Delirium and Dementia

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vascular dementia (15% to 25%), Lewy body dementia (5%), and Parkinson dementia (5%).

DELIRIUM

PATHOPHYSIOLOGY

The exact mechanism of delirium is not known, but it is believed to arise from an imbalance of neurotransmitters at the cortical and subcortical levels. The principal neurotransmitters implicated in causing delirium include dopamine, an excitatory neurotransmitter, and acetylcholine and γ-aminobutyric acid, inhibiting neurotransmitters. Physiologic stressors such as infection, medications, and metabolic disturbances can alter the balance of the levels of neurotransmitters and lead to changes in cognition and attention. Inflammatory mediators such as cytokines and histamines are thought to be involved as well.

PRESENTING SIGNS AND SYMPTOMS

Delirium is a syndrome and not a specific disease; therefore, identifying the underlying cause requires a comprehensive approach that includes a medical and family history, physical examination, bedside cognitive assessment, and diagnostic testing. The confusion assessment method is a useful tool to screen for delirium in the medical setting. In an uncooperative or severely confused patient, information obtained from emergency medical service personnel and the patient’s family, personal items brought in with the patient, and a detailed physical examination with close attention to vital signs are important.

Figure 104.1 provides a structured approach to assessing cognition at the bedside; patients who are oriented with immediate recall and the ability to sustain attention and recite months or digits in reverse but no delayed recall are unlikely to have delirium and should be suspected of having dementia. The challenge for the EP, who has not generally seen the patient previously, is recognizing delirium—an acute process—when it is superimposed on dementia—a chronic process. Therefore, a systematic approach to ED evaluation is necessary.

Infection

One of the most common causes of delirium in the elderly is infection. A simple urinary tract infection or pneumonia, which is easily handled by the immune system of a healthy adult, can have deleterious effects on the mental balance of an elderly patient who has little physiologic reserve. Progression to sepsis often worsens the delirium and can lead to
Metabolic, Fluid, and Electrolyte Disturbances

Hypoglycemia is a common cause of delirium seen in the ED and one that is readily treatable. Patients can have symptoms ranging from mild agitation to coma. As a note of caution, delirium from hypoglycemia may not be suspected in patients with a hypoglycemia-induced focal neurologic deficit or seizure. A history of diabetes, medications, and the time of the last meal are important; documentation of the administration of dextrose and other medications by the emergency medical service should be obtained.

Diabetic ketoacidosis and hyperosmolar hyperglycemic nonketotic coma can both be manifested as an acute confusional state. Hyperosmolar hyperglycemic nonketotic coma is seen more commonly in elderly patients with no history of diabetes or in patients with adult-onset diabetes and an underlying stressor such as infection.

Hyponatremia can cause delirium, but it is related to the rate of sodium reduction and not the absolute quantity. A patient with a slight, sudden decrease in serum sodium can have delirium, whereas a larger, more gradual reduction (over days) is well tolerated by many patients. Hyponatremia has many causes, from underlying medical conditions such as the...
syndrome of inappropriate secretion of antidiuretic hormone to intentional and unintentional water ingestion.

Hypercalcemia may be associated with delirium. The normal range of total serum calcium is between 8.5 and 10.5 mg/dL. Patients with calcium elevated above this range can exhibit confusion, depending on the rate of increase.

Patients with end-stage kidney and liver disease can also have delirium. The patient’s medical history or family members may document dialysis or a history of encephalopathy. The underlying process causing the encephalopathy, such as infection or lack of compliance with treatment, should be investigated.

**Drug Withdrawal**

Alcohol withdrawal in its severe form can cause delirium, which is known as delirium tremens. These patients will be seen in the ED with agitation and possible confusion. Visual or auditory hallucinations (or both) and delusions can also be part of the clinical findings and can contribute to misdiagnosis in these patients with a primary psychiatric disorder. Diagnosis of delirium tremens is based on a history of chronic alcohol abuse and symptoms of acute confusion and sympathetic hyperactivity. Typically, the last drink of alcohol was more than 48 hours before arrival at the ED. Vital signs may show severe hypertension, hyperthermia, and tachycardia. On physical examination, the patient often exhibits postural tremor and hyperreflexia.

Withdrawal from chronic benzodiazepine abuse can have a similar manifestation, although the onset of the symptoms varies, depending on the time of the last dose and the half-life of the drug.

**Drug Toxicity**

Alcohol intoxication is a common finding in the ED. The patient is often agitated, confused, and combative. This patient population is more susceptible to other causes of delirium, including infection, trauma, and concomitant ingestion of drugs; a thorough, unbiased evaluation is therefore important.

