Chapter 47: Delirium

Sharon K. Inouye; Matthew Growdon; Tamara Fong

This chapter addresses the following Geriatric Fellowship Curriculum Milestones: #29, #41, #42, #43, #55, #57, #58

LEARNING OBJECTIVES

Learning Objectives

Learn the epidemiology, pathophysiology, clinical presentations, evaluation, and management of delirium in older adults.

Understand the role of various predisposing and precipitating factors in increasing risk of older persons to delirium and associated prognosis and mortality.

Recognize the significance and limitations of routine as well as special laboratory and imaging tests commonly used to evaluate an older patient with delirium.

Learn the special relationship between dementia and delirium and the role of certain medications in predisposing older adults to delirium.

Gain a clear understanding of the specific indications and efficacy of various treatments, including pharmacologic and nonpharmacologic strategies commonly used to manage delirium.

Understand the latest concepts about special issues related to delirium, including patient preferences and decision making, delirium in nursing homes, and palliative and end-of-life care.

Key Clinical Points

1. **Delirium is commonly encountered in older adults in various clinical settings and associated with significant morbidity and mortality, especially in intensive care units, inpatient settings, nursing homes, and following major medical illnesses or surgery.**
2. **Delirium is commonly unrecognized in up to 70% of older patients and can lead to long-term functional and cognitive deficits.**
3. **The pathophysiology of delirium is currently unclear, but posited to be the end result of multiple pathogenic pathways eventually culminating in the dysfunction of various neurotransmitters and major brain networks.**
4. **Delirium is commonly due to multiple causes and the most effective treatment strategy is to identify and address as many predisposing and precipitating factors as possible.**
5. **Among the precipitating factors, decreased mobility is strongly associated with delirium and medical equipment and devices may further contribute to immobilization.**
6. **Dementia is the underlying risk factor in almost 75% of cases of delirium, and must be suspected in patients with slowly progressive cognitive and functional deficits.**
7. **Acute onset, varying levels of alertness, and inattention are cardinal features of delirium, and obtaining historical details from a close family member or friend is critical in making a correct diagnosis of delirium.**

8. **Lethargy and reduced psychomotor functioning are common presentations of delirium in older patients, in contrast to the hyperactive form more common in younger patients.**

9. **Nonpharmacologic strategies are the preferred treatment for delirium in older patients, and medications are reserved for more severe symptoms that affect either medical management or patient safety.**

Delirium, defined as an acute disorder of attention and global cognitive function, is a common, serious, and potentially preventable source of morbidity and mortality for hospitalized older persons. Delirium affects as many as half of all people over age 65 who are hospitalized. With the aging of the US population, delirium has assumed heightened importance because persons aged 65 and older presently account for more than 45% of all days of hospital care. Delirium increases hospital costs by an average of $1000 per patient and posthospital costs by over $10,000 per patient-year, so that annually over $164 billion (in 2011 US dollars) of US health care costs are attributable to delirium. Moreover, delirium is preventable in 30% to 40% of cases. Importantly, substantial additional costs linked to delirium accrue after hospital discharge because of the increased need for institutionalization, rehabilitation services, closer medical follow-up, and home health care. Delirium often initiates a cascade of events in older persons, leading to a downward spiral of functional decline, loss of independence, institutionalization, and ultimately, death. These statistics highlight the importance of delirium from both clinical and health policy perspectives. In fact, a recent consensus panel identified delirium as among the top three target conditions for quality-of-care improvement for vulnerable older adults. With its common occurrence, its frequently iatrogenic nature, and its close linkage to the processes of care, incident delirium can serve as a marker for the quality of hospital care and provides an important opportunity for quality improvement.

DEFINITION

The definition of and diagnostic criteria for delirium continue to evolve. The standardized criteria for delirium that appear in the American Psychiatric Association's *Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition* (DSM-5, 2013) is the current diagnostic standard. These criteria are based on: (A) a disturbance in attention and awaremeness; (B) an acute onset and fluctuating course; (C) an additional deficit in cognition (such as memory, orientation, language, or visuoperceptual ability); (D) impairments not better explained by dementia and do not occur in context of severely impaired level of consciousness or coma; and (E) evidence of an underlying medical etiology or multiple etiologies. Expert consensus was used to develop these criteria, however, and performance characteristics such as diagnostic sensitivity and specificity have not yet been reported for DSM-5 criteria. A standardized tool, the Confusion Assessment Method (CAM), provides a brief, validated diagnostic algorithm that is currently in widespread use for identification of delirium. The CAM algorithm relies on the presence of acute onset and fluctuating course, inattention, and either disorganized thinking or altered level of consciousness. The algorithm has a sensitivity of 94% to 100%, specificity of 90% to 95%, and high interrater reliability. Given the uncertainty of diagnostic criteria for delirium, a critical area for future investigation is to establish more definitive criteria, including epidemiologic and phenomenologic evaluations assisted by advances in functional neuroimaging and other potential diagnostic marker tests.

EPIDEMIOLOGY

Most of the epidemiologic studies of delirium involved hospitalized older patients, in whom the highest rates of delirium occur. Reported rates vary based on the subgroup of patients studied and the setting of care (eg, hospital, intensive care, surgical). Previous studies estimated the prevalence of delirium (present at the time of hospital admission) at 18% to 35% and the incidence of delirium (new cases arising during hospitalization) at 11% to 29%. The incidence rates of delirium in high-risk hospital venues, such as the intensive care unit and posthip fracture settings, range from 19% to 82% and 12% to 51%, respectively. Delirium occurs in up to 36% of patients in nursing homes or postacute settings, and in up to 83% of all patients at the end of life. The rates of delirium in all older persons presenting to the emergency department in several studies have ranged from 8% to 17%. While less frequent in the community setting, delirium is an important presenting symptom to emergency departments and community physicians, and often heralds serious underlying disease. Delirium is often unrecognized; previous studies have documented that clinicians fail to detect up to 70% of affected patients across all of these settings. Furthermore, the presence of delirium portends a potentially poor prognosis; hospital mortality rates in patients with delirium range from 22% to 76%, as high as mortality rates associated with acute myocardial infarction or sepsis. Following hospitalization, the additional 1-year mortality rate associated with cases of delirium is 35% to 40%.

