678-366-7933 x 316 or cs@ebmedicine.net for more information.

Copyright © 2015 EB Medicine. All rights reserved. Reprints: www.ebmedicine.net/empissues