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ED Management Of Delirium and Agitation

It is a hot and humid Friday night, and you are just starting your shift. The chart rack is stacked to the ceiling with patients to be seen, and you can see a sea of EMS gurneys waiting in line for the triage nurse. You suddenly hear a commotion at the ambulance triage area and all eyes are focused on a middle aged, disheveled, malodorous individual shouting obscenities at the triage nurse. The EMS workers tell you he is one of the "regulars" and was found on the street with alcohol-like smell on his breath. You cautiously approach the patient who has now successfully pulled his arms away from the EMTs and is attempting to punch the nurse. The nurse takes a step back and asks you what you want to do.

The next chart you pick up reads, "Patient from the nursing home for evaluation of fever and altered mental status." As you walk over to the patient, you find the nurse wrestling an elderly gentleman back onto his stretcher. You ask the patient how he is doing but the only response is, "Help! Help! Help me!" The nursing home referral sheet reads like a grocery list of medications and medical conditions, including dementia. There is no one in the ED familiar with the patient and the nurse is requesting that you order a B-52 (5 mg haloperidol and 2 mg lorazepam) since, "He's just demented."

You begin to think, "This is going to be a very long shift…"

Delirium, which often presents with agitation, is a diagnosis that every emergency physician must be diligent in recognizing, evaluating, and treating. Indeed, agitation should be presumed to be a manifestation of delirium until proven otherwise. A potentially life-threatening etiology must be searched for and addressed. If agitation is severe, it requires urgent intervention to reduce potential danger to both patient and staff. Managing the agitated patient requires a coordinated approach that gains control of the situation while facilitating the diagnostic work-up. This issue of *Emergency Medicine Practice* provides a review of the current literature on delirium and a systematic approach to the man-

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CME Objectives

Upon completion of this article, you should be able to:

1. Understand the epidemiology, pathophysiology, and clinical features of delirium.
2. Quickly evaluate and treat the acute, reversible causes of altered mental status.
3. Have a broad differential in the management of a delirious patient.
4. Know what studies to initiate in the workup of a delirious patient.
5. Understand the safe and proper use of pharmacotherapeutic options in the management of an agitated or delirious patient.

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See "Physician CME Information" on back page.

agement of undifferentiated agitation in the emergency department (ED).

Abbreviations Used In This Article

CAM: Confusion Assessment Method
CATIE: Clinical Antipsychotic Trials of Intervention Effectiveness
CNS: Central Nervous System
COPD: Chronic Obstructive Pulmonary Disease
DKA: Diabetic Ketoacidosis
GABA: Gamma Amino Butyric Acid
HHS: Hyperosmolar Hyperglycemic State
ICP: Increased Intracranial Pressure
IM: Intramuscular
IV: Intravenous
MMSE: Mini-Mental Status Examination

Critical Appraisal Of The Literature

The evidence to guide the evaluation and pharmacologic management of delirium and acute agitation is limited. A Medline search was performed using the search terms delirium, agitation, behavioral emergencies, aggression, chemical restraints, sedation, benzodiazepines, and antipsychotics, as well as searches of specific therapeutic agents. Additional references were obtained from the bibliographies of the articles reviewed.

A search of the Cochrane Database of Systematic Reviews yielded a review of haloperidol in chronic agitation in elderly demented patients.[1] The clinical guidelines clearinghouse at www.guidelines.gov and the American College of Emergency Physicians (ACEP) clinical policies were also searched. In 1999, ACEP published a "Clinical Policy for the Initial Approach to Patients Presenting with Altered Mental Status," which critically reviewed the literature and provided an evaluation framework; it did not address specific pharmacologic interventions.[2] In January 2006, ACEP published the clinical policy "Critical Issues in the Diagnosis and Management of the Psychiatric Patient in the Emergency Department."[3] This policy focused primarily on medically stable patients with acute psychiatric disturbances; however, the pharmacologic management section addressed undifferentiated agitation, including delirium. **(Table 1)**

In 1999, The American Psychiatric Association published "Practice Guideline for the Treatment of Patients with Delirium."[4] This document reviewed the literature and made graded recommendations based on the strength of evidence regarding psychiatric management, environmental and supportive interventions, and pharmacologic interventions. It provided a comprehensive analysis of delirium and emphasized the need for a multi-disciplinary approach. In 2001, an expert panel led by members of the American Association of Emergency Psychiatry (AAEP), published a consensus based guideline, "Treatment of Behavioral Emergencies," which focused on acute interventions in decompensated psychiatric patients.[5]

Table 1. ACEP / AAEP Clinical Policy: Level B Recommendations For The Pharmacologic Treatment Of The Acutely Agitated Patient In The ED

- For patients with undifferentiated agitation (delirium), treat with monotherapy using lorazepam, midazolam, droperidol, or haloperidol
- If an antipsychotic is used, consider droperidol instead of haloperidol if rapid sedation is required
- In patients with agitation and psychosis, treat with monotherapy using a typical or atypical antipsychotic

Etiology, Pathophysiology, And Epidemiology

Delirium: Definition And Diagnosis

Delirium is an organic mental syndrome defined by a global disturbance in consciousness and cognition. It is characterized by a global cognitive impairment due to a medical condition, which develops abruptly and often fluctuates over the course of the day.[6] The underlying mechanism of delirium is poorly understood and its pathophysiology has not been well elucidated. Delirium is common among medically compromised patients; the elderly are also highly vulnerable to its development.

Hallmarks of delirium include a disturbance in

Table 2: Key Features Of Delirium

- Altered level of consciousness, ranging from stupor to agitation
- Inattention, decreased ability to focus
- Fluctuating course over hours or days
- Disturbance in sleep / wake cycle
- Precipitated by medical illness, substance intoxication / withdrawal, or medication effect

attention and impairment in memory. Deficits in attention are characterized by ease of distractibility with a reduced ability to focus, sustain, or shift attention, resulting in difficulty following commands. Patients may have trouble maintaining conversation; conversation may be rambling or incoherent. Memory impairment usually involves recent memory; patients may be disoriented to time or place, but only rarely to person. Perceptual disturbances that may occur include misinterpretations, illusions, or hallucinations. Often, there are alterations in the patient's sleep / wake cycle. A fluctuating course is characteristic and lucid intervals may be misleading. **(Table 2)**

The clinical manifestations of delirium are highly variable. Patients with delirium may present subtly or dramatically. If subtle, delirium may go unrecognized without a formal mental status evaluation. Patients may present with psychomotor retardation with varying degrees of lethargy, withdrawal, and somnolence. Alternatively, delirium may present dramatically with disruptive psychomotor agitation, emotional lability and hallucinations. In one prospective study of 229 hospitalized elderly patients with delirium, agitation was present in less than one-third of cases.[7]

Pathophysiology Of Delirium

Though the exact mechanism of delirium is not known, it is thought to be caused by an imbalance of neurotransmitters at the cortical and subcortical levels. The implicated neurotransmitters include dopamine, acetylcholine, serotonin, and GABA, which are responsible for neuronal excitation and inhibition.[8] Physiologic stressors, such as infections, medications, and metabolic disturbances, can alter the levels of the neurotransmitters leading to changes in cognition and attention. Inflammatory mediators, such as cytokines and histamines, are thought to be involved as well.