PATHOPHYSIOLOGY

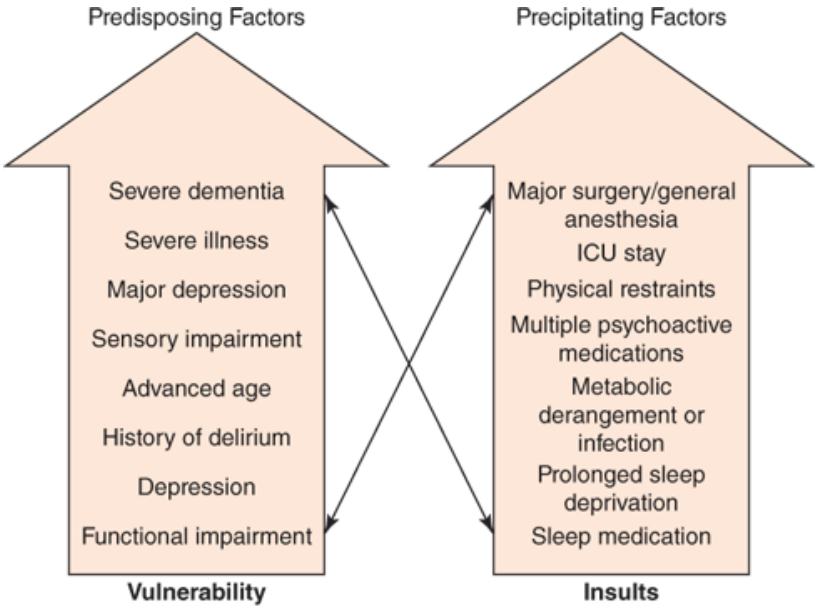
The fundamental pathophysiologic mechanisms of delirium remain unclear. Delirium is thought to represent a functional rather than structural lesion. The characteristic electroencephalographic (EEG) findings demonstrate global functional derangements and generalized slowing of cortical background (alpha) activity. Current hypotheses view delirium as the final common pathway of many different but interacting pathogenic mechanisms, causing dysfunction of multiple brain regions and neurotransmitter systems and culminating in disruption of large-scale networks. Evidence from EEG, evoked-potential studies, and neuroimaging studies in acute delirium suggest focal dysfunction localized to the prefrontal cortex, thalamus, basal ganglia, temporoparietal cortex, fusiform, and lingual gyri of the nondominant cortex. Studies using x-ray computed tomography (CT) or magnetic resonance imaging (MRI) have found lesions or structural abnormalities in the brains of patients with delirium. Several studies of cerebral blood flow (CBF) using single-photon emission computed tomography (SPECT) found that delirium is mostly associated with decreased blood flow. However, results from previous studies have been highly variable. Associated neurotransmitter abnormalities involve elevated brain dopaminergic function, reduced cholinergic function, or a relative imbalance of these systems. Serotonergic activity may interact to regulate or alter activity of these other two systems, and serotonin levels may be either increased or decreased. Extensive evidence supports the role of cholinergic deficiency. Acetylcholine plays a key role in consciousness and attentional process, and given that delirium is manifested by an acute confusional state often with alterations of consciousness, it is likely to have a cholinergic basis. Anticholinergic drugs can induce delirium in humans and animals, and serum anticholinergic activity is increased in patients with delirium. Physostigmine can reverse delirium associated with anticholinergic drugs, and cholinesterase inhibitors appear to have some benefit even in cases of delirium that are not induced by drugs. Neurotransmitter systems can also be affected indirectly. For instance, in sepsis, the systemic inflammatory response triggers a cascade of local (brain) neuroinflammation, leading to endothelial activation, impaired blood flow, neuronal apoptosis, and neurotransmitter dysfunction. Neuroinflammation can lead to microglial overactivation, resulting in a neurotoxic response with further neuronal injury. The stress response associated with severe medical illness or surgery involves sympathetic and immune system activation, including increased activity of the hypothalamic-pituitary-adrenal axis with hypercortisolism, and release of cerebral cytokines that alter neurotransmitter systems, the thyroid axis, and modification of blood-brain barrier permeability. Age-related changes in central neurotransmission, stress management, hormonal regulation, and immune response may contribute to the increased vulnerability of older persons to delirium. The description of delirium as “acute brain failure”—involving multiple neural circuits, neurotransmitters, and brain regions—suggests that understanding delirium may help to elucidate the essential underlying mechanisms of brain functioning.

ETIOLOGY

The etiology of delirium is usually multifactorial, like many other common geriatric syndromes, such as falls, incontinence, and pressure sores. Although there may be a single cause of delirium, more commonly in older persons, delirium results from the interrelationship between patient vulnerability (ie, predisposing factors) and the occurrence of noxious insults (ie, precipitating factors). For example, patients who are highly vulnerable to delirium at baseline (eg, such as patients with dementia or serious illness) can experience acute delirium after exposure to otherwise mild insults, such as a single dose of a sedative medication for sleep. On the other hand, older patients with few predisposing factors (low baseline vulnerability) are relatively resistant, with precipitation of delirium only after exposure to multiple potentially noxious insults, such as general anesthesia, major surgery, multiple psychoactive medications, immobilization, and infection (**Figure 47-1**). Moreover, based on validated predictive models for delirium, the effects of multiple risk factors appear to be cumulative. Clinically, the importance of the multifactorial nature of delirium is that removal or treatment of one risk factor alone often fails to resolve delirium. Instead, addressing many or all of the predisposing and precipitating factors for delirium is often required before the delirium symptoms will improve.

FIGURE 47-1.
Multifactorial model for delirium. The etiology of delirium involves a complex interrelationship between the patient’s underlying vulnerability or predisposing factors (*left axis*) and precipitating factors or noxious insults (*right axis*). For example, a patient with high vulnerability, such as with severe dementia, underlying severe illness, or hearing or vision impairment, might develop delirium with exposure to only one dose of a sleeping medication. Conversely, a patient with low vulnerability would

develop delirium only with exposure to many noxious insults, such as general anesthesia and major surgery, intensive care unit (ICU) stay, multiple psychoactive medications, and prolonged sleep deprivation.



Predisposing Factors

Predisposing factors for delirium include preexisting cognitive impairment or dementia, a history of delirium, advanced age (> 70 years), severe underlying illness and multimorbidity, functional impairment, depression, alcohol abuse, a history of stroke or transient ischemic attack, and sensory impairments (vision or hearing) (Table 47-1). Preexisting cognitive impairment, including dementia, is a powerful and consistent risk factor for delirium demonstrated across multiple studies, with patients with dementia having a two- to fivefold increased risk for delirium. Moreover, up to half of delirious patients have an underlying dementia. Nearly any chronic medical condition can predispose to delirium, ranging from diseases involving the central nervous system (eg, Parkinson disease, cerebrovascular disease, mass lesions, trauma, infection), to diseases outside the central nervous system, including infectious, metabolic, cardiac, pulmonary, endocrine, or neoplastic etiologies. Predictive risk models that identify predisposing factors in populations such as general medicine, intensive care, surgical patients (cardiac and noncardiac), cancer patients, and nursing home residents, have been developed and aid in the understanding of baseline patient characteristics contributing to delirium risk.

