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Altered Mental Status in Older Emergency Department Patients

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Synopsis

Altered mental status is a common chief complaint among older emergency department (ED) patients. Acute changes in mental status are more concerning and are usually secondary to delirium, stupor, and coma. These forms of acute brain dysfunction are commonly precipitated by an underlying medical illness that can be potentially life-threatening and are associated with a multitude of adverse outcomes. Though stupor and coma are easily identifiable, the clinical presentation of delirium can be subtle and is often missed without actively screening for it. For patients with acute brain dysfunction, the ED evaluation should focus on searching for the underlying etiology. Infection is one of the most common precipitants of delirium, but multiple etiologies may exist concurrently.

Keywords

delirium; coma; stupor emergency department; epidemiology; diagnosis; management

Introduction

Altered mental status is a common chief complaint among older emergency department (ED) patients. Despite the frequency of this complaint, the term “altered mental status” is vague and has several synonyms such as confusion, not acting right, altered behavior, generalized weakness, lethargy, agitation, psychosis, disorientation, inappropriate behavior, inattention, and hallucination.[1] Such lack of standardized terminology not only hinders the assessment and appropriate management of patients with altered mental status, but also the advancement of knowledge through research.

Altered mental status has varying time courses and degrees of severity. Acute changes in mental status are usually secondary to delirium, stupor, and coma, which are forms of acute brain dysfunction. These changes occur over a period of hours or days and are usually

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precipitated by an underlying medical illness that is potentially life threatening. Chronic alterations in mental status (e.g. dementia) occur over a period of months and years and are less likely to be precipitated by a life-threatening illness.[2] For these reasons, acute changes in mental status will be the focus of this review. Altered mental status is rarely caused by psychiatric illnesses such as depression or schizophrenia, and in elder patients, these should be diagnoses of exclusion. Acute brain dysfunction (delirium, stupor, and coma) and their underlying etiology should be ruled out prior to considering any psychiatric diagnoses, especially in patients without a previous history of psychiatric illness.

The ED plays a critical role in the evaluation and management of older patients with altered mental status. The ED is often the initial point of entry for geriatric hospital admissions,[3] and it is tasked with rapidly identifying those who are critically ill, while efficiently diagnosing the underlying etiology, and promptly initiating life saving therapies. In the United States alone, the ED sees approximately 18 million patients who are 65 years and older each year.[4] Because of the projected exponential growth of the US aging population over the next several decades, the number of elder ED patient visits will likely grow at a similar pace.[5] Hence, the emergency physician must be adept in evaluating and managing patients with acute alterations in mental status. This review will discuss the epidemiology of delirium, stupor and coma in the ED along with their effect on patient outcomes. This chapter will also review the mental status assessment of the patient with acute brain dysfunction, as well as their diagnostic workup and treatment. Of all the forms of acute brain dysfunction, delirium is probably the most well-studied and will be the focus of this review. However, the concepts pertinent to delirium can be generalized to stupor and coma, because there is significant overlap.

The Spectrum of Acute Brain Dysfunction

Delirium, stupor, and coma represent a broad spectrum of acute brain dysfunction (Figure 1) and are associated with an impairment of consciousness. There are two interrelated domains of neurologic function that are related to consciousness: content and level (also known as arousal) of consciousness.[6] The content of consciousness has many components such as orientation, perception, executive function, and memory, and is mediated at the cortical level. The level (or arousal) of consciousness signifies the patient's wakeful state and reactivity to surrounding stimuli. This is mediated at the ascending reticular activating system located in the brainstem.[6] Traditionally, terms such as lethargic, drowsy, or somnolent have been used to describe level or arousal of consciousness. Because these descriptors can have different meanings for different clinicians, using a structured arousal scale such as the Richmond Agitation Sedation Scale (RASS) may be a more reliable method to describe altered level of consciousness. This scale ranges from −5 (unresponsive to pain and voice) to +4 (extreme combativeness).[7,8] As the patient's level of consciousness becomes more disturbed, the concern for an underlying life threatening acute medical illness should similarly increase. Patients with acute brain dysfunction can not only fluctuate between different RASS scores, but can also transition between delirium, stupor, and coma.

Stupor and Coma: Definitions and their Epidemiology in the Emergency Department

Stupor and coma occurs in 5 to 9% of older ED patients and when present, are considered to be medical emergencies that require immediate evaluation.[9,10] These two forms of acute brain dysfunction occur over a period of hours to days and represent the most severe disruptions in both the level and content of consciousness. Stupor (RASS −4) is a condition of deep sleep or similar behavioral unresponsiveness from which the patient can be aroused only with vigorous and continuous stimulation. Coma (RASS −5) is defined as a state of unresponsiveness in which the patient cannot be aroused with any stimuli.

Delirium: Definitions and its Epidemiology in the Emergency Department

Delirium is an acute disturbance of consciousness (i.e. attention) that is accompanied by an acute loss in cognition that is not better explained by a preexisting dementia.[11] This form of acute brain dysfunction occurs in 8 to 10% of patients of older ED patients.[10,12–17] Similar to stupor and coma, delirium occurs over a period of hours and days, and its course tends to wax and wane throughout the day. In contrast to stupor and coma, however, some elements of the level and content of consciousness are maintained in patients with delirium. The degree of impairment in the level of consciousness can be variable, ranging from moderate sleepiness (RASS −3) to extreme combativeness (RASS +4). Patients with delirium also have inattention which is considered a cardinal feature of delirium.[18,19] The impairment of content of consciousness is similarly variable and leads to an acute loss in cognition. Examples of such impairments observed in delirious patients are disorganized thought, perceptual disturbances, and disorientation (See Box).[18]

Box

Examples of impairments in the cognitive domains that can be seen in patients with delirium

Disorganized thinking

The patient's thought process is disorganized and incoherent. The patient may ramble, make irrelevant statements, or have illogical flow of ideas. The following conversation is an example of disorganized thinking:

Physician: "Mr. B, how are feeling today?"

Mr. B: "I'm feeling horrible today. It reminds me of the day I visited Italy when I was younger… those were the days of yesterday, today, and the future. The future is irrelevant to the past, and this makes me happy."

Perceptual disturbances

The patient may be seeing things that aren't their (visual hallucinations) or hearing things that no one else can hear (auditory hallucinations). For example, a delirious patient with visual hallucinations is seen picking at his blanket thinking that he is picking up bugs, when in reality, none are present.

Disorientation

The patient may not know where he is or what the date is.

The Psychomotor Subtypes of Delirium

Delirium can be further classified into three psychomotor subtypes: hypoactive, hyperactive, and mixed.[20] Hypoactive (RASS < 0) delirium is described as "quiet" delirium and is characterized by psychomotor retardation; delirious patients with this subtype can appear drowsy, somnolent, or even lethargic. Because the clinical presentation can be very subtle, hypoactive delirium is frequently undetected by health care providers,[21] and is often attributed to other etiologies such as depression or fatigue.[22,23] To the contrary, patients with hyperactive delirium (RASS > 0) have increased psychomotor activity and may appear restless, anxious, agitated, or combative. Hyperactive delirium is more easily recognized by health care providers. Mixed-type delirium exhibits fluctuating levels of psychomotor activity; the patient can exhibit hypoactive symptomatology at one moment and hyperactive symptomatology several hours or even seconds later. Hypoactive delirium and mixed-type delirium appear to be the predominant subtypes in older patients regardless of the clinical setting.[14,24–29] In the ED specifically, hyperactive delirium is the least common subtype.[14]

It is hypothesized that each psychomotor subtype has different underlying pathophysiological mechanisms.[20,30] Though the mechanisms are unclear, it is hypothesized that each delirium subtypes has differential neurotransmitter activity (cholinergic, dopamine, serotonin, and gamma-aminobutyric acid).[20] Each psychomotor subtype may also be cause

by different etiologies. Delirium caused by an infection or metabolic derangement is more likely to be the hypoactive subtype, whereas delirium caused by alcohol or benzodiazepine withdrawal is more likely to be the hyperactive subtype.[31] The psychomotor subtypes of delirium may also have a differential effect on clinical course and outcomes.[32] In 225 older patients admitted to a post acute care facility, Kiely at al. observed that patients with hypoactive delirium had the highest 1-year mortality rate compared with the other subtypes.[33]

Delirium versus Dementia

Delirium is distinct from dementia (Table 1), yet many clinicians use these terms interchangeably. It is important to note, however, that dementia is an important predisposing factor to delirium, and patients can have both conditions concurrently. As previously mentioned, the loss of cognition observed in delirium tends to occur rapidly, and its course tends to fluctuate throughout the day. The loss of cognition observed in dementia is usually gradual (over months to years), and its course tends to be stable. Patients with delirium also have inattention, which is considered the cardinal feature of delirium where as attention is usually preserved in patients with dementia. Altered level of consciousness, disorganized thinking, sleep-wake cycle disturbances, and perceptual disturbances are also commonly observed in delirium, whereas these characteristics are typically absent in dementia.

There are instances when the clinical features of delirium and dementia overlap, making them difficult to distinguish from each other. This is especially the case in patients with end-stage dementia, where they can exhibit symptoms of inattention, altered level of consciousness, disorganized thinking, sleep-wake cycle disturbances, and perceptual disturbances in the absence of delirium.[34] When patients with end-stage dementia develop delirium, an acute change in mental status is still observed, and any pre-existing abnormalities in cognition and level of consciousness will likely worsen. For this reason, diagnosing delirium can be extremely challenging in patients with severe dementia and establishing their baseline mental status is critical to the diagnosis.