Common classes of abused drugs causing delirium include sympathomimetics such as cocaine and amphetamine and hallucinogens such as lysergic acid diethylamide (LSD) and ketamine. Close attention to vital signs and identification of a toxic syndrome (toxidrome) are essential in making the diagnosis. Patients with sympathomimetic toxicity may have significant increases in heart rate, blood pressure, and temperature with associated hyperactivity, agitation, and diaphoresis. Clinical findings associated with ketamine abuse include vertical and rotatory nystagmus, midpositioned pupils, hallucinations, labile affect, hyperthermia, and muscle rigidity. Mild tachycardia and hypertension may be seen. Investigation of personal belongings for pills and interview with family members may augment the diagnosis. Anticholinergic medications are also commonly used in the ED and outpatient settings. Delirium associated with mydriasis, hyperthermia, anhydrosis, and hyperemia is seen in this toxidrome.

Many commonly prescribed medications can cause delirium as a result of improper dosing, change in metabolism, intentional overdose, and drug-drug interactions (Box 104.2). Family members or the patient’s personal physician may be able to provide valuable information about recent changes in medication dosages or the addition of new medications.

**Cerebrovascular Disorders**

Delirium is a common complication after an acute stroke and is reported in up to 48% of patients. Despite case reports of delirium being the primary manifestation of an acute stroke, it is more frequently reported as a sequela of the event. Delirium has been associated with left-sided infarcts and thalamic and caudate nucleus strokes. Delirium after stroke has been linked to longer hospital stay and increased mortality.

Hypertensive emergency is associated with delirium if target organ damage affects the brain and causes hypertensive encephalopathy. Blood pressure is typically elevated significantly. Other signs of end-organ damage include heart failure and renal failure.

Delirium can develop as a result of a primary traumatic brain injury or the consequent secondary injury. Aggressive systematic evaluation of the reversible secondary causes of acute confusion after a traumatic brain injury is necessary while maintaining optimal cerebral perfusion and oxygenation. Intracerebral bleeding or edema, or both, must be suspected in patients in whom a change in mental status develops after a traumatic brain injury.

**Hypoxemia and Hypercapnia**

Acute elevations in PCO₂ and low Po₂ can cause alterations in cognition and awareness. Pulmonary disorders such as pneumonia, pulmonary embolism, asthma, and pneumothorax
can cause hypoxia. Abnormal chest excursion and rate, depth, and effort of breathing are significant findings on the physical examination. Symptoms important in the history include dyspnea, fever, cough, and pleuritic chest pain, as well as recent travel and a family history of connective tissue disease.

Hypercapnia is a normal finding in many patients with chronic obstructive pulmonary disease, but an acute rise in PaCO₂ can lead to an alteration in consciousness. Oxygenation is not an adequate measurement of ventilation, and therefore serial monitoring of the patient’s mental status should be initiated in the absence of bedside capnography.

Endocrine Disorders
Patients with endocrine disorders such as hyperthyroidism, hypothyroidism, Cushing syndrome, and hyperparathyroidism may have altered mental status when seen initially in the ED. Delirium is more common with severe manifestations of these diseases, as in the case of thyroid storm and myxedema coma. Abnormalities in vital signs, such as tachycardia and fever in thyroid storm and bradycardia and hypotension in myxedema coma, may be the only initial clues to the diagnosis.

Chemical Exposure
Delirium may be the initial symptom in patients exposed to a chemical weapon or contaminated environment. History of the exposure is important, but the patient often displays confusion and no history is available. If chemical exposure is suspected, the patient must be brought to the proper decontamination area immediately. Universal precautions should be practiced, as well as use of a proper-level hazmat suit. The patient should be stabilized and evaluated for findings on examination and vital signs suggesting the cause of the contamination and thus the antidote (Box 104.3).

Environmental Agents
Stroke from heat exposure occurs in the very young and the elderly, but exertional heatstroke can occur acutely in persons of all age. Heatstroke can be manifested as confusion, hyperthermia (temperature typically higher than 40°C), tachycardia, tachypnea, and hypotension. Delirium may be the initial finding because the central nervous system is often the first organ system to be affected by the elevation in temperature.

In contrast to heat illnesses, patients suffering from cold exposure can exhibit acute confusion. Patients with temperatures below 35°C can demonstrate apathy, slurred speech, confusion, forgetfulness, and shivering. As the temperature drops further, the symptoms progress from delirium to coma. Exposure to plants, insect stings, and animal bites may all result in delirium related to the toxin or chemical involved in the exposure. The initial finding may be related to the cause of the injury or rash, but progression to systemic complications can ensue rapidly.

Central Nervous System Disease
Depending on the location of the mass, intracerebral tumors can be manifested as delirium without focal motor deficits. Frontal lobe tumors are more commonly associated with acute changes in personality or behavior.