TABLE 47-1

PREDISPOSING AND PRECIPITATING FACTORS FOR DELIRIUM FROM VALIDATED PREDICTIVE MODELS

Predisposing factors • Dementia or underlying cognitive impairment • Severe illness • Comorbidity • Depression • Vision and/or hearing impairment • Functional impairment • History of transient ischemia or stroke • History of alcohol abuse • History of delirium • Advanced age (> 70)
Precipitating factors • Drugs, including polypharmacy, psychoactive, and sedatives or hypnotics • Use of physical restraints • Indwelling bladder catheters • Dehydration • Poor nutritional status, abnormal serum albumin • Iatrogenic complications • Major surgical procedure (eg, aortic aneurysm repair, noncardiac thoracic surgery, and neurosurgery) • Metabolic derangements (electrolytes, glucose, metabolic acidosis) • Infection • Trauma admission • Urgent admission • Coma

Precipitating Factors

Major precipitating factors identified in validated predictive models include medication use (see section on "Drug Use and Delirium"), use of indwelling bladder catheters, use of physical restraints, dehydration, malnutrition, iatrogenic events, infections, metabolic and electrolyte derangements, surgery, admissions that are urgent or involve trauma, and coma (see Table 47-1). Decreased mobility is strongly associated with delirium and concomitant functional decline. The use of medical equipment and devices (eg, indwelling bladder catheters and physical restraints) may further contribute to immobilization. Major iatrogenic events occur in 29% to 38% of older hospitalized adults (three to five times the risk when compared with adults younger than 65 years). Examples include complications related to diagnostic or therapeutic procedures, allergic reactions, and bleeding caused by over-anticoagulation. Many of these events potentially are preventable. Disorders of any major organ system, particularly renal or hepatic failure, can precipitate delirium. Occult respiratory failure has emerged as an increasing problem in older patients, who often lack the typical signs and symptoms of dyspnea and tachypnea. In older adults, acute myocardial infarction and congestive heart failure may present with delirium or "failure to thrive" as the cardinal feature, and minimal or none of the usual symptoms of angina or dyspnea. Occult infection, caused by pneumonia, urinary tract infection, endocarditis, abdominal abscess, or infected joint, is a particularly noteworthy cause of delirium because older patients may not present with leukocytosis or a typical febrile response. Metabolic and endocrinologic disorders, such as hyper- or hyponatremia, hypercalcemia, acid-base disorders, hypo- and hyperglycemia, and thyroid or adrenal disorders, may also contribute to delirium. The precipitating factors for delirium in hospitalized older patients that have been validated previously in a predictive model include use of physical restraints, malnutrition, more than three medications added during the previous day (more than 70% of these were psychoactive drugs), indwelling bladder catheter, and any iatrogenic event. The

presence of these independent factors contributes to delirium risk in a predictable and cumulative manner, yet each risk factor is potentially modifiable.

Drug Use and Delirium

In 40% or more of delirium cases, use of one or more specific medication contributes to its development. While medications often incite delirium, they are also the most common remediable cause of delirium. A broad array of medications and their metabolites can lead to delirium; the most common are those with known psychoactive effects, such as sedative hypnotics, anxiolytics, narcotics, H_2 blockers, and medications with anticholinergic activity (Table 47-2). In previous studies, use of any psychoactive medication was associated with a fourfold increased risk of delirium, while use of two or more psychoactive medications was associated with a fivefold increased risk. Sedative-hypnotic drugs are associated with a 3- to 12-fold increased risk of delirium; narcotics with a threefold risk; and anticholinergic drugs with a 5- to 12-fold risk. The incidence of delirium, similar to other adverse drug events, increases in direct proportion to the number of medications prescribed, because of the effects of the medications themselves, as well as to the increased risk of drug-drug and drug-disease interactions. Recent studies provide compelling evidence that suboptimal medication management, ranging from inappropriate use to overuse of psychoactive medications, occurs commonly in older adults in the hospital and in community settings, and suggests that many cases of delirium and other related adverse drug events may be preventable. As the number of prescription and over-the-counter drugs consumed by the older population increases, review of potentially problematic medications will remain an important step in the search for predisposing factors in the patient with delirium.

TABLE 47-2

MEDICATIONS ASSOCIATED WITH COGNITIVE IMPAIRMENT AND DELIRIUM (BEERS CRITERIA, 2012)

All tricyclic antidepressants Anticholinergics (including antihistamines, antiparkinsonian agents, skeletal muscle relaxants, antidepressants, antimuscarinics, antispasmodics) Benzodiazepines Chlorpromazine
Corticosteroids
H_2-receptor antagonists Meperidine Sedative hypnotics Thioridazine Zolpidem
Antipsychotics (chronic and as-needed use)

Data from American Geriatrics Society 2012 Beers Criteria Update Expert Panel. American Geriatrics Society updated Beers criteria for potentially inappropriate medication use in older adults. J Am Geriatr Soc. 2012;60(4):616–631.

Relationship Between Delirium and Dementia

While delirium and dementia are highly interrelated, the nature of their relationship remains poorly examined. The contribution of delirium itself to permanent cognitive impairment or dementia remains controversial; however, previous studies document that, after delirium, at least some patients never recover their baseline level of cognitive function. Thus, delirium and dementia may represent two ends along a spectrum of cognitive impairment with “chronic delirium” and “reversible dementia” falling along this continuum. Dementia is the leading risk factor for delirium, and fully two-thirds of cases of delirium occur in patients with dementia. Moreover, studies have shown that delirium and dementia are both associated with decreased cerebral metabolism, cholinergic deficiency, and inflammation, reflecting their overlapping clinical,

metabolic, and cellular mechanisms. Delirium can alter the course of an underlying dementia, with dramatic worsening of the trajectory of cognitive decline, resulting in more rapid progression of functional losses and worse long-term outcomes. In follow-up studies, patients with dementia in whom delirium develops have worse outcomes than those with dementia alone, including worsened cognitive function and increased rates of hospitalization, institutionalization, and death.

PRESENTATION

Cardinal Features

Acute onset and inattention are the central features of delirium. Determining the acuity of onset requires accurate knowledge of the patient's prior cognitive status. Pinpointing the origin and time course of changes in mental status often entails obtaining historical information from another close observer, such as a family member, caregiver, or nurse. Typically with delirium, the mental status changes occur over hours to days, in contrast to the changes that occur with dementia, which present insidiously over weeks to months. Another key feature is the fluctuating course of delirium, with symptoms tending to wax and wane in severity over a 24-hour period. Lucid intervals are characteristic, and the reversibility of symptoms within a short time can deceive even an experienced clinician. Inattention is manifested as difficulty focusing, maintaining, and shifting attention or concentration. With simple cognitive assessment, patients may display difficulty with straightforward repetition tasks, digit spans, or recitation of the months of the year backward. Delirious patients appear easily distracted, experience difficulty with multistep commands, cannot follow the flow of a conversation, and often perseverate with an answer to a previous question. Additional major features include a disorganization of thought and altered level of consciousness. Disorganized thoughts are a manifestation of underlying cognitive or perceptual disturbances, and can be recognized by disjointed and incoherent speech, or an unclear or illogical flow of ideas. Clouding of consciousness is typically manifested by lethargy, with a reduced awareness of the environment that may show diurnal variation. Although not cardinal elements, other frequently associated features include disorientation (more commonly to time and place than to self), cognitive impairments (eg, memory and problem-solving deficits, dysnomia), psychomotor agitation or retardation, perceptual disturbances (eg, hallucinations, misperceptions, illusions), paranoid delusions, emotional lability, and sleep-wake cycle disruption.