Epidemiology

Altered mental status is a presenting complaint in 5 to 10% of all ED visits.[9-12] Agitation in younger patients presenting to the ED is much more likely to be the result of substance abuse or underlying psychiatric disease (psychotic or mood disorder) than in the elderly population. In ED patients over 70 years old, it has been reported that up to 40% have an alteration in mental status, with approximately 25% diagnosed as having delirium.[13] Levkoff et al found that 24% of elderly patients from the community and 64% of those presenting from nursing homes were delirious upon hospital admission.[14]

Delirium is a medical emergency requiring prompt evaluation and treatment. It is generally reversible if the underlying cause is discovered and addressed. It can be fatal if overlooked and untreated. Hospital mortality rates in patients with delirium range from 25 to 33%. Elderly patients who develop delirium during hospitalization have a 22 to 76% chance of dying during that hospitalization. Interestingly, hospital mortality in patients who develop delirium is as high as the mortality rate associated with acute myocardial infarction or sepsis.[15-17]

Differential Diagnosis

The differential diagnosis of etiologies of delirium is extensive. **(Table 3)** Delirium is caused by a medical condition, substance intoxication or withdrawal, or medication side effect. It can be an occult manifestation of systemic illness. The underlying etiology must be identified and treated in order to attain resolution as soon as possible and, thus, decrease mortality. At times, as in the case of sepsis, therapeutic interventions may be initiated even before a specific underlying etiology is identified. Examples of reversible, immediately life threatening causes of delirium include hypoxia, hypoglycemia, and hypotension.

Table 3: Etiologies Of Delirium

- Hypoxemia / hypercarbia
- Hypoglycemia / hyperglycemia
- Hypotension and hypoperfusion
- Dehydration
- Electrolyte disturbance (sodium, calcium, magnesium, phosphorus)
- Infection / Sepsis (pneumonia, urinary tract infection)
- Alcohol and drug toxicity or withdrawal
- Medication / Vitamin deficiencies (Wernicke's)
- CNS lesion, injury, infection (CVA, subdural hematoma, meningitis, encephalitis)
- Endocrinopathies (thyroid, adrenal)
- Cardiac disease (myocardial infarction, congestive heart failure, arrhythmia)
- Hyperthermia or hypothermia

Hypoxemia and Hypercarbia

Hypoxia and hypercarbia are readily reversible causes of delirium. Common causes include pneumonia, pneumothorax, and pulmonary embolism as well as acute exacerbations of underlying illnesses, such as asthma and chronic obstructive pulmonary disease (COPD). Patients with COPD may have baseline elevations in pCO_2, but an acute rise can lead to lethargy and coma. In this subset of patients, as well as in asthmatics, bedside capnography is a useful tool. End-tidal partial pressure of CO_2 reliably estimates arterial partial pressure of CO_2 within 1 to 6 mmHg.[18]

Hypoglycemia And Hyperglycemia

Patients with hypoglycemia may present with confusion, agitation, or focal neurologic findings. In severe cases, coma and seizures can ensue. A history of diabetes or recent use of insulin may aide in the diagnosis. Diabetic ketoacidosis (DKA) and hyperosmolar hyperglycemia state (HHS) can present with altered mental status, lethargy, and coma. Both DKA and HHS have a high mortality even when managed in experienced centers, 5% and 15%, respectively.[19] ED care should be directed at resuscitation as well as a search for the precipitating illness.

Electrolyte Disturbances

Delirium may be the presenting symptom in patients with hyponatremia, though a mental status change is generally the rate of reduction rather than the absolute number.[20] Patients with sodium levels between 110 and 120 mEq/L can still maintain a normal mental status if the reduction was over many days to weeks, compared to a sudden decrease in serum sodium leading to seizures. Severe hypercalcemia from malignancy, hyperparathyroidism, or renal failure can present with agitation and confusion. Serum calcium levels above 14.0 mg/dL are typically associated with hypercalcemic crisis and mental status changes. Associated symptoms include nausea, vomiting, abdominal pain, joint pain, polyuria, and constipation.

Infection

Infection is one of the most common causes of delirium in the elderly, as high as 43% in one study; specifically, urinary tract infections have been implicated as a common cause.[21] After initial stabilization of an elderly patient with altered mental status, timely evaluation and antibiotic administration can be life saving. Infections of the central nervous system (CNS) are always a concern in patients with altered mental status. In a 10-year review of meningitis cases, Pzion et al recently reported that the most common symptoms in meningitis cases were fever (84%), followed by mental status change (25%), and headache (12%).[22] The classic triad of fever, neck stiffness, and headache was found in only 8% of the patients. Risk factors from this study included an immunocompromised host, recent neurosurgical procedure, and sinusitis. Sepsis can present with delirium or coma and management must focus on prompt antibiotic administration. In a recent retrospective chart review of 2731 sepsis patients, a correlation between time to antibiotic administration and survival was demonstrated.[23]

Alcohol And Drug Toxicity / Withdrawal

Alcohol related visits account for 10 to 46% of all ED visits each year.[24] Patients can present as agitated and confused from acute ingestion or from concomitant etiologies, such as subdural hematoma or hypoglycemia. Other drugs, including sympathomimetics and hallucinogens, may also present with delirium and the diagnosis is often made by recognizing the related toxidrome. Alcohol dependent patients with a sudden cessation can present with a severe form of withdrawal known as *delirium tremens*. In one study of patients admitted for alcohol withdrawal, prior history of delirium tremens was the only predictor of recurrence.[25] Patients are confused, often with visual or auditory hallucinations, agitated, and have exam findings of mydriasis, diaphoresis, and significant motor tremor. Vital signs are consistent with severe sympathetic hyperactivity (hypertension, hyperthermia, and tachycardia). By history, the last drink is typically more than 48 hours before presentation, with a range from one to five days. Withdrawal from chronic benzodiazepine use can present similarly.

Medications

Both over-the-counter medications as well as prescription medications can cause delirium. **(Table 4)** Typically, these reactions are due to improper dosing, drug-drug interactions, changes in metabolism, or intentional overdose.[26] Medications with anticholinergic properties are especially problematic. One study found that exposure to anticholinergic medication had an independent and specific association

with subsequent increase in delirium in the elderly patient in the inpatient setting.[27]

Some vitamin deficiencies can present with an acute confessional state. Severe vitamin B deficiency presenting with altered mental status (Wernicke's encephalopathy) can be treated with thiamine if properly identified. Patients present with ataxia, delirium, and ophthalmoplegia.

CNS Injury And Excitation

Central nervous system injury from ischemia, hemorrhage, or trauma can present with altered mental status. With the nationwide availability of stroke and trauma centers, timely recognition of injury must occur at the prehospital level and proper triage to the appropriate centers made. Though most strokes present with focal neurologic findings, confusion and a non-focal exam may reflect anterior cerebral artery strokes involving the frontal lobe as well as posterior cerebral artery infarctions.[28] Head trauma can cause altered mental status from diffuse axonal injury and intracerebral bleeds, which can lead to increased intracranial pressure (ICP) and herniation. Seizure patients may also present with delirium, either as part of the post-ictal phase or as a manifestation of the seizure itself. **(See the August 2005 issue of *Emergency Medicine Practice*, "Mild Traumatic Brain Injury; What To Do When There Is Nothing (Obviously) Wrong").**

Heat Stroke And Cold Exposure

Heat stroke can present with delirium and develop into coma. **(See the June 2006 issue of *Emergency Medicine Practice*, "The Evaluation And Management Of Heat Injuries In The Emergency Department").** The diagnosis is made in patients with CNS dysfunction and temperature greater than 40°C with a history of exposure or exertion. Hypothermia can also present with delirium with associated apathy, slurred speech, and forgetfulness. **(See December 2003 issue of *Emergency Medicine Practice*, "Hypothermia And Cold-Related Emergencies").** Temperatures are typically below 35°C when mental status changes are present.