Absence seizures, seen primarily in children 5 to 10 years of age, are characterized by acute-onset altered mental status without motor activity. The seizure episodes typically last for seconds and resolve without a postictal state. Complex partial seizures can also be accompanied by an acute change in mental status. Patients with nonconvulsive status epilepticus (absence or complex partial) may have a change in mental status that can vary in intensity and duration. Nonconvulsive status can occur in patients of all ages and without any previous history of a seizure disorder. Clinical findings vary from a minor change in mental status to full-blown psychotic or comatose states. The hallmark of nonconvulsive status epilepticus is a change in mental status that occurs in the absence of motor activity and is associated with characteristic electroencephalographic changes. Motor activity, when present, is subtle and in the form of mild twitching of the lips or the upper or lower extremities, but no clear tonic-clonic activity is present.

Vitamin Deficiency
Deficiency in certain vitamins can cause altered mental status. Patients with Wernicke encephalopathy, which is caused by a deficiency of thiamine (vitamin B₁), can exhibit delirium, ataxia, and ophthalmoplegia. Advanced cases of vitamin B₁₂ deficiency can also cause altered mental status, along with a history of paresthesias, weakness, diarrhea, and loss of appetite.

Differential Diagnosis and Medical Decision Making
If delirium is excluded after a thorough work-up of a patient with confusion, other causes of altered cognition should be considered. An elderly patient with newly recognized or worsening dementia may arrive at the ED with an acute decline in consciousness. Family members may recall changes in memory and function over a longer period, thus suggesting dementia rather than delirium (Table 104.1).

First-time manifestations of psychiatric disorders or exacerbation of underlying psychiatric disease can often be confused with delirium as a result of their similar characteristics. Because patients with psychiatric illness can exhibit delirium, medical and reversible causes of the confusion must be excluded before transfer of care to a psychiatrist (see the

### BOX 104.3 Chemical Agents Associated with Delirium

<table>
<thead>
<tr>
<th>Organophosphates</th>
<th>Sarin (isopropyl methylphosphonofluoridate)</th>
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<tbody>
<tr>
<td>Diethyl parathion</td>
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<tr>
<td>VX (O-ethyl S-2-[diisopropylamino]ethyl-methylphosphonothioate)</td>
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<tr>
<td>Carbamates</td>
<td>Aldicarb (Tres Pasitos)</td>
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<td></td>
<td>Propoxur (Baygon)</td>
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<tr>
<td>Organochlorines</td>
<td>DDT (dichlorodiphenyltrichloroethane)</td>
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<tr>
<td></td>
<td>Lindane</td>
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<tr>
<td>Other</td>
<td>DEET (diethyltoluamide)</td>
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<td></td>
<td>Pyrethrins</td>
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</tbody>
</table>

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Priority Actions box “Tests Useful in the Diagnosis of Delirium”).

TREATMENT
Once the cause of the delirium is discovered, appropriate treatment should be initiated immediately. Antibiotic therapy should be started in patients with suspected meningitis, hypoglycemia should be corrected with dextrose, and patients with hypoxia should receive oxygen supplementation. Delay in diagnosis and treatment can increase overall morbidity and mortality.

Pharmacologic management of agitation is sometimes necessary when a patient with delirium is a danger to self or others or if the agitation is impeding medical evaluation and management. Current pharmacologic options include typical and atypical antipsychotic agents and benzodiazepines. Both droperidol and haloperidol are generally safe and effective and cause less respiratory depression than benzodiazepines do. However, the benzodiazepines, midazolam or lorazepam, may be preferable in particular clinical scenarios such as drug withdrawal or overdose. It is important to remember to reduce dosing in elderly patients because they have altered pharmacodynamics and pharmacokinetics. There is currently no good literature to support the use of atypical antipsychotics in the acute management of delirium.

DEMENTIA

PATHOPHYSIOLOGY
At the anatomic level, Alzheimer dementia is characterized by atrophy of both cortical and subcortical structures, which is seen most prominently in the hippocampus and temporal cortex. Histologic examination reveals an accumulation of extracellular amyloid plaques and neurofibrillary tangles that attract inflammatory mediators and impede delivery of neurotransmitters along the axons, respectively. Deficiencies in the neurotransmitters acetylcholine and norepinephrine are also thought to be responsible for the dementia in Alzheimer disease. Pathophysiologic and clinical characteristics of the types of dementia are presented in Table 104.2.16
PRESENTING SIGNS AND SYMPTOMS

Alzheimer disease is characterized by a gradual onset of dementia, as defined by the Diagnostic and Statistical Manual of Mental Disorders, fourth edition (Box 104.4), with continuous functional decline. The cognitive impairment seen in Alzheimer disease is not explained by other causes of dementia. Most patients in the ED with Alzheimer disease will already carry the diagnosis and probably have an associated complication such as infection or exacerbation of the dementia.