Classification of Delirium

The clinical presentation of delirium can take two main forms, either hypoactive or hyperactive. The hypoactive form of delirium is characterized by lethargy and reduced psychomotor functioning, and is the more common form in older patients. Hypoactive delirium often goes unrecognized and carries an overall poorer prognosis. The reduced level of patient activity associated with hypoactive delirium, often attributed to low mood or fatigue, may contribute to its misdiagnosis or underrecognition. By contrast, the hyperactive form of delirium presents with symptoms of agitation, increased vigilance, and often concomitant hallucinations; its presentation rarely remains unnoticed by caregivers or clinicians. Importantly, patients can fluctuate between the hypoactive and hyperactive forms—the mixed type of delirium—presenting a challenge in distinguishing the presentation from other psychotic or mood disorders. Moreover, recent recognition of partial or subsyndromal forms of delirium has brought attention to the persistence of symptoms among older patients, particularly during the resolution stages of delirium, when manifestation of the full syndrome may not be apparent. Partial forms of delirium also adversely influence long-term clinical outcomes.

Prognosis

Delirium is an important independent determinant of prolonged length of hospital stay, increased mortality, increased rates of nursing home placement, and functional and cognitive decline—even after controlling for age, gender, dementia, illness severity, and baseline functional status.

Delirium has long been thought to be a reversible, transient condition; however, recent evidence brings this into question. Recent research on the duration of delirium symptoms, however, provides evidence that delirium may persist for much longer than previously recognized. In fact, delirium symptoms generally persist for a month or more; as few as 20% of patients attain complete symptom resolution at 6-months follow-up. In addition, those patients with extant cognitive impairment may experience greater deleterious effects than comparable patients without dementia. The chronic detrimental effects are likely related to the duration, severity, and underlying cause(s) of the delirium, in addition to the baseline vulnerability of the patient.

EVALUATION

Table 47-3 lists instruments for identification of delirium. Of these, the most widely used is the CAM, of which the four-item short form has been applied in over 4000 studies to date and translated into over 14 languages. The CAM has also been adapted for use in other settings, including the intensive care unit (CAM-ICU), nursing home (NH-CAM), and emergency department (CAM-ED and B-CAM). A new adaptation, called the 3D-CAM, provides a brief cognitive assessment that takes fewer than 3 minutes to complete, and identifies delirium with high sensitivity and specificity. The CAM-S derived from the CAM can be used to rate delirium severity, and has demonstrated predictive validity for relevant clinical outcomes. Other delirium severity instruments include the Delirium Rating Scale (DRS-98), the Memorial Delirium Assessment Scale (MDAS), and the Delirium Index (DI). Each instrument has strengths and limitations, and the choice among them depends on the goals for use.

TABLE 47-3

DELIRIUM SCREENING TESTS

DELIRIUM SCREENING TEST	BRIEF DESCRIPTION
4AT	2-min instrument for general practice includes 4 items; scores range from 0–12, with a score ≥ 4 suggesting possible delirium
Bedside Confusion Scale	2-min screening test requiring minimal training, involving observation of alertness and timed attention task, scores range from 0 to 5, with scores > 2 indicating confusion
Clinical Assessment of Confusion (CAC)	Nursing checklist of 25 psychomotor behaviors associated with confusion; range, 0–77, higher score indicates more severe confusion
Cognitive Test for Delirium (CTD)	15-min instrument designed for use in ICU settings; scores range from 0 to 30, with lower scores indicating delirium
Confusion Assessment Method (CAM)[a]	Widely adopted 5-min instrument to score 4-item algorithm based on 9 operationalized DSM-IIIR criteria for delirium; involves cognitive assessment; interviewer training recommended for optimal use
Confusion Assessment Method—ICU version (CAM-ICU)	Modification of CAM 4-feature algorithm with nonverbal tasks that can be used in the ICU setting
3D-CAM	3-min version of CAM requires minimal training; algorithm probes 4 cardinal features of delirium, with 2 essential features and at least 1 of 2 secondary features indicating delirium
Confusion Rating Scale (CRS)	Scale involving 4 behavioral domains designed for nurses during 8-h shifts, scores range from 0–24, with higher scores indicating more pronounced delirium
Delirium Index	Designed to be used with MMSE and to track delirium severity over time, includes 7 operationalized items from CAM, ranges from 0 to 21 with higher scores indicating greater severity
Delirium-O-Meter	Adapted from the CAM, 12-item behavioral observation scale, scores range from 0–36, with higher scores indicating higher severity of delirium
Delirium Observation Screening (DOS)	Thirteen-item scale based on DSM-IV criteria for delirium that can be observed during routine nursing care; presence of ≥ 3 items indicates delirium
Delirium Rating Sale Revised 1998 (DRS-98R)[a]	Scale for clinicians with psychiatric training with 2 sections, including 3 diagnostic items for initial ratings and 13 items on a scale ranging from 0 to 46, with higher scores indicating delirium
Delirium Symptoms Interview (DSI)	Structured interview for nonclinicians assesses 7 domains from DSM-III criteria for delirium, including 63 interview questions and 44 observations
Delirium Diagnostic Test—Provisional (DDT-Pro)	3-min, 3-item screening tool designed for nonclinicians and derived from CTD and DRS-98R, range 0–12 with lower scores indicating delirium; originally validated in patients rehabilitating from traumatic brain injury

DELIRIUM SCREENING TEST	BRIEF DESCRIPTION
Intensive Care Delirium Screening Checklist (ICDSC)	8-item screening tool involves focused bedside patient evaluation and observations during 24-h nursing shift, range 0–8, with scores ≥ 4 indicating delirium
Memorial Delirium Assessment Scale (MDAS)[a]	Physician-rated instrument requiring 10–15 min and designed for use multiple times in single day, scores range from 0 to 30 with higher scores indicating more severe delirium
NEECHAM Confusion Scale	Nursing questionnaire requiring 10 min with 3 subscales addressing cognition, behavior, and physiologic parameters, scores range from 0 to 30, with lower scores indicating higher risk of delirium
Nursing Delirium Screening Scale (Nu-DESC)	5-item, 1-min screening scale designed for use by nurses and used during routine care on the hospital floor, scores range from 0 to 10 with higher scores indicating delirium
Single Question in Delirium (SQiD)	Single question, “Do you think (name of patient) has been more confused lately?” posed to informant, positive response indicates delirium

[a]Generally considered too lengthy to serve as screening tools.

ICU, intensive care unit; MMSE, Mini Mental State Examination.