Prehospital Care

Prehospital care providers are often placed at risk for injury, especially when dealing with the agitated or violent patient. One study found that, of 490 surveyed prehospital care providers, 61% recounted assault during their career with 25% sustaining injury from the incident.[29] In an earlier study, 67% of prehospital providers reported injuries, with 97% requiring assistance by law enforcement officers.[30]

If the patient appears to be violent or agitated, appropriate steps should be taken to maintain control of the encounter, which may include the use of

Table 4: Medications Associated With Delirium

General Drug Class	Specific Drug Types	Example Medication
Anticholinergics	H_1 receptor blockers	diphenhydramine, meclizine, hydroxyzine
	Antiparkinson	benztropine
	Phenothiazine	promethazine
Antidepressants	Tricyclics	amitriptyline, nortriptyline
	SSRIs	fluoxetine, sertraline
Sedative	Benzodiazepines	alprazolam, diazepam
Analgesics	Opioids	codeine, morphine
Antiinflammatory	NSAIDs	aspirin, ibuprofen
	Corticosteroids	hydrocortisone, prednisone
Antihypertensives & Antiarrythmics	Beta blockers	metoprolol, propranolol
	Ace inhibitors	lisinopril, captopril
	Calcium channel blockers	amlodipine, nifedipine
	Other	digoxin
Antibiotics	Quinolones	levofloxacin, ciprofloxacin
	Macrolides	azithromycin, clarithromycin
Anticonvulsives	Barbiturates	phenobarbital

physical or chemical restraints. Unfortunately, the use of physical restraints has been associated with cases of sudden death secondary to positional asphyxiation and is an imperfect, but often necessary, form of patient restraint.[31] Though currently there are no national guidelines for the management of the violent or agitated patient in the prehospital setting, two studies exist with the use of droperidol in this patient population. Rosen et al compared 5 mg of droperidol IV to placebo in 46 patients. There was significantly greater sedation at 5 and 10 minutes, and no significant side effects except one occurrence of akathisia that had no associated morbidity.[32] Another study showed a reduction in agitation using intramuscular droperidol without significant adverse events.[33] Studies using benzodiazepines in the prehospital setting are currently limited to the treatment of status epilepticus, but its use in air medical transport has been documented.[34] Ultimately, it is at the discretion of the emergency medical director to establish a safe standard and protocol for the agitated or violent patient. Combinations of chemical and physical restraints seem to be a reasonable approach in this patient population, though further studies are needed.

Once provider and patient safety is assured, reversible causes of altered mental status must be quickly diagnosed and managed. Oxygen should generally be given to patients with delirium. Prehospital providers should be cautious in overzealous oxygenation in patients with COPD because their respiratory drive may depend on a relative hypoxia. If the patient is in respiratory distress or has agonal respirations, definitive airway management with endotracheal intubation may be necessary. Hypoglycemia has been reported as a cause of up to 10% of emergency patients with altered behavior, supporting the need for an early serum glucose determination as part of the initial care.[35] The "coma cocktail" has traditionally been given to all patients with altered mental status. The contents of the "coma cocktail" include thiamine, dextrose, and naloxone.[36] Theoretically, thiamine should be given prior to the dextrose for the prevention and treatment of Wernicke-Korsakoff syndrome in malnourished patients, though no controlled studies exist. If intravenous access cannot be obtained, intramuscular glucagon should be given, though recovery time may be increased.[37] Intramuscular glucagon appears to be superior to oral glucose paste in both ability to increase glucose level and patient compliance.[38] Intravenous naloxone has generally been found to be safe when given by prehospital providers in patients with suspected opiate overdose[39] and is a competitive antagonist at the opioid receptor. Recent studies have demonstrated intranasal naloxone as a safe alternative for patients with opioid overdose, without the risk of needlestick injury to the prehospital provider.[40]

ED Evaluation

Delirium is a syndrome and not a specific disease; thus, identifying the underlying etiology requires a comprehensive approach that includes history, physical exam, and diagnostic testing. **(Table 5)**

History

A detailed past medical history is important in elucidating the etiology of delirium. It is important to obtain information from as many sources as possible, including the patient, emergency medical service providers, witnesses, family, caregivers, and primary care providers. Information regarding the patient's baseline mental status and level of functioning should be ascertained. It is helpful to know if the patient has underlying dementia, if there has been an acute change, and what underlying medical conditions exist. A very thorough review of medication use is important, as medications are very common precipitants of delirium in the elderly.[41] The history should focus on causal factors related to the acute presentation, such as history of trauma or fall, lack of oral intake, presence of systemic disease including metabolic and cardiopulmonary disorders, symptoms of infection, and substance use or withdrawal.[2]

Table 5: Physical Assessment Of The Patient With Delirium

- Vital signs, including accurate temperature measurement
- Physical examination with thorough neurologic exam
- Oxygen saturation
- Rapid glucose determination
- Chemistry, including electrolytes, renal function, and liver function panels
- Urinalysis
- Chest x-ray
- Electrocardiogram
- Dependent upon the clinical scenario consider: Head CT, lumbar puncture, blood cultures, toxicology screening, thyroid function

Physical Exam

Vital signs should be carefully reviewed and an accurate temperature and oxygen saturation measurement obtained. A bedside glucose determination is often considered the "fifth vital sign" and is particularly important in the evaluation of the agitated patient.[35] A meticulous physical examination must be performed, including neurologic and mental status examination. The examination should search for evidence of medical or surgical causes for the patient's condition, including trauma, infections, and focal neurologic deficits.

Mental Status Evaluation: A mental status evaluation is crucial in the diagnosis of delirium. Disorientation to the environment begins with the inability to identify the date, progresses to day of week, time, month, and year, and eventually to place. Only in the most severe cases is the person unable to identify self. However, if the mental status exam is limited to orientation to person, place, and time, subtle cases of delirium may be missed.

The Mini-Mental Status Examination (MMSE) is an easy and reliable test that can be administered at the bedside. The MMSE is used to test for cognition, which includes orientation, registration (storing new information so that is can be retrieved later), attention and calculation, recall, visual-spatial ability, and language. A high score on the exam makes a cognitive deficit unlikely; however, a low score is nonspecific and not diagnostic of any specific disorder. For hospitalized patients, the MMSE has a sensitivity of 87% and specificity of 82% in detecting organic brain syndrome.[42,43] Note that the MMSE must be interpreted with care in delirium since the delirious patient has impaired attention, which interferes with exam performance.

The Confusion Assessment Method (CAM) **(Table 6)** has been developed as an easy to use, sensitive, specific, and reliable diagnostic tool for the rapid detection of delirium.[44] It has a sensitivity of 93% to 100% and specificity of 90% to 95% for the diagnosis of delirium. It has been used successfully for delirium screening in the ED.[45] This tool has four key features: Acute onset and fluctuating course, inattention, disorganized thinking, and altered level of consciousness. The first two features and one of the last two must be present to make the diagnosis of delirium.

Table 6: Confusion Assessment Method (CAM) Diagnostic Algorithm

1) Acute onset and fluctuating course
2) Inattention, distractibility
3) Disorganized thinking, illogical or unclear ideas
4) Alteration in consciousness

The diagnosis of delirium requires the presence of both features 1 AND 2, plus EITHER feature 3 or 4.

Adapted from: Inouye S, van Dyck C, Alessi C, et al: Clarifying confusion: The confusion assessment method. Ann Intern Med 113:941, 1990.