Delirium is classically thought of as reversible and is usually precipitated by an underlying medical illness. However, there are also a proportion of patients whose delirium is not transient, and their symptoms can persist for months or even years.[35,36] Dementia is thought of as irreversible and not secondary to an underlying medical illness. However, there are circumstances in which dementia may be reversible. Hypothyroidism, normal pressure hydrocephalus, vitamin B12 deficiency, and depression are examples of illnesses that can cause reversible dementia or a dementia-like illness (pseudodementia). One meta-analysis comprised of 39 articles reported that 9% of dementia were potentially reversible, but only 0.6% of the dementia cases showed any improvement in cognition after the reversible cause was addressed.[2]

Dementia with Lewy bodies is the second most common type of dementia (after Alzheimer's) and deserves special mention because it can be very challenging to distinguish from delirium.[37] Similar to delirium, the loss of cognition observed in dementia with Lewy bodies can be rapid, and it can fluctuate over several hours or days. Perceptual disturbances are also commonly observed in dementia with Lewy bodies. Patients with dementia with Lewy bodies, however, have Parkinsonian motor symptoms such as cog wheeling, shuffling gait, stiff movements, and reduced arm-swing during walking; these motor symptoms are usually absent in patients with delirium. Differentiating between dementia with Lewy bodies and delirium can be difficult in the ED and may require a detailed evaluation by a neurologist or psychiatrist.

Other Illnesses That Can Mimic Delirium, Stupor, and Coma

In patients with altered mental status, the emergency physician must also consider other neurologic diagnoses. In patients who appear unresponsive, locked-in syndrome should be considered and is caused by focal injury to the ventral pons secondary to an infarct, hemorrhage, or trauma. If secondary to an infarct, the distal basilar artery is usually occluded. Multiple sclerosis and central pontine myelinosis can also cause locked-in syndrome. Though the clinical presentation is variable, quadriplegia and anarthria is usually present, but vertical eye gaze and upper eyelid movement are usually retained.[38] Despite having the outward appearance of being unresponsive, patients with locked-in syndrome have normal levels of consciousness and are fully aware of their surroundings. If locked-in syndrome is suspected, then prompt neuroimaging and neurology consultation are warranted. Patients with a suspected thromboembolic cause of locked-in syndrome should immediately go to interventional radiology for intra-arterial thrombolytic therapy, even if the symptoms have being ongoing for more than the traditional 3-hour window.[39] Without emergent intervention, survival and neurological recovery for these patients can be poor.

Non-convulsive status epilepticus (NCSE) should also be considered in patients who have altered mental status, especially if no obvious cause for their mental status changes is found. This diagnosis should strongly be considered if the patient has a seizure history or had a seizure prior to arriving to the ED. One systematic review reported that NCSE occurred in 8% – 30% of patients with altered mental status (mean prevalence = 22%).[40] This systematic review consisted of 5 studies that predominantly enrolled patients in the hospital setting.[40] NCSE is an underrecognized and important form of altered mental status that can only be diagnosed with electroencephalography (EEG). If this cause of altered mental status is considered, then neurology consultation should be obtained promptly; the treatment of NSCE (benzodiazepine and anti-epileptic medications) is significantly different from other causes of altered mental status.

Risk Factors for Developing Acute Brain Dysfunction

The etiology of delirium (and other forms of acute brain dysfunction) involves a complex interplay between patient vulnerability (or predisposing) factors and precipitating factors (Figure 2).[41–43] Patients who are highly vulnerable (e.g. 92 year old with severe dementia, poor functional status, and multiple comorbidities) will require a relatively benign insult to develop delirium. For these patients, a relatively benign insult such as a simple urinary tract infection or small dose of narcotic medication can precipitate delirium. Because elderly patients are more likely to have multiple vulnerability factors, they are more susceptible to becoming delirious compared with their younger counterparts. Nursing home patients are particularly vulnerable.[44] For patients who are less vulnerable (e.g. 67 year old with no dementia, little comorbidity burden, and who is still functionally independent), higher doses of noxious stimuli such as severe sepsis are required to develop delirium. Consequently, when a patient with little or no vulnerability factors presents to the ED with delirium, stupor, or coma, the clinician should have more concern for an underlying life threatening illness. To develop stupor of coma, even higher doses of noxious stimuli are required.

Patient Vulnerability Factors for Acute Brain Dysfunction

A multitude of patient vulnerability factors for delirium have been identified in the hospital literature (Table 2) and can likely be extrapolated to stupor and coma.[45–48] Dementia is the most consistently observed vulnerability factor for delirium regardless of clinical setting.[41,45,49–55] A dose-response relationship seems to exist; as the severity of dementia worsens, the risk of developing delirium increases.[56] Similarly, low education attainment also increases the patient's susceptibility to developing delirium.[57] Both dementia and

education attainment may be indicative of poor cognitive reserve and reflect the inability of the brain to adequately compensate for any noxious or stressful physiological insult. Other commonly observed vulnerability factors for delirium include poor functional status,[50,55] advanced age,[49,54] home psychoactive medication use such as narcotics, benzodiazepines,[49,58] and medications with anticholinergic properties,[51] history of alcohol abuse,[50,55] visual impairment,[41] high comorbidity burden,[55] and malnutrition.[42] There are limited data from the ED setting, but one study identified dementia, premorbid functional impairment, and hearing impairment as risk factors for delirium in the ED.[14] Another ED study also identified dementia as a risk factor for delirium.[59] They also observed that patients with advanced age, or a past history of cerebrovascular disease and seizure disorder were more likely to be delirious in the ED.[59]

Precipitating Factors for Acute Brain Dysfunction

There are numerous precipitating factors of delirium that have been reported in the hospital literature (Table 3).[46–48] Generally speaking, patients with higher severities of illness are more likely to develop delirium,[41,58] and even higher doses are required to cause stupor and coma. Infections are probably the most common causes of delirium occurring in 16 to 67% of cases;[49,52–54,60–63] urinary tract infection and pneumonia are common infectious etiologies. Other precipitants for delirium include electrolyte abnormalities such as hyponatremia, hypernatremia, hypercalcemia, and hypocalcemia,[58,64] organ failure,[58,64] Wernicke's encephalopathy, thyroid dysfunction,[65] central nervous system insults such as cerebrovascular accidents, intracerebral hemorrhage, epidural and subdural hematomas, and subarachnoid hemorrhage,[52,53,60,63] ethanol and benzodiazepine withdrawal,[66–68] dehydration,[41] and cardiovascular illnesses such as congestive heart failure,[53,54] and acute myocardial infarction.[69] Poorly controlled somatic pain (i.e. extremity fracture patients) can also precipitate delirium.[70–72] Vital sign abnormalities (hypertensive encephalopathy, hypotension, hyperthermia or hypothermia, or hypoxia), endocrine disorders (hyperglycemia, hypoglycemia, adrenal insufficiency), and hypercarbia can also precipitate delirium.[73,74] More often than not, multiple delirium precipitants will exist concurrently,[58] but in 13% of cases, no obvious etiologic agent will be found.[63] Delirium can also be precipitated by iatrogenic events in the ED. Inouye et al. observed that the use of physical restraints, bladder catheters, or the addition of more than three medications were associated with delirium development.[42]

Medication Risk Factors for Delirium

Medications are important vulnerability and precipitating risk factors factor for delirium, because polypharmacy is highly prevalent in the older patient population. Clegg et al. performed a systematic review and observed that benzodiazepines, opioids, dihydropyridines (e.g. nifedpine), and antihistamines may increase the risk for delirium.[75] Of the opioids, meperidine is probably the most deliriogenic.[72,76–79] These medications, especially benzodiazepines and opioids, can also induce stupor and coma at higher doses.

Medications with anticholinergic properties are thought to be frequent causes of delirium. There are over 600 medications with anticholinergic properties, and of these, 11% are frequently prescribed to the older patients.[80] Some examples of commonly prescribed medications with anticholinergic properties are diphenhydramine, promethazine, hydroxyzine, meclizine, lomotil, and heterocyclic antidepressants (e.g. amitriptyline, nortriptyline, doxepin). In acute stroke patients, Caerio et al. found that that patients on home medications with anticholinergic properties were more susceptible to developing delirium during hospitalization.[81] In 278 older medical patients, Han et al. observed that anticholinergic medications were associated with increased delirium severity.[82] However, the evidence linking medications with anticholinergic properties and delirium is not

consistently observed. Agostini et al. observed a trend towards increase risk (relative risk = 2.1, 95%CI: 0.9 – 4.7) of developing delirium in older hospitalized patients when diphenhydramine was used.[83] Luukkanen et al. found that older patients who used more than one medication with anticholinergic properties were more likely to have delirium in the unadjusted analysis (27.0% versus 16.7%, p-value = 0.05). However, this relationship became non-significant after adjusting for age, gender, and comorbidity.[84] In 147 hospitalized older patients, Campbell et al. observed that anticholinergic medications were not associated with delirium that developed in the hospital. [85] These discrepant observations may be a result of patient characteristics (stroke versus non-stroke, race, etc.,) or the method in which anticholinergic burden was measured. Despite these discrepant findings, the general consensus among geriatric and psychiatric experts is that medications with anticholinergic properties in older patients should be avoided, especially if safer alternatives exist.[86,87]

The Effect of Acute Brain Dysfunction in the Emergency Department on Outcomes

There is a dearth of data with regard to acute brain dysfunction in the ED and its effect on patient outcomes. Much of what is known is based upon studies conducted in older hospitalized patients. Studies investigating the role of stupor and coma are mainly limited to the intensive care unit setting. It is clear that the development of stupor and coma portend adverse outcomes; multiple studies have observed that these patients are more likely to die and have poor functional outcomes regardless of underlying etiology.[88–92]