The acute evaluation of suspected or confirmed delirium centers on three main tasks that occur simultaneously: (1) establishing the diagnosis of delirium; (2) determining the potential cause(s) and ruling out life-threatening contributors; and (3) managing the symptoms while assuring patient safety. Delirium is a clinical diagnosis, relying on astute observation at the bedside, careful cognitive assessment, and history-taking from a knowledgeable informant to establish a change from the patient’s baseline functioning. Identifying the potentially multifactorial contributors to the delirium is of paramount importance, because many of these factors are treatable, and if left untreated, may result in substantial morbidity and mortality. Because the potential contributors are myriad, the search requires a thorough medical evaluation guided by clinical judgment. The challenge is enhanced by the frequently nonspecific or atypical presentation of the underlying illness in older persons. In fact, delirium is often the *only* sign of life-threatening illness, such as sepsis, pneumonia, or myocardial infarction in older persons. The NICE guidelines on delirium provide a recent systematic review and evidence-based approach to delirium (http://www.nice.org.uk/guidance/CG103). These guidelines highlight both the importance of delirium in older persons, and the need for better recognition and prevention of delirium.

History and Physical Examination

A thorough history and physical examination constitute the foundation of the medical evaluation of suspected delirium. The first step in evaluation should be to establish the diagnosis of delirium through careful cognitive assessment and to determine the acuity of change from the patient’s baseline cognitive state. Because cognitive impairment may easily be missed during routine conversation, brief cognitive screening tests, such as the Short Portable Mental Status Questionnaire, Mini-Cog test, or 3D-CAM assessment, should be used to rate the CAM. The degree of attention should be further assessed with simple tests such as a forward digit span (inattention indicated by an inability to repeat five digits forward or three digits backwards) or recitation of the months of the year backward. A targeted history, focusing on baseline cognitive status and chronology of recent mental status changes, should be elicited from a reliable informant (eg, family member or health professional). In addition, such historical data as intercurrent illnesses, recent adjustments in medications, the possibility of alcohol withdrawal, and pertinent environmental changes may point to potential precipitating factors of delirium.

The physical examination should include a detailed review that focuses on potential etiologic clues to an underlying or inciting disease process. Vital sign assessment is important to identify fever, tachycardia, or decreased oxygen saturation, each of which may point to specific disease processes. Ausculatory examination may suggest pneumonia or pulmonary effusion. A new cardiac murmur or dysrhythmia may suggest ischemia or congestive heart failure. Gastrointestinal examination should focus on evidence of an acute abdominal process, such as occult bleeding, perforated viscus, or infection. Patients with delirium may also demonstrate nonspecific focal findings on neurologic examination, such as asterixis or tremor, although the presence of any new neurologic deficit should raise suspicion of an acute cerebrovascular event or subdural hematoma. It is worthy of emphasis that in many older patients and in those with cognitive impairment, delirium may be the initial manifestation of a serious new disease process. Therefore, attention to early localizing signs on serial physical examinations is important.

A complete medication review, including over-the-counter medications, is critical, and any medications with known psychoactive effects should be discontinued or minimized whenever possible. Because of pharmacodynamic and pharmacokinetic changes in aging adults, these medications may cause deleterious psychoactive effects even when prescribed at customary doses and with serum drug levels that are within the “therapeutic range.”

Laboratory Tests and Imaging

Despite the growing recognition of geriatric syndromes such as delirium, there is little evidence-based research that assesses the predictive value of laboratory and other diagnostic testing in the evaluation of delirium. Consequently, laboratory evaluation should be guided by clinical judgment and take into account specific patient characteristics and historical data. An astute history and physical examination, medication review, focused laboratory testing (eg, complete blood count, chemistries, glucose, renal and liver function tests, urinalysis, oxygen saturation), and search for occult infection should help to identify the majority of potential contributors to the delirium. Obtaining additional laboratory testing such as thyroid function tests, B_{12} level, cortisol level, drug levels or toxicology screen, syphilis serologies, and ammonia level should be based on a patient’s distinct clinical presentation. Further diagnostic work-up with an electrocardiogram, chest radiograph, and/or arterial blood gas determination may be appropriate for patients with pulmonary or cardiac conditions. The indications for cerebrospinal fluid examination, brain imaging, or EEG remain controversial. Their overall diagnostic yield is low, and these procedures are probably indicated in fewer than 5% to 10% of delirium cases. Lumbar puncture with cerebrospinal fluid examination is indicated for the febrile delirious patient when meningitis or encephalitis is suspected. Brain imaging (such as CT or MRI) should be reserved for cases with new focal neurologic signs, with history or signs of head trauma, or without another identifiable cause of the delirium. Of note, some neurologic symptoms are associated with delirium, including tremor and asterixis. EEG, which has a false-negative rate of 17% and a false-positive rate of 22% for distinguishing between delirious and nondelirious patients, plays a limited role and is most commonly employed to detect subclinical seizure disorders and to differentiate delirium from nonorganic psychiatric conditions.

Differential Diagnosis

Distinguishing a long-standing confusional state (dementia) from delirium alone, or from delirium superimposed on dementia, is an important, but often difficult, diagnostic step. These two conditions can be differentiated by the acute onset of symptoms in delirium, with dementia presenting much more insidiously and by the impaired attention and altered level of consciousness associated with delirium.

The differential diagnosis of delirium can be extensive and includes other psychiatric conditions such as depression and nonorganic psychotic disorders (**Table 47-4**). Although perceptual disturbances, such as illusions and hallucinations, can occur with delirium in about 15% of cases, recognition of the key features of acute onset, inattention, altered level of consciousness, and global cognitive impairment will enhance the identification of delirium. Differentiating among diagnoses is critical because delirium carries a more serious prognosis without proper evaluation and management, and treatment for certain conditions such as depression or affective disorders may involve use of drugs with anticholinergic activity, for example, which could exacerbate an unrecognized case of delirium. At times, working through the differential diagnosis can be quite challenging, particularly with an uncooperative patient or when an accurate history is unavailable, and the diagnosis of delirium may remain uncertain. Because of the potentially life-threatening nature of delirium, however, it is prudent to manage the patient as having delirium and search for underlying precipitants (eg, intercurrent illness, metabolic abnormalities, adverse medication effects) until further information can be obtained.