Diagnostic Studies

Delirium requires an extensive evaluation that is further directed by clinical suspicion and response to interventions. **(Table 5)** Laboratory evaluation usually includes a complete blood count, electrolytes, glucose, renal, and hepatic testing. A urinalysis and chest x-ray should be obtained to rule-out infection. As already mentioned, urinary tract infections are one of the most common causes of delirium in the elderly, making a urinalysis essential.[46]

An electrocardiogram is indicated to evaluate for myocardial ischemia, arrhythmia, and to assess for QTc prolongation. **(See pharmacologic management below).** Additional tests, including toxicologic screens, serum drug-levels (alcohol, aspirin, acetaminophen), and thyroid function tests, may be indicated if a cause is not found on initial evaluation.

A history of falls, suspected trauma, or focal findings on physical exam are indications for early neuroimaging.[47] Neuroimaging should also be considered if no etiology for the delirium is identified after an initial evaluation is completed.[48] Examination of the cerebrospinal fluid is needed when meningitis or encephalitis are suspected.

Pharmacologic Management

One goal of pharmacologic treatment of the agitated patient is to create a safe environment for the patient, other patients in the ED, and the medical staff. The other goal is to facilitate the physical evaluation and diagnostic testing. The ideal agent for treating the undifferentiated acutely agitated patient would be one that is effective with a rapid onset of action and minimal or no side effects. Patients often require emergent sedation before full knowledge of their medical history and presenting illness is known. Pharmacologic therapy in the medically ill and elder-

ly is complicated by their underlying disease process as well as altered pharmacokinetics and pharmacodynamics. The elderly are particularly susceptible to drug side effects due to decreased renal and hepatic function, as well as confounding polypharmacy. In general, drugs should be administered in the lowest effective dose.

Unfortunately, there is limited evidence in the literature to guide the pharmacologic treatment of acute agitation in delirium, particularly in the elderly. Most studies of the emergent sedation of acutely agitated patients are in a younger patient population and typically include substance abusers and patients with underlying psychiatric disturbances (e.g., psychotic or mood disorders), often without other concomitant medical problems. There are several studies that evaluate the long-term management of chronic agitation, but not acute agitation in the demented elderly; (these will be discussed later in the text).

Pharmacologic options include benzodiazepines and the typical and atypical antipsychotics. For rapid sedation of an acutely psychotic patient, the intravenous (IV) route is preferred. In situations where establishing an IV is difficult or hazardous because of the patient's agitation, the intramuscular (IM) route may be necessary. In general, oral sedation has little role in the uncooperative acutely agitated patient in an emergency setting. However, an oral agent may be an appropriate option if symptoms of agitation are not severe, and may be considered prior to the escalation of symptoms.[3]

Typical (First Generation) Antipsychotics

Typical or conventional antipsychotics block dopamine D-2 receptors in the brain. The mechanism by which they reduce agitation has not been elucidated, although they are used extensively for this purpose. Typical antipsychotics are grouped into high, mid, and low potency agents. High potency typical antipsychotics include haloperidol and droperidol. The low potency typical antipsychotics include the phenothiazines (chlorpromazine) and thioridazine. Typical antipsychotics are associated with extrapyramidal symptoms (including rigidity, dystonia, bradykinesia, tremor, akathisia, and tardive dyskinesia) and anticholinergic side effects (including dry mouth, urinary retention and decreased cognitive function). Caution should be used in treating patients suffering from Parkinson's disease with typical antipsychotics because of the significant risk of worsening of the extrapyramidal features of the disease. A rare side effect of antipsychotic medication is the neuroleptic malignant syndrome, which is manifested by high fever, rigidity, mental status changes, and autonomic instability. Patients on long-term antipsychotic therapy are at cumulative risk for the development of tardive dyskinesia, which is characterized by involuntary choreoathetoid movements. Low potency antipsychotics are associated with a high incidence of anticholinergic side effects (which can worsen cognitive function); they are much more sedating due to their antihistaminergic effects, and their alpha-adrenergic blocking effects may lower blood pressure. The side effect profile of the low potency agents limits their usefulness, particularly in medically ill and elderly patients.

Haloperidol is commonly used for the treatment of agitation because its use is rarely associated with respiratory depression, hypotension, and anticholinergic side effects. Haloperidol is not FDA approved for IV administration, although it is commonly administered by this route and thought to be safe. Numerous studies have demonstrated its efficacy in treating aggression; however, most of these studies were of younger patients with a known psychiatric disorder.[3,49] Haloperidol was recommended as a drug of choice for managing the patient with delirium by the American Psychiatric Association in their 1999 practice guideline.[4] In one retrospective case series of 136 disruptive ED patients with a mean age 33 years old, haloperidol was demonstrated to be safe and effective.[50] In a randomized, double blind study of hospitalized AIDS patients with delirium, haloperidol or chlorpromazine were found to be superior to lorazepam in controlling symptoms.[51]

In the management of chronic behavioral symptoms in the demented elderly, the efficacy and safety of haloperidol has been evaluated. A Cochrane Systematic Review of five randomized, placebo-controlled trials showed that demented subjects receiving haloperidol exhibited no significant improvement in overall agitation scores when compared to those treated with a placebo, but did find that aggression, one subtype of agitation, decreased in the haloperidol group when compared to controls.[1] Unfortunately, in these studies, outcomes were measured no earlier than three weeks after initiation of treatment. Patients receiving haloperidol reported more adverse reactions but there was no significant difference in the drop-out rate from the studies between haldoperidol treated subjects and placebo controls.

Droperidol has been used effectively for the

rapid tranquilization of acutely agitated and violent patients in the ED.[52] Droperidol is more potent, more sedating, has a more rapid onset, and has a shorter half-life than haloperidol. IM droperidol has been demonstrated to have a more rapid onset and greater efficacy than IM haloperidol alone for patients with acute psychosis.[53,54] In 2001, the FDA placed a "black box" warning for droperidol because of reports of death associated with QTc prolongation and development of torsades de pointes. Some controversy exists in the literature regarding the boxed warning issued to droperidol given the decades of successful clinical use.[55, 56] A retrospective review of its use and safety in 2500 ED patients, including 141 patients over the age of 66, found negligible complications.[57] In a review of 12,000 patients treated with droperidol for agitation, no dysrhythmic events were observed.[58] There is evidence to suggest that haloperidol, as well as all of the other antipsychotics, are also associated with QTc prolongation and torsades de pointes.[59-61]