The link between delirium and patient outcomes is well established in older hospitalized patients. A recent meta-analysis that included 21 studies observed that hospitalized patients with delirium are twice as likely to die, have a 2-fold increased odds of being institutionalized, and have a 12-fold increased odds of developing dementia compared with patients without delirium.[93] Delirium also accelerates the rate of cognitive decline in patients with pre-existing dementia, and it is hypothesized that delirium may cause irreversible brain injury.[94,95] In addition, delirium is associated with accelerated functional decline,[96] prolonged hospitalizations,[58] and higher health care expenditures.[97] The duration of delirium appears to be an important prognostic indicator as for every 48 hours of delirium increases the risk of 3-month death by 11%.[98] Furthermore, many patients with delirium can remember their delirious experience and this can cause significant distress in 70 to 80% patients.[99,100]

The consequences of acute brain dysfunction in the ED remain unclear. Although older patient cohorts are similar between the ED and hospital settings, caution must be taken when attempting to generalize the results of studies from one setting to another especially with delirium. ED patients who are discharged home represent a significant proportion of older ED patients and are not represented in hospital-based studies. Up to 25% of delirious older ED patients are discharged home,[12,101] and likely represent a unique population. Additionally, most hospital-based delirium studies enrolled patients 24 to 48 hours after admission,[27,55,96,102,103] and this may not reflect what the patient's delirium status was in the ED. Delirium can rapidly fluctuate and can quickly resolve in less than one day in 20% – 51% of patients;[104–106] hospitalized patients who were classified as non-delirious in the hospital may have been delirious in the ED. Conversely, patients who were not delirious in the ED may have become delirious in the hospital at the time of enrollment. Such misclassification can also occur in stupor and coma studies that enrolled patients in the hospital; such patients may have been delirious or had normal mental status in the ED.

Though there are no studies investigating the role of stupor and coma in the ED on outcomes, there are limited data on the effect of ED delirium. Delirium in older ED patients appear to be a predictor of long-term mortality, and this relationship is independent of age, comorbidity burden, severity of illness, dementia, functional dependence, and nursing home residence.[107] Delirium is also a marker for death for those who are discharged from the ED. Kakuma et al. observed that in older ED patients who were discharged from the ED, delirium was independently associated with 6-month mortality.[17] Older ED patients with delirium are also more likely to have prolonged hospitalizations.[101] Only one ED study has investigated the relationship between delirium and long-term functional outcomes. Vida et al. observed that delirium in the ED was associated with accelerated functional decline in patients without pre-existing dementia in the unadjusted analysis only.[108] However, this relationship disappeared after potential confounders were adjusted for in the multivariable model.[108] Even with the relatively small number of ED studies, it is likely that delirium in the ED is a marker for adverse patient outcomes.

Under-recognition of Delirium in the Emergency Department

Because of the severity of impairment observed, emergency physicians readily recognize stupor and coma with little difficulty. However, emergency physicians miss delirium in 57 to 83% of the cases,[10,12–17] because its clinical presentation can be subtle and can be missed if it is not actively sought. Missing delirium is considered by many to be a medical error and may have important downstream implications for clinical care.[109] Patients with delirium may be unable to provide an accurate reason of why they are in the ED,[110] and this may lead to inappropriate or inadequate diagnostic workups. Delirium may be ascribed to another psychiatric illness such as depression.[23] These patients may be erroneously admitted to a psychiatric ward and there may be delay in the diagnosis of their underlying medical illness.[111] Up to 25% of delirious older ED patients are discharged home,[12,101] a significant proportion may not be able to comprehend their discharge instructions,[110] leading to non-compliance.[112] Older ED patients who are discharged home with unrecognized delirium are more likely to die at 6-months compared with those whose delirium was recognized.[17] Hustey et al. observed that out of the five older ED patients who were discharged home with delirium, one patient fell and two patients returned to the ED within three days and were eventually hospitalized.[12] Lastly, if the patient is admitted, over 90% of delirium that is missed in the ED will also be missed in the hospital setting.[14]

Assessment of the Dysfunctional Brain in the Emergency Department

In any ED patient with acute alterations in mental status, the first step is to assess for the level of consciousness using a validated arousal scale such as the RASS. If the patient in a sleep-like state, then it is necessary to determine the intensity of stimulation that is needed to arouse the patient.[6] If a patient is unarousable to loud voice and vigorous shaking, then a painful stimulus should be introduced, but every effort should be made to avoid causing tissue damage. Painful stimuli can be introduced by moderate compression of the nail beds, the supraorbital ridge, or the temporomandibular joint.[6] Patients with a RASS −4 and −5 are considered to be stuporous or comatose, respectively; these patients should then be assessed with a validated coma scale (See Assessment of Stupor and Coma). Patients with a RASS of −3 and above should be assessed for delirium (See Assessment of Delirium).

Assessment of Stupor and Coma

If the patient's RASS is −4 or −5, then the patient is likely to be stuporous or comatose for which several scoring assessments exist. The Glasgow Coma Scale (GCS) is probably the most widely used coma scale, and rates eye, verbal, and motor response to verbal and painful stimuli (Table 4).[113] Scores range from 3 (unresponsive) to 15 (normal). The GCS

has prognostic significance as it predicts mortality,[114,115] but has several limitations as the verbal score is difficult to obtain in patients who are intubated or aphasic. The GCS can also have low inter-rater reliability because it is difficult to remember.[116] The Full Outline of Unresponsiveness (FOUR) is another coma score that assesses for eye response, motor response, pupillary reflexes, and breathing.[117] Because the FOUR Score does not evaluate verbal response, this scale can be performed in patients who are intubated or aphasic. However, the FOUR score is relatively complicated and is also difficult to remember. Hence, the FOUR score may have limited utility in the ED.

The AVPU is another commonly used scale to help describe impaired level of consciousness. It stands for alert, responsive to verbal stimuli, responsive to painful stimuli, and unresponsive. The benefit of the AVPU scale is that it is easy to remember and allows for quick communication of the patient's global picture of level of responsiveness. However, it lacks granularity to detect subtle impairments.[118]

Assessment of Delirium

For patients with altered mental status with a RASS of -3 or greater (arousable to verbal stimuli), the patient should be assessed for delirium. It is important to remember that the minority of patients with delirium will have the chief complaint of "altered mental status" and the clinical manifestation of delirium can be subtle especially if it is the hypoactive subtype. As a result, many cases of delirium will be missed unless it is actively screened for using validated delirium assessments. Recently, delirium screening has been proposed to be one of the key quality indicators for emergency geriatric care,[119] and a core competency for emergency medicine resident education.[120]

A psychiatrist evaluation using Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, Text Revision (DSM-IV-TR) criteria is considered to be the gold standard for delirium diagnosis.[11] To meet DSM-IV-TR criteria for delirium, a patient must have all of the following: 1) a disturbance of consciousness (i.e., reduced clarity of awareness of the environment) with reduced ability to focus, sustain or shift attention, 2) a change in cognition or the development of a perceptual disturbance that is not better accounted for by a preexisting, established or evolving dementia, 3) the disturbance develops over a short period of time (usually hours to days) and tends to fluctuate during the course of the day, and 4) there is evidence that the disturbance is caused by the direct physiological consequence of a general medical condition or substance. Determining these criteria require a comprehensive neurocognitive testing and a detailed interview with a person who knows the patient well (i.e. proxy or caregiver).

Obtaining routine psychiatric consultation to perform these DSM-IV-TR delirium evaluations may not be feasible for most hospitals and these criteria are not routinely applied by non-psychiatrists. The Confusion Assessment Method (CAM) was developed for non-psychiatrists and is probably the most widely used delirium assessment in the medical setting,[121] and has undergone the most extensive validation.[122] The CAM operationalizes the Diagnostic and Statistical Manual of Mental Disorders criteria for delirium and consists of 4 features: 1) altered mental status and fluctuating course, 2) inattention, 3) disorganized thinking and 4) altered level of consciousness. Feature 1 (altered mental status and fluctuating course) is obtained through collateral history from a person who knows the patient's baseline cognition (i.e. family member, caregiver, nursing home, or primary care provider). Time of onset of the change in mental status should be established as well as the presence fluctuations ("Did the symptoms you noticed tend to come and go, or get worse and better over time"). In the ED, approximately 40% of older patients may not have a proxy available in the ED, and they may need to be contacted by telephone.[123] If the patient is grossly altered and a proxy is not readily available, information from the patient's medical

record may be useful to help establish their mental status baseline. For example, if a patient is unable to follow simple commands and barely able to stay awake to verbal stimuli (RASS −3), but was able to provide a detailed history in a recent primary care provider clinic visit, this patient likely has an acute change in mental status. Feature 2 is inattention and considered to be a cardinal feature of delirium.[18,19,124] Patients with inattention are easily distractible to irrelevant stimuli and can have difficulty maintaining a conversation. Questions often have to be repeated to the patient when inattention is present. Patients who are inattentive may also fall asleep during the interview when disengaged. Inattention is also commonly assessed for by asking the patient to recite the months of year backwards, recite the days of the week backwards, or count backwards from 20 to 1.[124,125] Patients with disorganized thinking (feature 3) exhibit incoherent thought processes; they may ramble or have irrelevant conversations. They may also display illogical flow or of ideas, circumstantiality, or tangential thoughts. Feature 4 is altered level of consciousness and is patient who is drowsy, lethargic, anxious, restless, or agitated (RASS other than 0).