TABLE 47-4

DIFFERENTIAL DIAGNOSIS OF ALTERED MENTAL STATUS

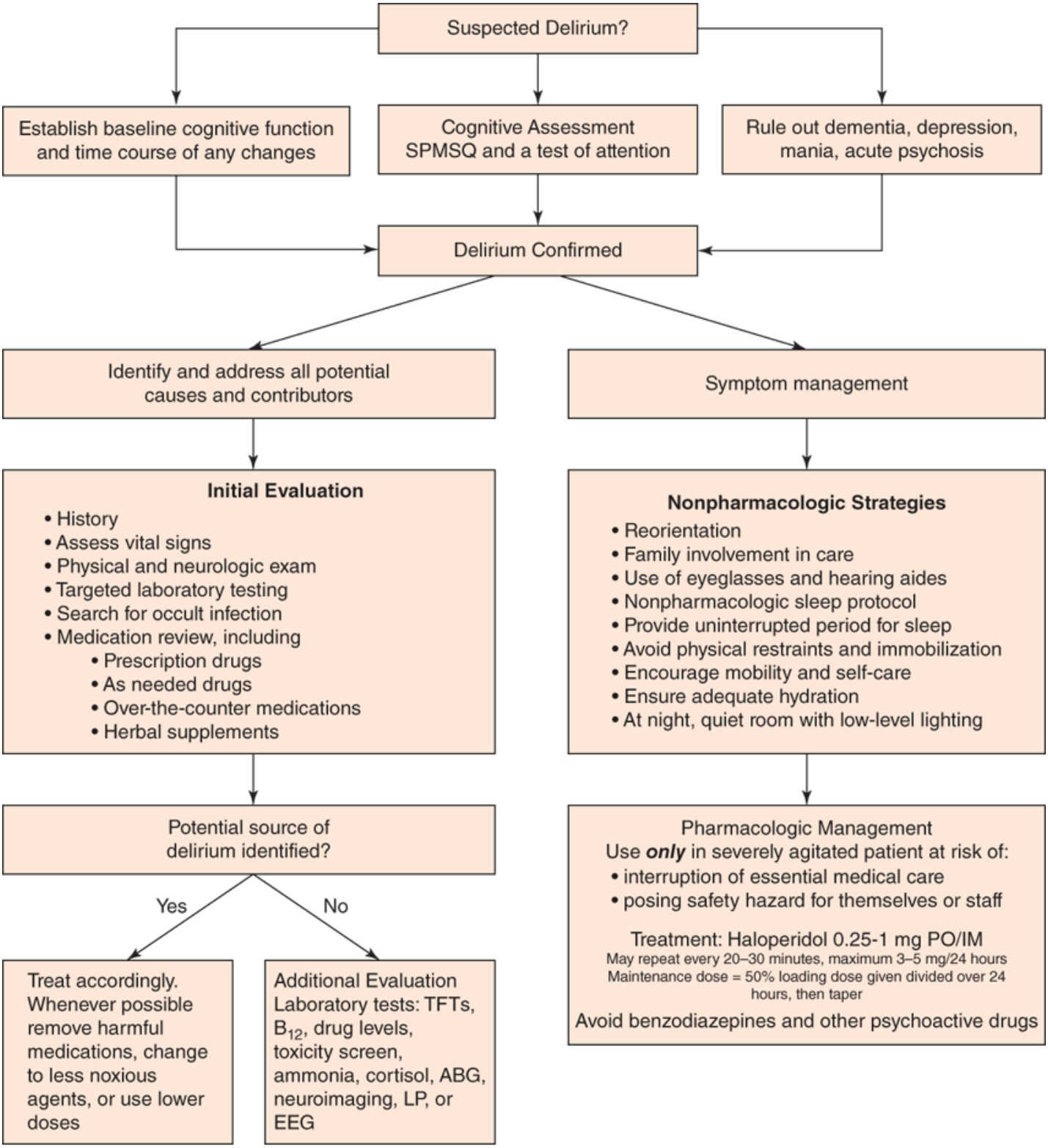
CHARACTERISTIC	DELIRIUM	DEMENTIA	DEPRESSION	ACUTE PSYCHOSIS
Onset	Acute (hours to days)	Progressive, insidious (weeks to months)	Either acute or insidious	Acute
Course over time	Waxing and waning	Unrelenting	Variable	Episodic
Attention	Impaired, a hallmark of delirium	Usually intact, until end-stage disease	Decreased concentration and attention to detail	Variable
Level of consciousness	Altered, from lethargic to hyperalert	Normal, until end-stage disease	Normal	Normal
Memory	Impaired commonly	Prominent short- and/or long-term memory impairment	Normal, some short-term forgetfulness	Usually normal
Orientation	Disoriented	Normal, until end-stage disease	Usually normal	Usually normal
Speech	Disorganized, incoherent, illogical	Notable for parsimony, aphasia, anomia	Normal, but often slowing of speech (psychomotor retardation)	Variable, often disorganized
Delusions	Common	Common	Uncommon	Common, often complex
Hallucinations	Usually visual	Sometimes	Rare	Usually auditory and more complex
Organic etiology	Yes	Yes	No	No

Algorithm for the Evaluation of Altered Mental Status

Figure 47-2 presents an algorithm for the evaluation of altered mental status in the older patient. The initial steps center on establishing the patient's baseline cognitive functioning and the onset and timing of any cognitive changes. Chronic impairments, representing changes that occur over months to years, are most likely attributable to a dementia, which should be evaluated accordingly (see Chapter 66). Acute alterations, representing abrupt deteriorations in mental status, occur over hours to weeks, although they may be superimposed on an underlying dementia. They should be further evaluated with cognitive testing to establish the presence of delirium. In the absence of notable delirium features (see "Presentation" earlier in this chapter), subsequent evaluation should focus on the possibility of major depression, acute psychotic disorder, or other psychiatric disorders (see Chapters 71,72,73).

FIGURE 47-2.

Flowchart for evaluation of suspected delirium in an older person. ABG, arterial blood gas; B_{12}, cyanocobalamin or vitamin B_{12} level; CAM, Confusion Assessment Method; EEG, electroencephalography; IM, intramuscular; LP, lumbar puncture; PO, by mouth; SPMSQ, Short Portable Mental Status Questionnaire; TFT, thyroid function tests (eg, T_4, thyroid index, thyroid-stimulating hormone).



PREVENTION

Primary prevention—preventing delirium before it develops—is the most effective strategy for reducing delirium and its associated adverse outcomes, which range from functional disability to longer lengths of hospital stay, institutionalization, and

death. Table 47-5 describes well-documented delirium risk factors and tested preventive interventions to address each risk factor. A controlled clinical trial demonstrated the effectiveness of a delirium prevention strategy targeted toward these risk factors. The selection of risk factors was based on their clinical relevance and the degree to which they could be modified by employing practical and feasible interventions. Compared with standard care, implementation of these preventive interventions resulted in a 40% risk reduction for delirium in hospitalized older patients.

TABLE 47-5

DELIRIUM RISK FACTORS AND TESTED INTERVENTIONS

RISK FACTOR	INTERVENTION PROTOCOL
Cognitive impairment	• Orienting communication, including orientation board • Therapeutic activities program
Immobilization	• Early mobilization (eg, ambulation or bedside exercises) • Minimizing immobilizing equipment (eg, restraints, bladder catheters)
Psychoactive medications	• Restricted use of PRN sleep and psychoactive medications (eg, sedative-hypnotics, narcotics, anticholinergic drugs) • Nonpharmacologic protocols for management of sleep and anxiety
Sleep deprivation	• Noise-reduction strategies • Scheduling of nighttime medications, procedures, and nursing activities to allow uninterrupted period of sleep
Vision impairment	• Provision of vision aids (eg, magnifiers, special lighting) • Provision of adaptive equipment (eg, illuminated phone dials, large-print books)
Hearing impairment	• Provision of amplifying devices; repair hearing aids • Instruct staff in communication methods
Dehydration	• Early recognition and volume repletion

Data from Inouye SK, Bogardus ST Jr, Charpentier PA, et al. A clinical trial of a multicomponent intervention to prevent delirium in hospitalized older patients. N Engl J Med. 1990;340:669.