Atypical (Second Generation) Antipsychotics

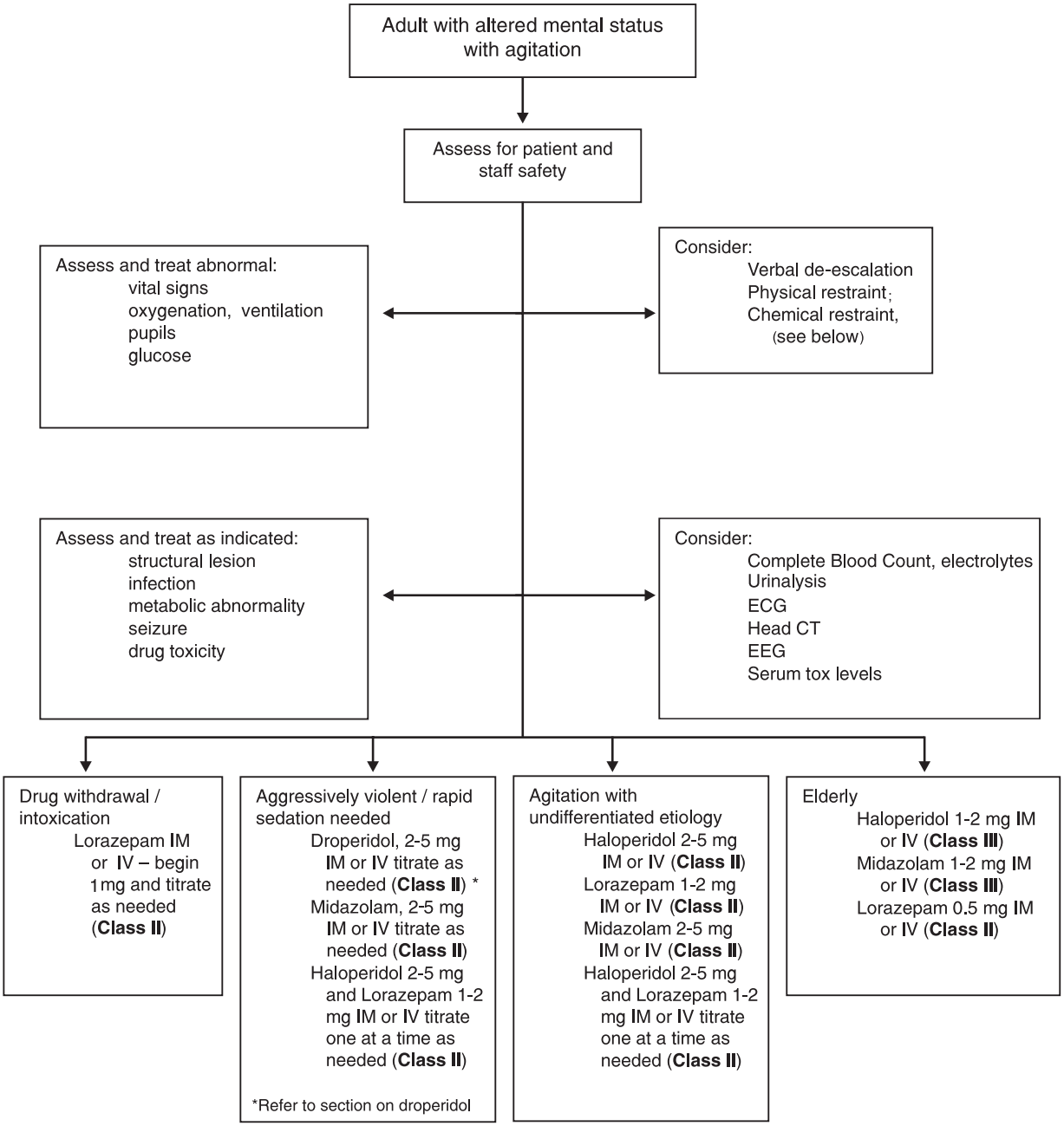
Atypical antipsychotics act at both serotonin and dopamine receptors. In recent years, numerous agents have been developed with the anticipation of an improved side effect profile compared with typical or first generation antipsychotics. Atypical antipsychotics have been marketed as having safety profiles with less akathisia, parkinsonism, tardive dyskinesia, sedation, peripheral and central anticholinergic effects, postural hypotension, and cardiac conduction defects. The recently published Clinical Antipsychotic Trials of Intervention Effectiveness (CATIE) that compared the effectiveness of atypical antipsychotic agents with older agents in patients with chronic schizophrenia, introduces doubt on the advantage of atypical agents over typical antipsychotics.[62] This study found no statistically significant difference in efficacy or the incidence of extrapyramidal side effects.

The atypical antipsychotics, as with the typical antipsychotics, have been approved by the FDA for the treatment of schizophrenia; they have not been approved for the treatment of undifferentiated agitation. The Expert Consensus Guidelines for the Treatment of Dementia and its Behavioral Disturbances recommended the use of atypical antipsychotics over conventional antipsychotics.[63] However, since initially marketed, significant concerns have arisen regarding the safety of the atypical antipsychotics; (see next section).

Olanzapine: Olanzapine is available in oral and IM formulations. Two studies of IM olanzapine have demonstrated it to be as effective as haloperidol in controlling acute agitation in patients with schizophrenia.[64,65] Olanzapine has been reported to be effective in the treatment of chronic agitation in the elderly patient. Most studies have focused on the management of behavioral disturbances in nursing home patients over the course of days to weeks and not on the treatment of acute agitation.[66-68] There is some data to support the use of olanzapine in the management of acute agitation in the elderly. IM olanzapine was compared to haloperidol and lorazepam in the treatment of acute agitation in the ED for patients with schizophrenia and bipolar mania (greater than 18 years of age) and dementia (greater than 55 years of age).[69] Agitation was significantly reduced by olanzapine (2.5 mg) when compared with placebo with no more sedation than lorazepam (1.0 mg) in the dementia group. In the dementia group, olanzapine was not compared to haloperidol. In a double-blind study comparing the efficacy and safety of rapid-acting IM olanzapine in treating agitation associated with Alzheimer's disease and vascular dementia, 272 acutely agitated patients were randomized to treatment with olanzapine (dosages of 2.5 and 5.0 mg), lorazepam (1.0 mg) or placebo.[70] At two hours, both olanzapine (2.5 and 5.0 mg) and lorazepam showed superiority over placebo in terms of reduced agitation. At 24 hours, both olanzapine groups maintained superiority over placebo, while lorazepam did not. There were no significant differences in sedation, adverse events, extrapyramidal symptoms, QT interval, or vital signs among all groups. Currently, data supporting the use of olanzapine for acute agitation in the elderly is limited.

Ziprasidone: IM ziprasidone is effective in controlling acute agitation in patients with schizophrenia and has been FDA approved for this indication.[71,72] A study by Martel et al of acute undifferentiated agitation in patients with a mean age of 37 years (range 19 to 68) compared 5.0 mg of IM midazolam with 5.0 mg of IM droperidol and 20 mg of IM ziprasidone.[73] All three agents were found to be effective sedative agents; however, the ziprasidone group was more likely to remain agitated at 15 minutes. In a double-blind, randomized study in a younger population (79 subjects, age 20 to 62 years), ziprasidone was shown to be effective in reducing acute agitation associated with psychosis with an

Clinical Pathway: Managing The Adult Patient With Delirium And Agitation



The **evidence for recommendations** is graded using the following scale. For complete definitions, see back page. **Class I:** Definitely recommended. Definitive, excellent evidence provides support. **Class II:** Acceptable and useful. Good evidence provides support. **Class III:** May be acceptable, possibly useful. Fair-to-good evidence provides support. **Indeterminate:** Continuing area of research.

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.

excellent side effect profile.[74] A retrospective study of the safety of IM ziprasidone in agitated elderly patients admitted to a neuropsychiatric service found no significant differences in QTc intervals of treated patients.[75] A case series of five patients with Parkinson's disease demonstrated no deterioration of motor function or other relevant side effects in patients treated with IM ziprasidone for acute agitation.[76] Data is limited to support or refute the use of ziprasidone for acutely agitated elderly patients.

Risperidone: Risperidone has been extensively studied for the management of psychosis and behavioral disturbances in patients with dementia. The only currently available parenteral formulation is an extended-acting slow release formulation that is dosed bi-weekly and therefore not suitable for use in acute agitation. However, there is an available rapidly dissolving oral tablet. A number of studies have demonstrated its efficacy and safety for the longer-term management of agitation in the elderly.[77-79] There is one study suggesting the efficacy of risperidone in controlling the agitation of delirium over several days.[80] In this retrospective review, 41 subjects received risperidone and 36 received haloperidol, with both agents demonstrating effectiveness. However, the use of risperidone to immediately control acute agitation has not been studied.