For a patient to meet criteria for delirium, both features 1 and 2, and either 3 or 4 must be present. The original CAM validation study was conducted in hospitalized patients, and was found to have excellent sensitivity (94 – 100%) and specificity (90 – 95%) compared with a psychiatrist's assessment using DSM-III-R criteria.[121] The CAM is the only delirium assessment to be validated in the ED setting, albeit in patients from Brazil.[126] In 100 patients who were 60 years or older, the CAM's sensitivity was 94.1% and its specificity was 97.4% when performed by a geriatrician.[126] The psychiatrist's DSM-IV assessment was the reference standard for this study. In order to assess all of the CAM's features, the training manual recommends performing the Modified Mini-Cog and the Digit Span test, and can take approximately 5 minutes to complete.[127] If the patient is delirious or demented, the CAM may take even longer.[128] The CAM requires significant training and may be less sensitive when used by raters with less clinical experience.[129,130]

Detecting delirium in the ED can be challenging, because it is fast paced and the ED staff is usually under immense time constraints. As a result, spending 5 minutes performing a delirium assessment may not be feasible and briefer (<2 minutes) delirium assessments may be needed in this difficult setting. The Confusion Assessment Method of the Intensive Care Unit (CAM-ICU) is based upon the CAM and may be feasible to perform in the ED, because it takes less than 2 minutes to complete.[131] The CAM-ICU (Figure 3) has been recently restructured and allows for early stoppage. For a patient to meet criteria for feature 1, a patient must have either altered mental status or fluctuating course; this is slightly different than the CAM which requires both to be present. The CAM-ICU uses brief objective assessments to test for inattention and disorganized thinking. To test for inattention (feature 2), the CAM-ICU rater gives a series of 10 letters ("SAVEAHAART") and asks the patient to squeeze the rater's hand whenever the letter "A" is heard. A picture recognition test, which tests the patient's short term memory, is also used to test for inattention. To test for disorganized thinking, four yes/no questions are asked as well as a simple command. The CAM-ICU incorporates the RASS to assess for altered level of consciousness (Feature 3); a score other than 0 indicates altered level of consciousness. Additional details are available in www.icudelirium.org.

The CAM-ICU has excellent diagnostic performance in the critically-ill patient population, but there are limited data evaluating the CAM-ICU's diagnostic performance in those who are non-critically ill. Neufeld et al. evaluated the CAM-ICU performed by a layperson in 139 noncritically ill medical oncology inpatients where the median age was 57 years old. They found that its sensitivity was 18% and its specificity was 99% compared with a psychiatrist's DSM-IV assessment.[132] In 129 patients with acute stroke and a median age of 72.5 years, the CAM-ICU's sensitivity and specificity was 76% and 98%, respectively.[133] It

is unclear why the sensitivities are so discrepant, but it may be secondary to differences in median age, underlying disease, and severities of illness. Recently, the CAM-ICU was modified into the Brief Confusion Assessment Method (B-CAM) to improve its sensitivity. The B-CAM and CAM-ICU primarily differ on how they test for inattention. The B-CAM simply asks the patient to recite the months of the year backwards from December to July. The CAM-ICU, B-CAM, and other brief delirium assessments specifically designed for the ED are currently being validated in the older ED patients.

Several very brief delirium assessments have been validated in other settings and may have promise for the ED. The Delirium Diagnostic Tool-Provisional (DDT-Pro) is brief delirium assessment that assesses for disorganized thinking, inattention, and sleep-wake cycle disturbances. In 36 patients with traumatic brain injury, the DDT-Pro was 100% sensitive and 94% specific when performed by a layperson compared with a psychiatrist's assessment.[134] However, the median age was 44 years old, and patients were recruited from a rehabilitation hospital, indicating significant brain injury; the diagnostic performance may be different in older ED patients without head injury. The Single Question in Delirium (SQiD) is another promising delirium assessment that asks the patient's family or friend the following question: "'Do you think [name of patient] has been more confused lately?" In 33 oncology inpatients, the SQiD was 80% sensitive and 71% specific compared with a psychiatrist's assessment.[135] Lastly, the modified Richmond Agitation and Sedation Scale (mRASS) may also have clinical utility in the ED; this assessment takes less than 30 seconds to complete and can easily be integrated into the ED clinical workflow.[135] The mRASS is based upon the RASS, but also incorporates the rater's observations of the patient's attentiveness. Using the psychiatrist's assessment as the reference standard, a mRASS other than 0 (altered level of consciousness or inattentive) is 64% sensitive and 93% specific for delirium in older hospitalized patients.[135] Performing serial mRASS assessments increases the sensitivity to 74% with a specificity of 92%.[135]

Initial Management of Patients with Altered Mental Status in the Emergency Department

When a patient with altered mental status arrives to the ED, the first step is to determine whether this patient is critically ill or not. As the level of consciousness becomes more disturbed (i.e. RASS −5 or RASS +4), the index of suspicion for a life threatening illness that precipitated the acute change in mental status should similarly increase. This is particularly the case for patients who are stuporous or comatose. These patients should become the emergency physician's immediate priority, and the primary goal should be to promptly assess and stabilize the patient with as little delay as possible.

The initial evaluation and management for ED patients with altered mental status is summarized in Table 5. The patient's airway, breathing, circulation, and disability should be rapidly evaluated and addressed; the patient should be fully exposed to facilitate evaluation and treatment. Concomitantly, the patient should be placed on pulse oximeter and cardiac monitor, and an intravenous line should be established; if the patient is hemodynamically unstable, then two large bore intravenous lines should be started in the antecubital fossa. Finger stick blood glucose should be obtained immediately to rule out hypoglycemia. Vital signs should also be rapidly measured and if possible, a rectal temperature should be performed to accurately rule out hypo- or hyperthermia.

If opioid overdose is suspected, then intravenous nalaxone should be given especially if the patient is comatose or stuporous. The initial dose of nalaxone is not well established, but is generally considered to be 0.4mg; this initial dose should be diluted in 10cc of normal saline and be administered slowly over several minutes to avoid severe withdrawal symptoms. If

there is no response, then the dose can be escalated to 2mg and up to 10mg intravenously; higher doses may be needed if the patient is on a long-acting opioid medication such as methadone. Transdermal fentanyl patches should also be looked for while exposing the patient and if present, it should be removed immediately. Reversing benzodiazepine overdoses with flumazenil is not routinely recommended because it may elicit life threatening withdrawal and seizures in patients who are chronic users. If the finger stick blood sugar indicates hypoglycemia, one ampule (50cc) of D50 should be administered intravenously; if intravenous access is difficult to obtain, 2mg glucagon can given intramuscularly. Thiamine 100mg given parenterally or intramuscularly can also be considered if Wernicke's encephalopathy is suspected; clinicians should have a high index of suspicion of this in patients who have a history of ethanol abuse or appear malnourished. Thiamine should be given prior to glucose administration. Based upon animal models, there is a theoretical risk that glucose administration may worsen encephalopathy in those who are thiamine deficient.[136]

The Diagnostic Evaluation of Patients with Acute Brain Dysfunction

In patients with delirium, stupor, or coma, the diagnostic evaluation should be focused on uncovering the underlying etiology. Though other causes of acute brain dysfunction are common, the emergency physician's first priority is to consider life threatening causes. Life threatening causes of acute brain dysfunction can be remembered using the mnemonic device "WHHHHIMPS" (Table 6).[73] Many of these life-threatening causes such as hypoglycemia or hypoxemia can be ruled out within the initial assessment mentioned in the previous section. Other diagnoses, such as meningitis, require a more extensive evaluation and should be considered if no other cause for the patient's acute brain dysfunction is found. Once these life threatening causes have been considered, the ED evaluation can then focus on ruling out other less life threatening causes of acute brain dysfunction as listed in Table 3.

History

Because a patient with acute brain dysfunction, including delirium, is unlikely to provide an accurate history,[110] obtaining a detailed history from a proxy is critical to uncovering the underlying etiology. This may be from a family member, caregiver, or a nursing home staff if the patient resides in one. Because so many medications can be deliriogenic, it is important to carefully review the patient's medication history. Medication histories obtained from triage or from electronic medical record are notoriously inaccurate and should be confirmed with the caregiver or their pharmacy.[137,138] A history of any recent changes or additions to the patient's home medication regimen should be elicited as well as increased dosages; the clinician should determine if these changes are temporally related to the development of symptoms. In addition to prescribed medications, history of taking over the counter medications and alternative medications should also be obtained. A careful substance history should also be obtained, preferably from a proxy. A significant proportion of elderly patients are abusers of ethanol and sedative-hypnotics;[139,140] significant ingestion or withdrawal from these substances can precipitate delirium.

Physical Examination

The detailed physical examination (Figure 4) is also crucial to uncovering the underlying etiology of delirium, especially if no collateral history is available. A head examination should look for any signs of recent trauma; the presence of trauma should increase one's suspicion for a subdural hematoma, subarachnoid hemorrhage, or other traumatic intracranial injury. A pupillary examination should also be performed looking for the presence of fixed or dilated pupils. The presence of miosis and mydriasis may also indicate opioid and anticholinergic medication toxicity, respectively. The pupillary exam may be

difficult to assess in elderly patients with eye diseases, prior surgery, or in those who use opthalmic eye drops. A fundoscopic examination can also be considered looking for papilledema suggestive of increased intracranial pressure or retinal subhyaloid hemorrhage suggestive of subarachnoid hemorrhage. If possible, an extraocular muscle examination should also be performed especially in patients who appear to be unresponsive; the presence of vertical extraocular eye movements may suggest locked-in syndrome. Ophthalmoplegia can also be seen in patients with Wernicke's encephalopathy or increased intracranial pressure. The presence of nystagmus may indicate intoxication with alcohol or other drugs.