The Hospital Elder Life Program (HELP; www.hospitalelderlifeprogram.org) represents an innovative strategy of hospital care for older patients, designed to incorporate the tested delirium prevention strategies and to improve overall quality of hospital care. Programs, such as HELP, underscore the importance of an interdisciplinary team's contributions to the prevention of delirium. For example, trained volunteers and family members can play roles in daily orientation, therapeutic recreation activities, and feeding assistance. Physical rehabilitation experts and nurses can assist with mobilization and the incorporation of daily exercises to prevent functional decline. Dietitians can help to maximize appropriate caloric intake and oral hydration in acutely ill patients. Consultant pharmacists, chaplains, and social workers also may provide specialized expertise to address patient care issues pertinent to individuals at risk for delirium.

Proactive geriatric consultation has been demonstrated to reduce the risk of delirium posthip fracture by 40% in a randomized controlled trial. The targeted multicomponent consultation strategy focused on 10 domains, namely, adequate brain oxygen delivery, fluid/electrolyte balance, pain management, reduction in psychoactive medications, bowel/bladder function,

nutrition, early mobilization, prevention of postoperative complications, appropriate environmental stimuli, and treatment of delirium (Table 47-6). The recommendations were carried out with good adherence (77%) and provided a feasible and effective approach to address a leading complication of hip fracture surgery.

TABLE 47-6

PREVENTIVE INTERVENTIONS AFTER HIP FRACTURE

RISK FACTOR	INTERVENTION
Hypoxia	• Supplemental oxygen • Raise systolic blood pressure • Transfusion to hematocrit > 30%
Fluid/electrolyte imbalance	• Restore serum sodium, potassium, glucose • Treat fluid overload or dehydration
Pain	• Around-the-clock acetaminophen • Low-dose morphine, oxycodone for breakthrough pain
Psychoactive medications	• Minimize benzodiazepines, anticholinergics, antihistamines • Eliminate drug interactions and redundancies
Bowel/bladder dysfunction	• Treat constipation • Discontinue urinary catheter by postoperative day 2, screen for retention or incontinence
Poor nutrition	• Provide dentures, assistance • Supplements or enteral nutrition
Immobilization	• Early mobilization (out of bed postoperative day 1) • Physical therapy
Postoperative complications	• Monitor and treat for: Myocardial ischemia Atrial arrhythmias Pneumonia Pulmonary embolus Urinary tract infection
Sensory deprivation	• Use glasses and hearing aids • Provide clock and calendar • Provide radio and soft lighting
Treatment of agitation	• Diagnostic work-up • Reassurance, family presence, sitter • If pharmacologic management necessary, use haloperidol

Adapted with permission from Marcantonio ER, Flacker JM, Wright RJ, et al. Reducing delirium after hip fracture: a randomized trial. J Am Geriatr Soc. 2001;49:516.

At least 13 studies have examined primary prevention with nonpharmacologic multicomponent approaches to delirium in controlled trials with prospective sampling frameworks and validated delirium assessments. These studies have applied multifactorial interventions or educational strategies targeted toward health care professionals, staff, and families, and have demonstrated reductions in delirium rates, health care–associated costs, and/or duration. Multifactorial interventions consisted of staff education strategies combined with the administration of individually tailored treatment and management of patients with delirium, sometimes with proactive geriatric consultation. Educational interventions sought to increase awareness and knowledge of delirium among medical staff, in hopes of improving assessment, prevention, and management strategies of patients with delirium. One controlled trial found that home rehabilitation after acute hospitalization in the older adults was associated with lower risk of delirium, and greater patient satisfaction, when compared with the hospital setting. Taken together, results from controlled trials suggest that 30% to 50% of cases of delirium may be preventable and that prevention strategies should begin early during hospitalization.

On a larger scale, preventive efforts for delirium will require system-wide changes and large-scale shifts in local and national policies and approaches to care. Recommended changes include routine cognitive and functional assessments on admission of all older patients; monitoring mental status as a “vital sign”; education of physicians and nurses to improve recognition and heighten awareness of the clinical implications; enhanced geriatric physician and nursing expertise at the bedside; incentives to change practice patterns that lead to delirium (eg, immobilization, use of sleep medications, bladder catheters, and physical restraints); and creation of systems that enhance high-quality geriatric care (eg, geriatric expertise, case management, clinical pathways, and quality monitoring for delirium). Implementing these changes will not only impact on delirium, but also result in high-quality hospital care more generally.

MANAGEMENT

Drugs

The recommended management approach for all delirious patients begins with nonpharmacologic strategies (see “Nonpharmacologic Management” and “Nonpharmacologic Sleep Protocol” later in this chapter), which usually result in successful symptom amelioration. In selected cases, such strategies must be supplemented with a pharmacologic approach, usually reserved for patients in whom delirium symptoms would result in interruption of needed medical therapies (eg, mechanical ventilation, central lines) or may endanger the safety of the patient or other persons. However, prescribing any drug requires balancing the benefits of delirium management against the potential for adverse medication effects because sedative drugs may prolong delirium and worsen clinical outcomes. Sometimes the decision to prescribe may be influenced by other members of the clinical team, the family, or caregivers. All interested parties should understand that the choice of almost any medication may further cloud the patient’s mental status, prolong delirium symptoms, and obscure efforts to monitor the course of the mental status change. Consequently, any drug chosen should be initiated at the lowest starting dose for the shortest time possible.

Antipsychotics

When required, antipsychotics are the preferred agents of treatment, with haloperidol being the agent in most widespread use, whose effectiveness has been established in a randomized clinical trial. Haloperidol is available in parenteral form and is associated with less postural blood pressure changes and fewer anticholinergic side effects compared with thioridazine; however, high-potency antipsychotics such as haloperidol are associated with a higher rate of extrapyramidal side effects and acute dystonias. The intravenous route should be reserved for use in monitored settings due to the risk of torsades and sudden death. Parenteral administration is required in cases where rapid onset of action is required with short duration of action, whereas oral or intramuscular use is associated with a more optimal duration of action. The recommended starting dose is 0.25 to 0.5 mg of haloperidol orally or parenterally. The dose may be repeated every 30 minutes after the vital signs have been rechecked and until sedation has been reached. The clinical end point should be an awake but manageable patient, a goal that can be achieved by following the general geriatric prescribing principle, “start low and go slow.” Most older patients naïve to prior treatment with a neuroleptic should require a total loading dose of no more than 3 to 5 mg of haloperidol. A subsequent maintenance dose consisting of one-half of the loading dose should be administered in divided doses over the next 24 hours, with doses tapered over the ensuing 48 hours as the agitation resolves.