FDA Warning: A recent FDA advisory with a mandatory boxed warning on manufacturers labeling has been issued advising against the use of the atypical antipsychotics in treating agitation in patients with dementia.[81,82] The FDA determined that the treatment of behavioral disorders in elderly patients with dementia with atypical (second generation) antipsychotic medications is associated with increased mortality. Analyses of 17 placebo-controlled studies with enrollment of 5106 patients receiving four different drugs (olanzapine, aripiprazole, risperidone, and quetiapine) had a death rate 1.6 to 1.7 times higher than placebo. The FDA concluded that the effect is probably related to the common pharmacologic effects of all atypical antipsychotic medications, including those that have not been studied in the dementia population. Over the course of these trials, averaging 10 weeks in duration, the death rate in the treated groups were 4.5% compared to the rate in the placebo groups of 2.6%. The causes of death varied, though most were either cardiovascular or infectious in etiology. The FDA has considered adding a similar warning to the labeling for typical antipsychotic medications because the limited data suggest a similar increase in mortality for these drugs.

Benzodiazepines

Benzodiazepines potentiate the effect of gamma amino butyric acid (GABA) by binding to GABA receptors in the brain. Benzodiazepines are effective and commonly used to sedate violent and severely agitated younger patients. In younger patients, benzodiazepines produce a rapid decrease in agitation with minimal side effects. However, they are respiratory depressants and respiratory status must be closely monitored after administration. There is little data in the literature regarding the use of benzodiazepines for the control of acute agitation in the elderly. Diazepam has no role in the treatment of acute agitation because of its prolonged half-life and active metabolites.

Midazolam: Midazolam is the benzodiazepine that has the fastest onset of action and the shortest duration of effect. In a study by Nobay et al in younger patients (mean age 41 years old) IM midazolam had significantly shorter onset of action and shorter duration than both IM haloperidol and IM lorazepam.[83] In a study comparing IM midazolam, IM ziprasidone, and IM droperidol,[73] respiratory depression requiring supplemental oxygen administration (but no intubation nor bag mask ventilation) was a frequent adverse effect in the midazolam group. Additionally, patients who received midazolam were more likely to require subsequent rescue medication to maintain sedation. An Australian study of patients primarily with psychiatric disturbances and substance abusers compared IV midazolam with IV droperidol. Both agents achieved rapid adequate sedation; however, patients receiving midazolam were more likely to need airway management (including one patient who required intubation) and to require further sedation at 60 minutes.[84]

Lorazepam: Numerous studies have demonstrated the efficacy of intramuscular lorazepam for the sedation of the agitated young patient in the ED.[83,85,86] Only one randomized, controlled trial investigated its use in the delirious elderly patient.[70] In this study, lorazepam was more effective than placebo in reducing agitation and was well tolerated; however, risk of respiratory depression was not specifically assessed.

Caveat: There are many recommendations in the literature advising against the use of benzodiazepines in the elderly. Elderly demented patients with chronic agitation treated with benzodiazepines are at an increased risk of falls, sedation, and cognitive impairment.[87-89] However, these adverse effects are probably not relevant to the acute temporary management of an agitated patient.

There is a body of evidence regarding safety and efficacy information of benzodiazepines in elderly patients undergoing conscious sedation for elective procedures or receiving them as pre-anesthetic adjuncts. Randomized trials do not reveal a significant risk of post-sedation cognitive impairment in elderly patients receiving intravenous midazolam for conscious sedation.[90,91] Clinical trials have identified a risk of hypoxia and respiratory depression with IV administration of midazolam when administered alone in the elderly.[92] This risk may be higher in the elderly than in younger patients.[93] There may also be an increased risk of hypoxia in patients with underlying respiratory disease, such as COPD.

There is little data to support concerns of potential behavioral disinhibition or paradoxical agitation in response to benzodiazepine administration in the elderly. The literature is generally limited to case series,[94,95] and there is no strong evidence that the elderly are at any increased risk of this adverse effect.

In several clinical scenarios, benzodiazepines confer an advantage over antipsychotics. Benzodiazepines are the treatment of choice for delirium related to alcohol or benzodiazepine withdrawal.[4, 96] Benzodiazepines are particularly effective in agitated patients with sympathomimetic toxidromes, such as in cocaine and phencyclidine intoxication.[52] In patients with Parkinson's disease, benzodiazepines should be considered because they are not associated with extrapyramidal symptoms as the antipsychotics drugs are. If lowering the seizure threshold is a concern, then benzodiazepines may be the preferred sedative.

Combination Therapy

The combination of an antipsychotic and a benzodiazepine is often used for the rapid tranquilization of acutely agitated, violent, younger patients. A study of haldoperidol and lorazepam, in patients with an average age of only 34.2 years, demonstrated that the combination of the two were more effective than either drug alone.[86] In studies in agitated psychiatric patients by Garza-Trevino[97] and Bieniek,[98] the combination of IM lorazepam and IM haloperidol resulted in more rapid onset of sedation than monotherapy. A review by Yildiz et al of previously published studies of primarily psychiatric ED patients concluded that a combination of haloperidol and lorazepam was an effective rapid tranquilization method.[99] The treatment of elderly agitated patients with a combination drug therapy has not been studied and, in general, it is thought best to minimize the number of medications when treating elderly patients. However, the American Psychiatric Association's Practice Guideline for the treatment of delirium cited combination therapy with a typical antipsychotic and a benzodiazepine as potentially beneficial in that it allows for the use of a lower dose of each medication and thus lowers the risk of each drug's side effects.[4]

Summary Of Pharmacologic Management

The typical antipsychotics, haloperidol and droperidol, are effective sedative agents for the management of acutely agitated patients. There is evidence that both haloperidol and droperidol, as well as the new generation atypical antipsychotics, are relatively safe, although all have been associated with QTc interval prolongation. The FDA warning for droperidol introduced concerns regarding usage of this agent, though subsequent analyses question validity of the

Table 7: Recommendations For The Pharmacologic Management Of Acute Agitation*

Agent	Dose Range	Comments
Haloperidol**	1 mg to 5 mg IM or IV	Most evidence supports its use
Droperidol	1 mg to 5 mg IM or IV	FDA warning, see text on pages 9 and 12
Lorazepam**	0.5 mg to 5 mg IM or IV	Preferred in alcohol and drug withdrawal
Midazolam	1 mg to 5 mg IM or IV	Rapid onset and shorter duration

*Caution for all agents: Use the lower dose in elderly patients and in patients with respiratory depression and / or low blood pressure.

**Consider use of combination therapy, lorazepam and haloperidol, as an alternative to monotherapy in certain populations, refer to Clinical Pathway.

FDAs warning. Indeed, the 2006 ACEP Clinical Policy recommends that droperidol be considered when rapid sedation is required.