Because the clinical manifestation of dementia is subtle and gradual, it is important to maintain a high index of suspicion in the evaluation of elderly patients in the ED. Initial symptoms, such as depression, fatigue, insomnia, and irritability, can be nonspecific. Inquiring about missing appointments and increased forgetfulness can be helpful, but patients often avoid discussing difficulties in cognitive abilities by changing the subject. Family members or caregivers may bring patients to the ED because they are unable to care for them or because the patients are no longer able to care for themselves. It is important to recognize early dementia (mild cognitive impairment) in the ED setting to prevent secondary complications such as injuries from falls and fires, noncompliance with medications, and malnutrition and dehydration. Evaluation for a reversible cause of dementia and delirium must be initiated.

Although dementia has a reversible cause in less than 5% of these patients, a thorough history and physical examination must be undertaken to identify this subcategory (see the Priority Actions box “Tests Useful in the Diagnosis of Reversible Causes of Dementia”). Normal-pressure hydrocephalus is characterized by ataxia, urinary incontinence, and dementia, all of which are reversible. Diagnosis is made by CT scan of the head and the finding of elevated opening pressure on lumbar puncture. Treatment is surgical insertion of a shunt.

DIFFERENTIAL DIAGNOSIS AND MEDICAL DECISION MAKING

Pseudodementia is a term used to describe patients who appear to be demented but are actually severely depressed. Differences from genuine dementia can be subtle; patients with pseudodementia usually have a preexisting history of depression with acute onset (often after a specific event), emphasize and appear more distressed about the cognitive deficits, and have preserved attention. If the diagnosis of depression is suspected, patients should be asked about thoughts of suicidality and their social support structure. Appropriate consultation and follow-up with a psychiatrist or social worker or hospitalization may be necessary to ensure the patient’s safety.

**Table 104.2** Clinical and Pathophysiologic Symptoms and Signs in Types of Dementia

<table>
<thead>
<tr>
<th>DISORDER</th>
<th>CLINICAL</th>
<th>SYMPTOMS AND SIGNS</th>
<th>PATHOPHYSIOLOGIC</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alzheimer disease</td>
<td>Gradual and continuing functional decline not explained by another cause of dementia</td>
<td>Amyloid plaques, neurofibrillary tangles, hippocampal and temporal atrophy</td>
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<tr>
<td>Vascular dementia</td>
<td>Sudden onset, focal neurologic findings, stepwise deterioration</td>
<td>Multiple infarcts</td>
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<tr>
<td>Lewy body dementia</td>
<td>Visual hallucinations, fluctuating cognition, mild parkinsonism seen less than 1yr before dementia</td>
<td>Lewy bodies, Lewy neuritis</td>
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<tr>
<td>Parkinson dementia</td>
<td>Extrapyramidal signs, visual hallucinations, fluctuating cognition</td>
<td>Lewy bodies, Lewy neuritis</td>
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<tr>
<td>Frontotemporal dementia (Pick disease)</td>
<td>Personality changes, restlessness, disinhibition, impulsiveness, ataxia, parkinsonism</td>
<td>Pick bodies, frontal and temporal atrophy</td>
<td></td>
</tr>
<tr>
<td>Infectious dementia (Creutzfeldt-Jakob)</td>
<td>Visual disturbances, ataxia, myoclonus, progressive dementia</td>
<td>Prion protein accumulation, spongiform change of brain</td>
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</table>
TREATMENT
As with the treatment of delirium, reversible causes of dementia should be addressed and treatment initiated immediately. Frequently, the dementia will have no reversible cause; the patient has a new diagnosis of dementia or worsening of an underlying condition. In such cases, disposition is based on the patient’s ability to function independently at home or on the family’s capacity to care for the patient. If the family is unable to further care for the patient, admission to the hospital for evaluation for nursing home placement or assisted home care is necessary. If there is adequate support by family and patient safety can be ensured, the work-up of patients with new-onset dementia can be done in an outpatient setting with appropriate coordinated care by the primary physician.

Cholinesterase inhibitors are often used in the treatment of mild to moderate Alzheimer-type dementia; vitamin E has also been recommended to slow the progression of Alzheimer dementia.\textsuperscript{17} Cholinesterase inhibitors have been recommended to improve quality of life and cognitive function. However, despite the frequent use of these medications, the literature on the benefit of cholinesterase inhibitors remains controversial.\textsuperscript{18}

FOLLOW-UP, NEXT STEPS IN CARE, AND PATIENT EDUCATION
Disposition depends on the cause of the delirium or dementia and the patient’s response to treatment. If the patient does not improve or the cause is not found, the patient should be transferred to the appropriate inpatient facility. In some cases, with improvement in baseline values the patient can be discharged home.

SUGGESTED READINGS

REFERENCES
References can be found on Expert Consult @ www.expertconsult.com.
REFERENCES