A neck examination should look for thyromegaly and meningismus. Though the presence of meningismus greatly increases the likelihood of meningitis, its absence does not reliably rule it out. A lung examination should look for any signs of pulmonary edema or pneumonia. If febrile, the cardiac exam should be focused on looking for new murmurs that may suggest endocarditis. An abdominal examination is needed to rule out any acute surgical emergencies such as acute appendicitis, diverticulitis, or cholecystitis. The patient should also be completely exposed and the skin should be examined for medication patches (e.g. fentanyl or scopolamine), signs of infection, petechiae, and sequelae of liver failure. A genitourinary examination should be performed to look for infected decubiti ulcers or perirectal or perianal abscesses. A rectal examination should be performed in patients with end stage liver disease as esophageal variceal bleeds can precipitate hepatic encephalopathy.

A focused neurological examination should be also performed. The presence of focal, lateralizing neurological symptoms is suggestive of a central nervous system insult (e.g. cerebrovascular accident, intraparenchymal hemorrhage, or mass effect). Additionally, the presence of repetitive movement of the eyelids, eyes, or extremities may be suggestive of seizure. The presence of gait ataxia may also be seen in patients with Wernicke's encephalopathy or medication overdoses.

Laboratory Testing

Laboratory tests are routinely performed in patients with delirium, stupor, and coma. Because urinary tract infections are common delirium precipitants, a urinalysis should be performed in all patients. Serum electrolytes should also be routinely obtained to rule-out electrolyte abnormalities such as hypernatremia, hyponatremia, hypercalcemia, or hypocalcemia. Because uremia can precipitate delirium, a blood urea nitrogen and serum creatinine should be ordered. In patients with respiratory complaints or issues, an arterial or venous blood gas should be considered if hypercarbia is suspected. In patients with physical findings suggestive of end stage liver disease, transaminases and ammonia levels can also be ordered. Thyroid stimulating hormone and free T4 can also be considered to rule out hyperthyroidism and hypothyroidism. Serum drug levels should also be ordered if the patient is on medications that can be measured in the serum (i.e. anticonvulsants, theophylline, and digoxin). Occasionally, patients with acute myocardial infarction can also present with delirium without chest pain;[69,141] hence, a 12-lead electrocardiogram and cardiac biomarkers should be considered, but their diagnostic yield in ED patients with delirium remains unknown. A lumbar puncture, though not routinely performed, should be strongly considered if there is a clinical suspicion for meningitis or encephalitis or if the patient has a fever or leukocytosis without an obvious source.[142,143] This diagnostic procedure can also be considered if no other etiologies for delirium, stupor, or coma are found. A urine drug screen can also be ordered but should be interpreted with caution as it can mislead the clinician into thinking that the patient has a toxicological etiology for their acute brain dysfunction, when in fact another underlying illness, such as meningitis, exists. A patient who is on home opioids and benzodiazepines will likely have a positive urine drug screen for these substances. It also does not provide serum levels, and false positive and negative results can occur.[144]

Radiographic and Other Testing

With regard to radiological testing, a chest x-ray can be considered to rule out pneumonia or pulmonary edema, especially in the setting of a history of cough and dyspnea, hypoxemia, or tachypnea. An abdominal ultrasound or abdomen and pelvis computed tomography (CT) should be considered if the patient has abdominal pain. For patients who are stuporous or comatose, they should promptly receive a head CT emergently to rule out any structural lesions. For delirious patients, however, there is little evidence based guidance to when a head CT is appropriate; their routine use is not recommended as its diagnostic yield may be low.[9] Based upon two studies, a head CT's diagnostic yield is increased when performed in delirious patients with impaired level consciousness, a recent history of a fall or head trauma, or a focal neurological deficit.[9,145] It can also be considered when no other cause for delirium is found. Clinical judgment should be used when deciding whether or not a delirious patient requires a head CT.

Magnetic resonance imaging of the brain (brain MRI) and electroencephalography (EEG) are occasionally performed in patients with acute brain dysfunction including delirium, but their optimal role in the ED is yet to be determined. In addition, these diagnostic modalities may not be readily available in all settings further limiting their use. Patients with cerebrovascular accidents involving the right parietal lobe can present with delirium as the sole manifestation and without any focal neurological findings.[146] Early in the clinical course (several hours), the head CT may be non-diagnostic, and a brain MRI can help rule in this diagnosis. Non-convulsive status epilepticus can also manifest as unusual mental status changes including delirium, but making this diagnosis can be challenging without an EEG. An early EEG should be considered in patients who had a reported seizure prior to ED arrival or have a seizure history. Though EEGs are difficult to obtain in the ED, the development of abbreviated (5-minute) EEG protocols[147] and portable EEG monitoring devices may improve the feasibility of obtaining this diagnostic modality quickly.[148] Early diagnosis of cerebrovascular accidents or non-convulsive status epilepticus is important, because earlier intervention may improve patient outcomes. If either of these diagnoses is being considered as a cause for altered mental status, then prompt neurologic consultation in the ED is recommended to facilitate both diagnostic evaluation and therapeutic intervention.

Emergency Department Management of Patients with Delirium

The single most effective treatment for acute brain dysfunction is to diagnose and treat the underlying etiology. Beyond this, the clinical management of acute brain dysfunction is unclear especially for delirium and is secondary to the limited evidence available. Delirium care is slowly evolving, and non-pharmacologic and pharmacologic interventions currently exist, especially for those who are agitated. In general, non-pharmacologic interventions are favored as the initial management and pharmacologic means should be used as a last resort. The following sections can also be applied to patients in stupor or coma, as many of these patients will eventually transition into delirium.

Non-Pharmacologic Management

Though hyperactive delirium occurs less frequently in older ED patients, its management can be challenging if they are agitated or combative, and especially if patient, caregiver, and ED staff safety is a concern. Non-pharmacologic interventions should be attempted prior to considering pharmacologic interventions. Initial steps would be to modify the environment and may involve dimming or turning off lights, minimizing auditory stimulation from beeping cardiac monitors or intravenous infusion pumps, and having family members and familiar objects from home at the patient's bedside.[47,149]

Flaherty et al. recommend the "TADA" approach as a non-pharmacologic means to managing and preventing agitation. It stands for "Tolerate, Anticipate, Don't Agitate".[150] *Tolerating* behaviors that may appear to be potentially dangerous is the first step and is contrary to the nature of health care providers. For example, a delirious patient may attempt to get out of bed without assistance or pull on intravenous lines, oxygen tubing or cardiac monitoring devices. However, tolerating such behaviors allows patients to respond naturally to their circumstances and may provide them a sense of control while in their confused state. These behaviors may also be a cue that something is bothering them; they are so cognitively impaired that they are unable to communicate what's wrong. For example, a patient who is agitated and getting out bed may really need to go to the bathroom. Tolerating behaviors require close supervision to maintain patient safety.[150] *Anticipating* behaviors is where the health care provider prepares for what the patient might do and avoids inciting agents that may exacerbate agitation. This includes avoiding unnatural attachments or tethers that are not absolutely necessary for clinical care.[150] Examples of tethers are multiple intravenous lines, nasal cannula oxygen, and monitoring devices. Instead of giving intravenous normal saline continuously for maintenance fluids, intermittent boluses should be considered. Supplemental oxygen is not needed if the patient is not hypoxic or in respiratory compromise. Blood pressure cuffs, pulse oximeter, and cardiac monitoring devices should also be minimized if continuous monitoring is not necessary; intermittent vital sign measurements should be used whenever possible.[150] Getting out of bed is also anticipated and encouraged by this approach as long as patient's safety can be ensured. *Don't Agitate* is the final step and considered the golden rule of this approach.[150] Some agitators are obvious (i.e. urinary bladder catheters) and some are not. Reorientation can be unpredictable as it can occasionally worsen agitation and should only be attempted if the patient is amenable to it.

Indwelling urinary bladder catheters deserve special mention because they are frequently placed in patients with acute brain dysfunction. They should be avoided in delirious patients when there is no clear medical indication. Urinary bladder catheters can not only agitate the patient further, but their use is associated with increased in-hospital and 90-day mortality, longer hospital lengths of stays, and a higher risk of developing delirium.[42,151] If the delirious patient has urinary incontinence and urine is needed for a urinalysis, straight catheterization should be used. Avoiding or removing urinary bladder catheters can not only reduce agitation, but can also help minimize urethral trauma from forced self-removal and reduce the risk of catheter associated infections.

Similarly, physical restraints should be avoided as they are associated with a four-fold increase in delirium development during hospitalization and is associated with increased delirium severity.[42] If placed for patient or provider safety, physical restraints should be a temporary measure and should be removed once non-pharmacological or pharmacological alternatives have taken effect. Having family members in the room or using sitters can help reduce the need for physical restraints; they can provide feedback to patients when they initiate dangerous behaviors such as climbing out of bed or attempting to go the bathroom without assistance.