At this time, there is no compelling evidence to support the use of the newer atypical antipsychotics over the older sedative agents for treatment of acute agitation in the non-psychiatric ED setting. Benzodiazepines are effective sedative agents. However, benzodiazepines are more often associated with respiratory depression and more likely to lower blood pressure than haloperidol. In several clinical scenarios, such as alcohol withdrawal, benzodiazepines are the preferred sedative agent. **(Table 7)**

Special Circumstances

Risk Factors, Supportive Care, And Non-pharmacologic Interventions

Delirium is a multifactorial disorder and the elderly are particularly vulnerable to its development. It is important to try to prevent delirium before it occurs; implementation of preventive interventions has been demonstrated to substantially reduce the risk of delirium in hospitalized older patients.[100-102] Patients should be provided with an optimum level of sensory stimulation. Environmental cues and family members should be available to help re-orient patients. Patients are particularly vulnerable to the development of delirium if they are sleep deprived, dehydrated, immobilized, or have vision or hearing impairments. Patients who require hearing aids or eyeglasses should have them available to prevent sensory deprivation. Excess noise should be avoided when possible and patients should be allowed to have uninterrupted sleep. Oral fluids should be encouraged and, if oral fluids are contraindicated, intravenous hydration should be provided. Physical restraints should be avoided as they may increase agitation and are associated with injury and death.[103]

Dementia

Patients with dementia are at risk for the development of delirium. Additionally, behavioral disturbances, including agitation, are common among patients with dementia. Agitation in dementia may include aggression, combativeness, delusions, or hallucinations. Agitation may develop either as part of the clinical course or as a response to a new illness. An etiology for the agitation in patients with dementia must be sought, as agitation can be precipitated by pain and acute illness. When confronted with a confused, elderly patient in the ED or hospital ward, it may not be apparent if the confused state is superimposed on a preexisting altered mental state. It may not be possible to immediately distinguish between delirium and dementia, or determine which patients are suffering from both.

Controversies And Cutting Edge

With the continued rise in ED visits each year, up 26% from 1993 to 2003, and the increasing number of "boarded" patients, emergency physicians have been developing innovative methods to quickly, safely, and accurately diagnose and disposition patients. For example, the incorporation of the point-of-care test, brain natriuretic peptide (BNP), has lead to improvements in the timely diagnosis and manage-

Key Points

- Assume the etiology of the agitation is delirium and search for correctable underlying etiologies
- The CAM score is a useful tool for diagnosing delirium in the ED
- Pharmacological agents should be considered when the patient has the potential to harm themselves or others, or is impeding medical evaluation and management
- There is no good evidence to support not using benzodiazepines to manage agitation in the elderly
- Monotherapy with haloperidol, droperidol, lorazepam, or midazolam is generally preferred over polytherapy in the management of acute agitation
- Pharmacologic agents must be used in age-adjusted doses
- All of the typical and atypical antipsychotics can cause QTc prolongation
- Some of the atypical antipsychotics have been associated with increased mortality when used in treating agitation in patients with dementia

ment for congestive heart failure.[104,105] Though there is currently no bedside blood test for the diagnosis of delirium, the confusion assessment method (CAM), as discussed in the section on **"ED Evaluation on page 9,"** has been proposed as a sensitive and specific test for screening delirious patients.[44,106] Many who argue against the use of the CAM test state that, in busy ED's, the addition of a bedside screening test is both impractical and time consuming. However, when taking into consideration the mortality associated with delirium, the CAM test may be the first step in a valuable risk management strategy. Unfortunately, one study found that, even when the results of the CAM test were provided to emergency physicians who missed the diagnosis of delirium in five patients, management was unchanged, and patients were still sent home.[11] The author of that study suggested it may be a quality-of-care issue, and ED physicians may need further education regarding the significance of delirium. Three of the five patients required a return visit and admission or were given a new diagnosis.

Because patients with delirium represent a high risk population in both mortality and morbidity, the high prevalence of mental status impairment in the elderly population (26% to 40%), and the increasing number of elderly patients presenting to the emergency department, due diligence is needed in addressing this at risk population. The CAM test appears to be a useful test in the screening of patients with delirium in the ED setting, though further studies are needed to assess whether it alters management and, ultimately, patient care.

Disposition

It is important to remember that delirium is associated with high morbidity and mortality. Elderly patients with delirium should be admitted to the hospital to allow for a thorough search for an underlying cause of the delirium and allow for its treatment. Particularly in the elderly, there may be multifactorial etiologies contributing to the delirium that need to be addressed. In younger patients with substance abuse etiologies of delirium, selected patients may be observed in the ED and safely discharged once the condition resolves.

Cost Effective Strategies For The Management Of Delirium And Agitation

1. **Always check the fingerstick glucose.**

   Hypoglycemia is a common and readily reversible cause of altered mental status. Missing the diagnosis can cause the patient harm and expose them to unnecessary diagnostic testing.

2. **Check oxygen saturation and, if possible, capnography.**

   Oxygen supplementation or non-invasive assisted ventilation may reverse delirium or agitation caused by hypoxia or hypercapnia. Failure to recognize either can quickly lead to respiratory failure, severe acidosis, and cardiac arrest or anoxic brain injury, which may necessitate costly ICU stays and interventions.

3. **Examine the pupils and respiratory rate.**

   The diagnosis of opioid overdose can be made in the patient with pinpoint pupils and bradypnea. A small dose of titrated naloxone may reverse the altered mental status and respiratory depression from the opioid and can be both a diagnostic and therapeutic maneuver.

4. **Try to obtain information from family members, caretakers, or ambulance personnel.**

   Obtaining a careful history from caretakers may prevent unnecessary testing and workup. Eliciting information about the patient's baseline mental status is key in the evaluation of delirium and agitation. The patient may be in the ED for a foley change and the mental status may be their baseline dementia. If there is a doubt, a full workup of altered mental status should be initiated.

5. **Ask about new medications.**

   Change in medication dosages or the addition of medications, especially in the elderly, are common causes of delirium and agitation. Ask family members about all of the patient's medications, paying special attention to those listed in **Table 4 on page 5**. A drug with anticholinergic side effects can cause urinary retention, pain, and agitation in an elderly patient who is demented.

Ten Pitfalls To Avoid

1. **"I was just letting him sleep it off until morning. I didn't realize he was actually sick until we couldn't arouse him at shift change in the morning."**

   Don't assume the disoriented, verbally abusive patient is only drunk or intoxicated without performing a thorough assessment.

2. **"He was acting bizarrely and I thought he had a psychiatric problem. I didn't know he was agitated because he was post-ictal."**

   Patients exhibiting agitation must be evaluated for a possible precipitating medical condition. Don't assume the combative and agitated patient is just suffering from an exacerbation of an underlying psychiatric disease. Remember that patients with psychiatric disorders may have underlying medical problems.

3. **"She was from a nursing home. I thought the confusion was her baseline. I didn't realize this was a change in mental status for her."**

   Don't assume the confused elderly patient is suffering only from dementia. Always evaluate a confused, elderly patient for possible delirium. Remember that patients with baseline dementia may have a superimposed delirium. When possible, obtain the patient's baseline mental status from family members or caretakers.

4. **"He was so agitated we decided to come back later to evaluate him after he had calmed down. When we went back, he was unarousable. It turned out that he had diabetes and his glucose was really low."**

   Do not fail to immediately identify and intervene when life-threatening causes of agitation, such as hypoxia, hypoperfusion, or hypoglycemia, are present.

5. **"The EMS crew said he was just drunk. We didn't realize he had fallen and that he wasn't moving his right side normally. Luckily the nurse pointed out the hematoma on the back of his head. It turned out he had a huge subdural."**

   Patients with altered mental status need a prompt and thorough workup to identify an etiology for delirium, including full exposure and focused neurologic exam.

6. **"He was so agitated the nurse couldn't get vital signs on him. How were we supposed to know he was hypoxic if he wouldn't let us check a pulse oximetry? We couldn't know he would go into cardiopulmonary arrest."**

   Do not fail to sedate a patient to assist in the proper medical assessment and management of a patient who is agitated or violent.

7. **"She never complained of chest pain. Her family only that said she seemed disoriented. I can't believe she had an MI."**

   Patients with cardiac disease, as well as disease of any major organ system, can present with delirium. Remember to obtain an ECG in an elderly patient with altered mental status.

8. **"She was acting so strangely we thought it must be Alzheimer's or that she was really crazy. Later, her daughter brought in the diphenhydramine that the patient had started using to help her sleep."**

   Do not fail to obtain a thorough medication history in a delirious patient. Elderly patients are particularly prone to medication-induced delirium.