Other Pharmacologic Approaches

Benzodiazepines (eg, lorazepam) are not recommended as first-line agents in the treatment of delirium because of their increased propensity to cause oversedation and to exacerbate acute mental status changes. However, they remain the treatment of choice for delirium caused by seizures and alcohol- and medication-related withdrawal syndromes. While other drugs have been advocated for use in treatment of delirium, evaluation of their use has resulted in discrepant findings, and there is no consensus recommendation for their general use. These drugs include the newer atypical antipsychotic agents, procholinergic agents (such as donepezil), serotonin receptor antagonists (such as trazodone), α_2-agonists (clonidine), and sedatives (such as dexmedetomidine). The atypical antipsychotic drugs (such as risperidone, olanzapine, and quetiapine) have the potential for fewer sedative and extrapyramidal effects. There is some evidence, however, that treatment with antipsychotic drugs may prolong delirium and result in poor clinical outcomes; thus, the current recommendation is that their use be restricted to patients with severe agitation that poses a threat to their safety. Moreover, official warnings have been issued regarding the increased mortality associated with use of atypical antipsychotics in dementia patients.

Nonpharmacologic Management

Nonpharmacologic approaches are the mainstays of treatment for every delirious patient. These approaches include strategies for reorientation and behavioral intervention, such as ensuring the presence of family members, use of sitters, and transferring a disruptive patient to a private room or closer to the nurse's station for increased supervision. Orienting influences such as calendars, clocks, and the day's schedule should be prominently displayed, along with familiar personal objects from the patient's home environment (eg, photographs and religious artifacts). Personal contact and communication are critical to reinforce patient awareness and encourage patient participation as much as possible. Communication should incorporate repeated reorientation strategies, clear instructions, and frequent eye contact. Correction of sensory impairments (ie, vision and hearing) should be maximized as applicable for individual patients by encouraging the use of eyeglasses and hearing aids during the hospital stay. Mobility and independence should be promoted; physical restraints should be avoided because they lead to decreased mobility, increased agitation, and greater risk of injury and worsening delirium. Patient involvement in self-care and decision making should also be encouraged. Other environmental interventions include limiting room and staff changes and providing a quiet patient care setting with low-level lighting at night. An environment with decreased noise allowing for an uninterrupted period for sleep at night is of crucial importance in the management of delirium. This may require unit-wide changes in the coordination and scheduling of nursing and medical procedures, including medication dispensing, vital sign recording, and administration of intravenous medications and other treatments. Hospital-wide changes may be needed to ensure a low level of noise at night, including minimizing hallway noise, overhead paging, and staff conversations.

Nonpharmacologic Sleep Protocol

Nonpharmacologic approaches for relaxation and sleep can be effective for management of agitation in delirious patients and for prevention of delirium through minimization of psychoactive medications. The nonpharmacologic sleep protocol includes three components: (1) a glass of warm milk or herbal tea, (2) relaxation music or tapes, and (3) back massage. This protocol was demonstrated to be feasible and effective. Use of the protocol reduced the use of sleeping medications from 54% to 31% ($p < 0.002$) in a hospital environment.

SPECIAL ISSUES

Patient Preference and Decision Making

In a condition characterized by acute fluctuations in attention and decision-making capacity, delirium presents formidable challenges to the ethical care of afflicted patients (see Chapters 12 and 61). Recent research has highlighted the importance of determining and appropriately documenting cognitive impairment prior to initiating nonemergent treatments. Cognitive assessments in patients with suspected delirium help to ensure that patients can be involved in decision making wherever possible and that appropriate surrogate decision makers (eg, family members or caregivers) are involved in representing a patient's wishes and understanding the risks and benefits of procedures and treatments. Because the patient may exhibit periods of lucidity in delirium, there may be times during which the decision-making and informed consent process can and

must involve the patient. Following resolution of an acute delirium episode, the clinician should be cognizant of ongoing subclinical manifestations of delirium, or partial forms of delirium, which may be important for considerations of both the long-term management and decision-making capacity of the patient.

Nursing Home Setting

The patient population in nursing homes can be divided into two distinct groups: postacute patients who receive short-term rehabilitative care in nursing homes after an acute hospitalization, and long-term care patients who reside in nursing homes long term as a result of severe cognitive and functional impairments. Both are high-risk groups for delirium, though the epidemiology differs between the two populations.

For the postacute population, persistent delirium after an acute hospitalization is the major issue. A recent study demonstrated that 16% of new admissions to postacute care met full CAM criteria for delirium, while another 50% demonstrated signs of subsyndromal (partial) delirium. Patients with delirium on admission to postacute care experience more complications such as falls, have higher rehospitalization rates, and higher mortality. Delirium among postacute patients is also persistent—of those admitted with delirium, over 50% are still delirious 1 month later. Persistence of delirium prevents functional recovery in the postacute setting; only those patients whose delirium cleared within 2 weeks of admission recovered to their prehospitalization functional status. Persistent delirium is also associated with higher mortality.

The long-term care population represents a high-risk group for delirium, with a high prevalence of dementia and functional impairments. In these individuals it is incident, rather than prevalent delirium, which is the primary concern. Large-scale epidemiologic studies of delirium in these patients have not been performed, but data from the minimum data set suggest that incident delirium is common in this population, and frequently heralds the onset of an acute illness that results in hospitalization and/or death.

Interventions for delirium in the nursing homes are challenging. First, because of the high prevalence of dementia in both postacute and long-term care populations, case identification can be challenging. This is compounded in the postacute population by a lack of knowledge of the patient's baseline cognitive state. Poor nursing staffing ratios, high turnover, and competing concerns make attention to delirium challenging in this setting. Nonetheless, these patients represent among the most vulnerable of all elders, and further attention to delirium in this setting is warranted. Adaptations of the HELP delirium prevention strategies are currently under way in the nursing home setting.

Palliative and End-of-Life Care

Management of delirium at the end of life poses particular challenges. Because delirium occurs in more than 80% of patients at the end of life, it is considered nearly inevitable in the terminal stages by most hospice care providers and may serve as a herald of approaching death. Establishing the goals of care with the patient and family is a crucial step, including discussions about the potential causes of the delirium, intensity of medical evaluations considered appropriate, and the need for titration between alertness and adequate control of pain and agitation. For example, some patients may wish to preserve their ability to communicate as long as possible, while others may focus on comfort perhaps at the expense of alertness. Physicians must be cognizant that even in the terminal phase, many causes of delirium are potentially reversible, and may be amenable to interventions (eg, medication adjustments, treatment of dehydration, hypoglycemia, or hypoxia) that may improve comfort and quality of life. However, the burdens of evaluation (eg, invasive testing) or treatment (eg, reduction in narcotic dose) may not be consistent with the goals for care. In all cases, symptom management should begin immediately, while evaluation is under way. Nonpharmacologic approaches should be instituted in all patients, with pharmacologic approaches for selected cases. Haloperidol remains the first-line therapy for delirium in terminally ill patients. In end-of-life care, there is a lower threshold for the use of sedative agents. Sedation may be indicated as an additional therapy for management of severe agitated delirium in the terminally ill patient, which can cause considerable distress for the patient and family. Because sedation poses the risks of decreased meaningful interaction with family, increased confusion, and respiratory depression, this choice should be made in conjunction with the family according to the goals for care. If sedation is indicated, an agent that is short acting and easily titrated to effect is recommended. Lorazepam (starting dose 0.5–1.0 mg PO, IV, or SQ) is the recommended agent of choice.

FURTHER READING

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