Pharmacologic Management

Pharmacologic management is mainly focused on the agitated delirious patient (hyperactive) and can be considered if non-pharmacologic interventions fail. Benzodiazepines should be avoided as monotherapy in delirious patients whenever possible,[47,152] because they have high side effect profiles and can exacerbate delirium. Breitbart et al. performed a randomized control trial that compared antipsychotic medications with lorazepam, and observed a higher prevalence of treatment limiting side effects such as over-sedation and increased confusion in the lorazepam arm.[153]

The National Institute of Health and Clinical Excellence (NICE) delirium guidelines recommend using antipsychotic medications in patients with agitation and who are at high risk for harming themselves and others.[152] However, these medications should be used only if verbal and non-verbal de-escalation techniques have failed, and if used, the lowest dose possible should be given.[152] Antipsychotic medications are also used in delirious patients with behavioral disturbances and overt psychotic manifestations (i.e. visual hallucinations and delusions). However, their routine use is controversial because most studies investigating the use of antipsychotics are limited by their non-blinded trial design, poor randomization, or inadequate power. Two systematic reviews investigated the role of antipsychotic medications in delirium management, and they concluded that there was little evidence to support their routine use and that additional studies using more rigorous methodology were needed.[154,155]

Haloperidol is one of the most studied and widely used antipsychotic medication because its lacks anticholinergic properties and can be administered orally, intramuscularly, or intravenously.[47] Hu et al. compared haloperidol with placebo, and observed that 70.4% of delirious patients who received haloperidol showed improvement in their delirium severity at the end of one week compared with 29.7% of the placebo group.[156] For agitated elderly patients, 0.25 – 1.0 mg of haloperidol can be given every 30 to 60 minutes in the intravenous or intramuscular form. Special care must be taken when given in the intravenous formulation, because torsades de point has been reported when given in this form.[157] If possible, a 12-lead electrocardiogram should be obtained prior to intravenous haloperidol administration to evaluate the patient's QTc interval, and should be avoided if the QTc interval is greater than 500ms. The benefit of the intravenous haloperidol is that it is the least likely to cause extrapyramidal symptoms whereas the intramuscular formulation is associated with the highest incidence.

Atypical antipsychotic medications such as olanzapine, risperidone, and quetiapine are also commonly used by psychiatrists and geriatricians for the treatment of delirium. The advantage of these medications is the decreased incidence of extrapyramidal side effects compared with haloperidol.[158] Most atypical antipsychotics are given orally, but recently, olanzapine, risperidone, ziprasidone, and aripiprazole have been made available in intramuscular formulations. Unfortunately, these forms may not be readily available in many EDs. Similar to haloperidol, there is limited evidence on the effectiveness of atypical antipsychotics and few have been compared to placebo. Compared with placebo, olanzapine has been shown to improve delirium severity in one randomized control trial,[156] but its effectiveness may be attenuated in patients who are 70 years and older.[159] Tahir et al. performed a double-blinded randomized control trial in 42 delirious patients and observed that patients in the quetiapine arm recovered faster than those who received placebo.[160]

In patients with Diffuse Lewis Body dementia or Parkinson's disease, antipsychotic medications should be should be avoided or used with extreme caution.[161] These patients are highly sensitive to these medications and easily develop extrapyramidal side effects.[152] If antipsychotic medications must be given in these patients, quetiapine is the least likely to have extrapyramidal side effects.[162] Regardless, if these patients are agitated and non-pharmacologic measures have failed, psychiatric and / or geriatric consultation may be warranted.

As previously mentioned, benzodiazepines should be avoided for the management of delirious patients. The exception to this recommendation is for patients who are withdrawing from ethanol (delirium tremens) or benzodiazepines. [47,163] Giving benzodiazepines to these patients will improve delirium severity and may also improve mortality and morbidity.[163] Because poorly controlled somatic pain can precipitate delirium, [70–72] using opioid

medications in this subgroup may be beneficial and help reduce agitation.[71] Pain control can also be achieved by using regional anesthesia such as femoral nerve blocks in patients with lower extremity fractures.

Medications to Avoid in Patients with Delirium

Part of the management of patients with acute brain dysfunction is to avoid medications known to be precipitate or worsen delirium. Recently, the Beers Criteria for Potentially Inappropriate Medication Use in Older Adults was updated. Based upon "moderate quality evidence and strong strength of recommendation" from the panel, they recommend avoiding tricyclic antidepressants, medications with anticholinergic properties, benzodiazepines and other sedative-hypnotics, corticosteroids, and histamine-2 receptor antagonists in older patients because they may worsen or exacerbate delirium.[86] If the patient is on multiple medications with anticholinergic properties, reducing these medications may improve delirium severity; in a study of 34 delirious nursing home patients who were on at least one anticholinergic medication, subjects were randomly assigned to receive an intervention that reduced their anticholinergic load by 25%.[164] Those who received the intervention had significant improvements in delirium symptomatology.[164] There several reports of histamine-2 blockers (cimetidine, ranitidine, and famotidine) precipitating delirium,[165] and they should be avoided in delirious patients since safer alternatives such as proton pump inhibitors are available.

Disposition

Patients who are stuporous or comatose need a hospital admission and likely require an intensive care unit. With delirium, however, there is little evidence-based guidance regarding the appropriate disposition of older ED patients. Most delirious patients will require hospitalization, especially if they have severe symptoms, have poor social support at home, or poor access to follow-up care. There is also evidence to suggest that older ED patients with delirium who are discharged home are more likely to die than their non-delirious counterparts; this relationship is further magnified when the delirium is missed by the ED.[17] However, for a small minority of delirious patients with reliable caregivers and accessible transportation, ED discharge can be considered. This is if the etiology is unequivocally obvious and the delirium symptoms resolve (e.g. accidental opioid overdose reversed with nalaxone) or are mild, the patient can be closely supervised at home, and close outpatient follow-up can be arranged.

If admitted to the hospital, delirious patients should preferably be admitted to specialized geriatric unit such as an Acute Care for Elderly unit or a Delirium Room.[166,167] These units typically have multidisciplinary team of physicians, nurses, and social workers or case managers who specialize in geriatrics care and have expertise in managing delirious patients. They also implement non-pharmacologic, multi-component delirium interventions which 1) minimize the use of psychoactive medications such as benzodiazepines and medications with anticholinergic properties, 2) maximize mobility and limit the use of urinary bladder catheters and physical restraints, 3) implement the TADA approach as described above, 4) reduce sensory deprivation by offering eye-glasses or hearing devices, 5) provide cognitive stimulation and reorientation, and 5) encourage normal sleep-wake cycles (e.g. minimize nighttime noise, use ear plugs at night).[149,167,168] However, the efficacy of these interventions is equivocal, especially for delirious medical inpatients.[169] Pitkala et al. found that a multi-component delirium intervention enhanced delirium resolution in the hospital and improved cognition and health related quality of life at 6-months.[170,171] However, they did not observe any differences in long-term mortality or institutionalization.[170,171] Regardless of which inpatient unit delirious patients are admitted to, their time spent in the ED should probably be minimized. Inouye et al. observed that patients who were in the ED

for longer than 12 hours were two-times more likely to develop delirium in the hospital setting.[42]

Communication During Transitions of Care

Regardless of the patient's disposition, the patient's mental status in the ED should be communicated to the physician at the next level of care. The patient's delirium status and the delirium assessment used to make the diagnosis, the suspected underlying etiology, and treatments administered should be communicated. Communicating the patient's level of consciousness using an arousal scale such as the RASS may also be useful provide information on the patient's psychomotor status (normal, hypoactive, or hyperactive). Additionally, knowing a baseline RASS may be useful as changes in RASS increases the likelihood that the patient has delirium.[135] If the delirious patient is being admitted, then this information should be conveyed to the admitting physician. If the patient is being discharged home, then his or her primary care provider should be notified. Similar communication should occur between ED physicians and nurses during shift change.

Improving Delirium Recognition in the Emergency Department - Challenges and Future Research

Delirium is currently missed in the majority of older ED patients,[10,12–17] because EDs do not screen for this form of acute brain dysfunction. Improving delirium recognition in the ED will be challenging. Emergency physicians are usually under huge time constraints and have a limited amount of time to spend with the patient. They often take care of large numbers of patients at once and their patient evaluations are also frequently interrupted (i.e. radiological testing or a higher acuity patient arrives). This limits the feasibility of a prolonged mental status examination. Brief and efficient approaches to delirium monitoring that are specifically tailored for the ED setting are needed. Future research should focus developing these approaches. This may entail validating brief (< 2 minutes) delirium assessments in older ED patients. These assessments should balance brevity with diagnostic accuracy, be easy to use, and be reliable when performed by non-physicians such as nurses, paramedics, or patient care technicians. Non-physicians may play a more instrumental role in ED delirium monitoring, because they may also have more time to spend with the patient at multiple time points compared with physicians.[172]

In addition, the utility serial measurements of global tests of cognition should be investigated. Decreasing scores in these cognitive assessments, such as the Mini-Mental State Examination, may be diagnostic of delirium.[173] However, the Mini-Mental State Examination can take 5 – 10 minutes to perform and may not be feasible to perform in the ED.[128] Brief cognitive assessments such as the Six-Item Screener[174,175] Mini-Cog,[175] Ottawa 3DY,[176] and Brief Alzheimer's Screen exist[176] but it is unclear how sensitive these assessments are in detecting changes in cognition observed in delirium. This would also require that routine cognitive screening be performed in outpatient clinic and possibly the ED setting during non-delirious episodes in order to establish a baseline.

Delirium surveillance in the ED can further be optimized by performing assessments on patients who are higher risk for having delirium. Ideally, the process of identifying of high risk patients should be automated and incorporated into the electronic medical record system in order to minimize ED staff workload. Currently, there are little data to suggest what risk factors should be used to identify older ED patients at high risk for delirium. Future research should focus on developing and validating such clinical decision rules; these rules should use patient characteristics that are immediately and easily available to the clinician.

Perhaps the most significant obstacle to routine ED delirium monitoring is the absence of cost-effective interventions for delirious ED patients. Thus far, uncovering the underlying etiology remains the most effective treatment for delirium. Several non-pharmacological multi-component interventions have been developed (see Disposition), but as previously mentioned, their efficacy is questionable in medical delirious patients. Perhaps initiating these interventions in the ED instead of the hospital setting would improve their efficacy. Additionally, the role of antipsychotic medications in older ED patients with delirium remains unknown. It is also possible that there is a subgroup of delirious of patients that may more benefit from these non-pharmacologic and pharmacologic interventions. Future studies using randomized control trial methodology are needed to test these hypotheses.