9. **"That elderly patient was agitated and trying to jump off the stretcher so we gave her a benzodiazepine. While she was waiting for her admission bed, she had a respiratory arrest and required a crash intubation."**

   Always carefully monitor respiratory status in patients sedated with benzodiazepines. Elderly patients appear to be more prone to respiratory depression with benzodiazepines.

10. **"She didn't seem quite right and was a little drowsy. I gave her a prescription for antibiotics for a UTI and sent her home. The next day, she was brought in septic because she was confused and hadn't filled her prescription."**

    Patients with delirium have high rates of morbidity and mortality. Most elderly patients with delirium will require hospitalization. Some select patients, particularly those suffering from delirium induced by substance abuse, may be discharged after a period of observation in the ED.

Case Conclusions

The first patient appeared to be just another belligerent drunk. Security was called and, when the patient failed to calm down with a show of force, he was restrained and given 2 mg of IM lorazepam . . and then another 2 mg ... and then another 2 mg! His alcohol level was only 120 mg / dl and, when he failed to become more responsive four hours after presentation, a head CT was done which showed a subdural hematoma.

The second agitated patient from the nursing home also ended up to harbor an unsuspected surprise: Her agitation was easily controlled with 0.5 mg of IM midazolam … but the surprise came when her blood sugar, done an hour after presentation, was found to be 20 mg / dl. In the end, the patient had urosepsis and a very stormy hospital course … she never made it back to the nursing home.

Summary

The agitated or confused ED patient should be assumed to be delirious until proven otherwise. Delirium may be misdiagnosed and subtle cases may not be recognized. The differential diagnosis of etiologies of delirium is extensive, due to the fact that nearly any medical condition may precipitate it. Life-threatening etiologies must immediately be identified and treated. Pharmacologic management is necessary in more severe cases of agitation in which patients are a danger to themselves or others, or are impeding medical evaluation and care. Good evidence from well designed studies to guide pharmacologic treatment is limited. At the present time, the best available evidence supports the use of monotherapy with either the typical antipsychotics (haloperidol or droperidol) or a benzodiazepine, lorazepam or midazolam. The benzodiazepines are preferred in patients with drug related agitation or in patients with parkinsonism or at risk of anticholinergic complications.

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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, such as the type of study and the number of patients in the study, will be included in bold type following the reference, where available.

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CME QUESTIONS

1. Characteristics of delirium include:
a) It is a global impairment of consciousness and cognition.
b) It cannot be diagnosed in a patients with underlying dementia.
c) It occurs only in elderly patients.
d) It is a permanent decline in mental status.

2. Attributes of delirium include:
a) Altered level of consciousness ranging from stupor to agitation.
b) Inattention with a decreased ability to focus.
c) Fluctuating course over hours or days.
d) Often associated with sleep/wake cycle disturbance.
e) All of the above.

3. Which of the following statements regarding delirium is correct?
a) The mortality rate in hospitalized patients with delirium is insignificant.
b) Most patients with delirium can be safely discharged from the ED.
c) Delirium rarely occurs in ill elderly patients.
d) The presence of delirium warrants an evaluation to search for a precipitating medical condition.

4. Which of the following is characteristic in the diagnosis of delirium?
a) Delirium is always readily apparent and obvious to the clinician.
b) Delirium always presents as lethargy or reduced level of consciousness.
c) Delirium can sometimes be subtle and, therefore, requires a careful mental status assessment.
d) Delirium should be diagnosed only in patients exhibiting disruptive agitated behavior.

5. Which of the following is true regarding the Confusion Assessment Method (CAM):
a) Is a useful tool to assist in the diagnosis of dementia.
b) Is a useful tool to assist in the diagnosis of delirium.
c) Is used to determine the underlying cause of delirium.
d) Is used to predict prognosis in delirium.

6. Life-threatening causes of delirium that must be immediately identified and treated include:
a) Hypoglycemia
b) Hypotension
c) Sepsis
d) Acute Myocardial Infarction
e) All of the above

7. Which of the following statements regarding the workup of delirium is true?
a) All patients with delirium must have a lumbar puncture.
b) All patients with delirium must have a serum alcohol level measured.
c) All patients with delirium must have a head CT.
d) All patients with delirium must have a careful history and physical to elucidate the underlying cause of the delirium.

8. In the targeted workup of a delirious patient, the following tests may be indicated as directed by the history, physical exam, and initial assessment:
a) Toxicology screen
b) Abdominal CT
c) Thyroid function tests
d) Blood cultures
e) All of the above

9. Metabolic and endocrinologic etiologies of delirium include:
a) Hyperthyroidism
b) Hypoglycemia
c) Hyponatremia
d) Hypercalcemia
e) All of the above

10. Which of the following should be considered as a possible etiology of acute agitation in a 25-year-old male?
a) Alcohol or sedative/hypnotic drug withdrawal
b) Drug intoxication
c) Hypoxia
d) Head trauma with CNS injury
e) All of the above

11. Common causes of delirium in the elderly include:
a) Pneumonia
b) Urinary tract infection
c) Dehydration
d) Adverse medication effect
e) All of the above

12. All of the following interventions may be considered to calm an acutely agitated patient with dementia *EXCEPT*:
a) Haloperidol
b) Lorazepam
c) Olanzepine
d) Verbal reassurance and physical comfort

13. Which statement regarding the sedation of agitated patients is correct?
a) Newer atypical or second generation antipsychotics have been proven to be far more efficacious and safe than haloperidol.
b) A warning has been issued by the FDA linking droperidol to cardiac arrhythmias.
c) Sedation must be withheld until an etiology of the agitation has been determined.
d) Diazepam is preferred over midazolam because it is shorter acting.

14. Which statement regarding the use of haloperidol for agitation is correct?
a) It is FDA approved for intravenous administration.
b) It is frequently associated with severe respiratory depression.
c) A dystonic reaction is a potential adverse effect.
d) It can only be used in combination with a benzodiazepine.

15. Which statement regarding benzodiazepines is *INCORRECT*?
a) The benzodiazepine with the shortest half-life is diazepam.

b) Benzodiazepines can cause respiratory depression.
c) Benzodiazepines potentiate the effect of gamma amino butyric acid (GABA) in the brain.
d) Benzodiazepines are particularly effective calming agents in patients with sympathomimetic toxidromes, such as cocaine and phencyclidine (PCP) intoxication.

16. Which of the following would be the best drug for sedation of an agitated patient with acute alcohol withdrawal?
a) Lorazepam
b) Haloperidol
c) Olanzapine
d) Droperidol
e) Risperidone

Coming in Future Issues:

Altitude Illness
Complications in Pregnancy
Pediatric Toxicology

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

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

Class III
- May be acceptable
- Possibly useful
- Considered optional or alternative treatments

Level of Evidence:
- Generally lower or intermediate levels of evidence
- Case series, animal studies, consensus panels
- Occasionally positive results

Indeterminate
- Continuing area of research
- No recommendations until further research

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

Significantly modified from: The Emergency Cardiovascular Care Committees of the American Heart Association and representatives from the resuscitation councils of ILCOR: How to Develop Evidence-Based Guidelines for Emergency Cardiac Care: Quality of Evidence and Classes of Recommendations; also: Anonymous. Guidelines for cardiopulmonary resuscitation and emergency cardiac care. Emergency Cardiac Care Committee and Subcommittees, American Heart Association. Part IX. Ensuring effectiveness of community-wide emergency cardiac care. JAMA 1992;268(16):2289-2295.

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