The American Delirium Society

Delirium remains an underappreciated geriatric syndrome among clinicians outside of geriatrics, psychiatry, and neurology. To increase delirium's awareness, recognition, and advance its science, the American Delirium Society was recently created. The overall mission of this society is to "foster research, education, quality improvement, advocacy and implementation science to minimize the impact of delirium on short and long-term health and well being, and the effects of delirium on the health care system as a whole."[177] This organization consists of an interdisciplinary group of physicians, nurses, pharmacists, and social workers in psychiatry, geriatrics, emergency medicine, internal medicine, and critical care. Additional information can be found at www.americandeliriumsociety.org.

Conclusion

Altered mental status is a common complaint in older ED patients. Acute changes are more concerning because they are usually caused by an underlying medical illness and can be life threatening. Delirium, stupor, and coma are common causes of altered mental status, and these forms of acute brain dysfunction are associated with a multitude of adverse outcomes including higher death rates. Their etiology multifactorial and are a result of a complex interplay between patient vulnerability and precipitating factors. Patients with acute brain dysfunction can fluctuate and transition from one state to another. A patient who is initially comatose in the ED frequently transitions into delirium. The initial evaluation of a patient with acute brain dysfunction should begin by assessing the level of consciousness using a arousal scale such as the RASS. If the patient is unresponsive (RASS −5) or responsive to painful stimuli (RASS −4) only, then the patient is considered to be comatose or stuporous, respectively; a validated coma scale such as the GCS should be used. If the patient has a RASS of −3 and above, a delirium assessment such as the CAM should be used, but it takes 5 minutes to perform and may not be feasible for some EDs. Several briefer delirium assessments exist (CAM-ICU, B-CAM, SQiD, and mRASS) but require validation in older ED patients and such studies are ongoing. Once acute brain dysfunction is detected in the ED, the primary goal is to find and treat the underlying cause. For agitated patients, non-pharmacologic interventions, such as the TADA approach, should be attempted initially. If non-pharmacologic interventions fail, antipsychotic medications such as haloperidol can be considered. Benzodiazepines should be avoided as monotherapy unless the patient is withdrawing from ethanol or benzodiazepines. Patients with delirium, stupor, or coma generally require admission. The optimal method for delirium monitoring and treatment in the ED remains unclear and additional research is needed.

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Key Points

- Altered mental status is a common chief complaint among older emergency department (ED) patients.
- Patients with acute changes in mental status are likely to have delirium, stupor, and coma, and these changes are commonly precipitated by an underlying medical illness that can be potentially life-threatening.
- Though stupor and coma are easily identifiable, the clinical presentation of delirium can be subtle and is often missed without actively screening for it.
- The ED management of patients with altered mental status should initially be focused on stabilizing the patient (airway, breathing, circulation) while searching for the underlying etiology.

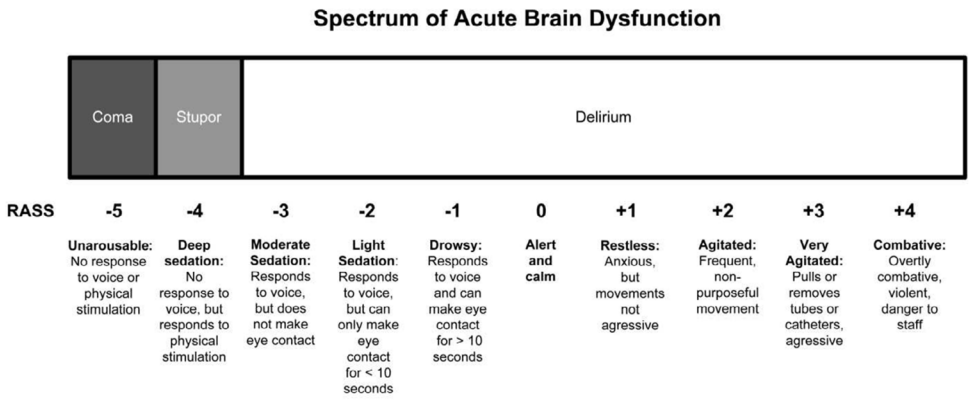

Figure 1.

Spectrum of acute brain dysfunction based upon the Richmond Agitation Sedation Scale (RASS). Courtesy of Vanderbilt University, Nashville, TN. Copyright © 2012. Used with Permission.

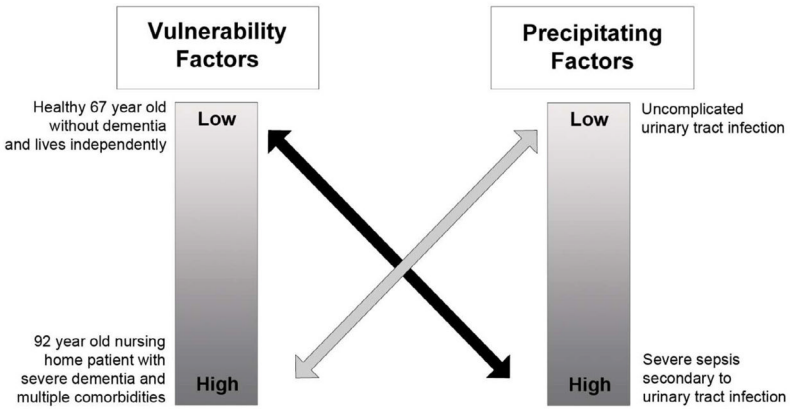

Figure 2.

Interrelationship between patient vulnerability and precipitating factors for developing acute brain dysfunction such as delirium. Patients who not vulnerable require significant noxious stimuli to develop acute brain dysfunction (black arrow). Patients who are highly vulnerable require only minor noxious stimuli to develop acute brain dysfunction (gray arrow). Adapted from Inouye et al. *JAMA* 1996;275:852–857.

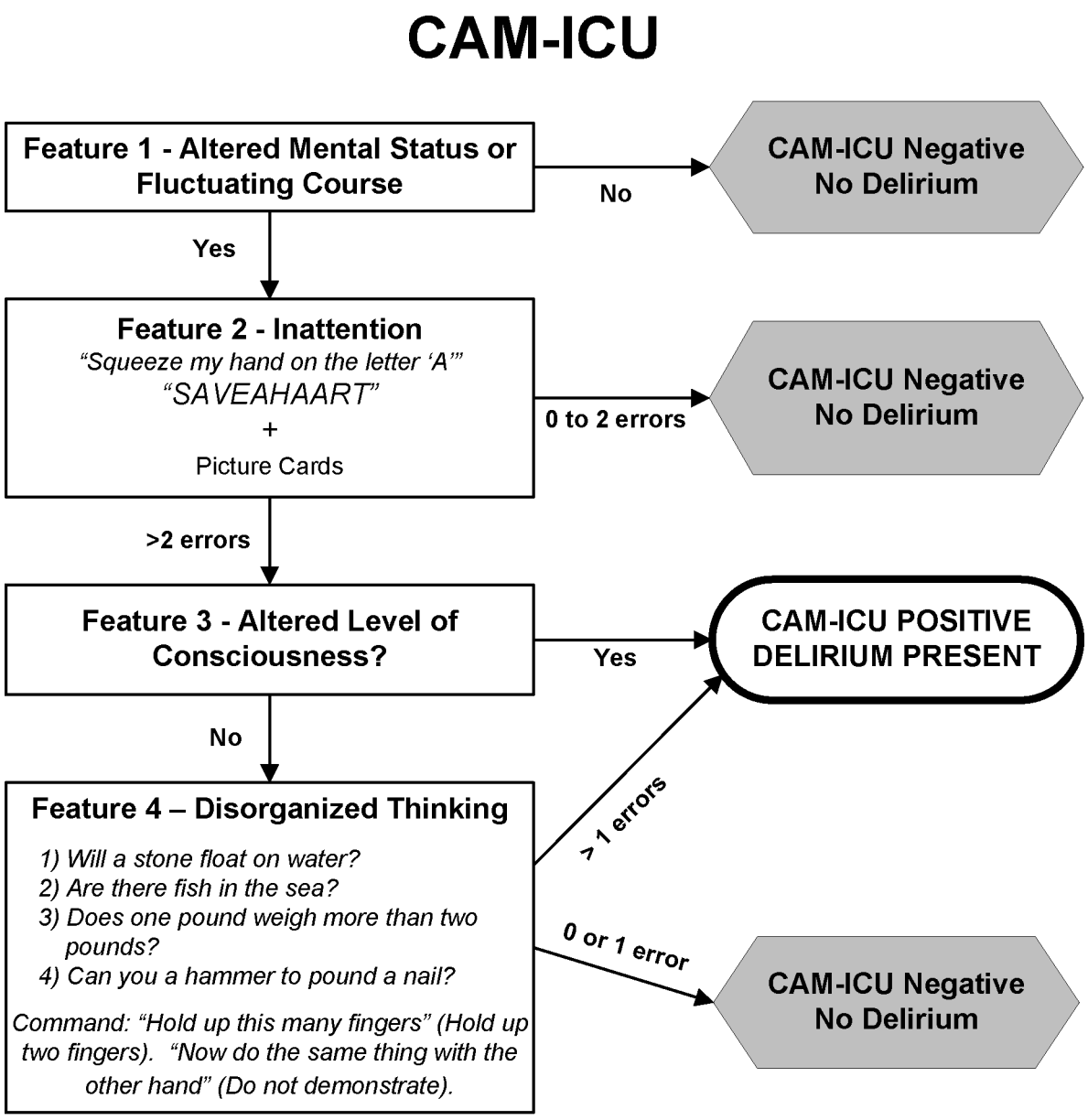

Figure 3.
Confusion Assessment Method for the Intensive Care Unit. Adapted from www.icudelirium.org. Courtesy of Dr. Wes Ely and Vanderbilt University, Nashville, TN. Copyright © 2002. Used with Permission.

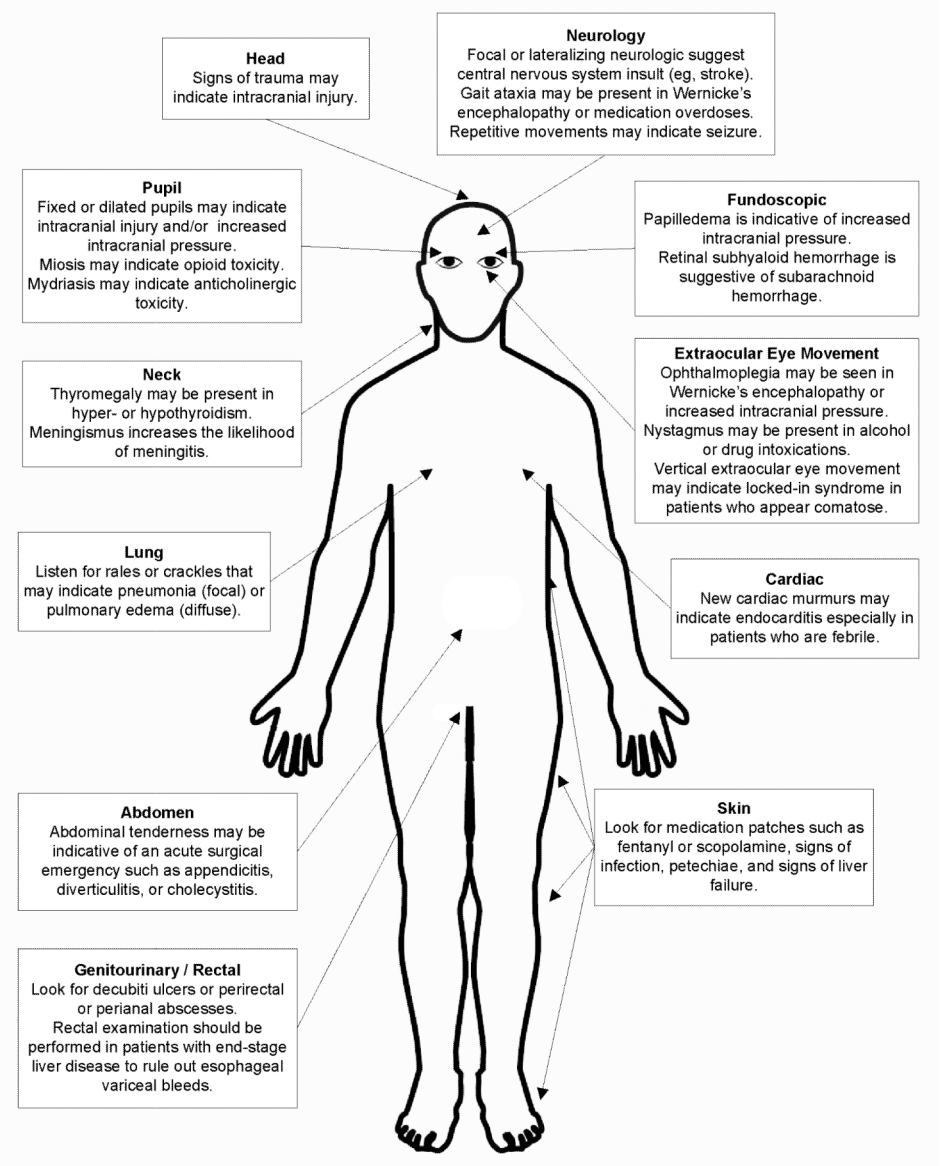

Figure 4.
The physical examination of the patient with delirium, stupor, or coma.

Table 1

Key Differences between delirium and dementia.

Characteristic	Delirium	Dementia
Onset	Rapid over a period of hours or days	Gradual over months and years
Course	Waxing and waning	Stable
Inattention	Present	*Absent
Altered of level of consciousness	Usually present	*Typically absent
Disorganized thinking present	May be present	*Typically absent
Sleep-wake cycle disturbance	Present	*Typically absent
Perceptual disturbances and hallucinations	May be present	*Typically absent
Is cognitive decline reversible?	Usually reversible	Rarely reversible

*May be present in patients with severe dementia.

Table 2

Patient Vulnerability Factors for Delirium

Vulnerability Factors	
Demographics	Medications and Drugs
• Advanced age	• Polypharmacy
• Male gender	• Baseline psychoactive medication use *
Comorbidity	• History of alcohol or other substance abuse
• Dementia	Sensory Impairment
• # of comorbid conditions	• Hearing impairment
• Chronic kidney disease	• Visual impairment
• End stage liver disease	Decreased oral intake
• Terminal illness	• Dehydration
Functional Status	• Malnutrition
• Functional impairment	Psychiatric
• Immobility	• Depression

Increased severity of these vulnerability factors will increase the patient's susceptibility to delirium. Modified from Pun et al, Fearing et al., and the American Psychiatry Association Delirium Guidelines.[46–48]

* Psychoactive medications include benzodiazepines, opioids, and medications with anticholinergic properties.

Table 3

Precipitating factors for delirium.

Precipitating Causes for Delirium	
Systemic	Metabolic
• Infection/sepsis	• Thiamine deficiency (Wernicke's encephalopathy)
• Inadequate pain control	• Hepatic or renal failure
• Trauma	• Hypo- and hypernatremia
• Dehydration	• Hypo- and hypercalcemia
• Hypo- or hyperthermia	• Hypoglycemia/hyperglycemia
	• Thyroid dysfunction
CNS	Cardiopulmonary
• Meningitis/encephalitis	• Acute myocardial infarction
• Cerebrovascular accident	• Congestive heart failure
• Intracerebral hemorrhage	• Hypoxemia
• Subarachnoid hemorrage	• Hypercarbia
• Subdural/epidural hematoma	• Hypertensive encephalopathy
	• Shock
Medications and Drugs	Iatrogenic
• Medications and medication changes	• Procedures or surgeries
• Recreational drug use or withdrawal	• Indwelling urinary catheters
	• Physical restraints

Modified from Pun et al, Fearing et al., and the American Psychiatry Association Delirium Guidelines.[46–48]

Table 4

Glasgow Coma Scale

Points	Scale Elements
	Eyes
4	Opens eyes spontaneously
3	Opens eyes in response to voice
2	Opens eyes in response to painful stimuli
1	Does not open eyes
	Verbal
5	Oriented, converses normally
4	Confused, disoriented
3	Utters inappropriate words
2	Incomprehensible sounds
1	Makes no sounds
	Motor
6	Obeys commands
5	Localizes painful stimuli
4	Flexion/withdrawal to painful stimuli
3	Abnormal flexion to painful stimuli (decorticate response)
2	Extension to painful stimuli (decerebrate response)
1	Makes no movements

Table 5

Initial Assessment and Management of a Patient with Altered Mental Status

	Assessment	Intervention
Airway	• Is patient protecting his/her airway? • Look for airway obstruction including foreign bodies	• Extend neck, provide chin lift or jaw thrust. • Suction oropharynx • In cases of trauma, provide cervical spine immobilization. • Nasopharyngeal airway • Oropharyngeal airway if no gag • Endotracheal intubation patient is not able to protect airway
Breathing	• Is there respiratory distress? • Is the patient hypoventilating? • Is the patient cyanotic or hypoxic? • Ascultate the chest	• Provide high flow oxygen * • Provide bag-valve mask ventilation if hypoventilating
Circulation	• Check for pulse while getting blood pressure measurement • Look for other signs of hypoperfusion (i.e. capillary refill, skin temperature). • Place on electrocardographic monitor to look for dysrhythmias • Look for obvious bleeding • If hypotensive or signs hypoperfusion, consider bedside ultrasound **	• Establish intravenous access • Two large bore intravenous lines are needed in patients who are hemodynamically unstable. • Fluid challenge with intravenous crystalloid if hypotensive or has other signs of hypoperfusion • Stop hemorrhage if accessible
Disability	• Examine pupils • Assess responsiveness using a scale such as the GCS • Check finger stick blood glucose • Consider toxicologic causes (i.e. opioid overdose)	• One amp (50cc) of D50 in hypoglycemia • Nalaxone in suspected opioid overdose
Exposure	• Expose the patient. Minimize heat loss in patients who are normothermic or hypothermic • Look for transdermal drug patches (e.g. fentanyl) that could cause mental status changes • Look for signs of infection	• Remove drug patches

* In patients who have chronic obstructive pulmonary disease, high flow oxygen may remove their respiratory drive especially in patients with chronic respiratory failure. Oxygen saturation should be titrated to the low 90s%.

** Bedside ultrasounds are commonly used in emergency departments and intensive care units to rapidly rule out causes of hypotension such as cardiac tamponade and intrabdominal blood. The inferior vena cava can also be assessed using the bedside ultrasound to assess whether a patient is hypovolemic (dehydration, hemorrhage) or hypervolemic (heart failure).

GCS, Glasgow Coma Scale

Table 6

Life-threatening causes of delirium

Adapted from Caplan GA et al. Delirium. In: Stern TA, ed. *Massachusetts General Hospital comprehensive Clinical Psychiatry*. 1st ed. Philadelphia, PA: Mosby/Elsevier; 2008.[73]

Wernicke's disease or ethanol withdrawal
Hypoxia or hypercarbia
Hypoglycemia
Hypertensive encephalopathy
Hyperthermia or hypothermia
Intracerebral hemorrhage
Meningitis/encephalitis
Poisoning (whether exogenous or iatrogenic)
Status epilepticus