



Delirium in the hospitalized elderly

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- **BACKGROUND** As many as one third of elderly hospitalized patients become delirious, and most do not fully recover. Delirium may impart a higher mortality rate and may be a marker for future cognitive decline.
- **OBJECTIVE** To review the clinical features, etiology, diagnosis, and management of delirium in elderly hospitalized patients.
- **SUMMARY** Delirium can be caused by primary intracranial disease, systemic diseases, withdrawal from alcohol or sedative hypnotic agents, or drug intoxication, the most common cause. Because delirium may present with diverse clinical features, physicians should suspect it in any elderly patient with a change in mental status, personality, or behavior. Bedside screening tools may help distinguish delirium from dementia and psychosis. Causative factors should be sought and removed or treated. Anticholinergic drugs are the worst offenders, but all drugs are suspect and should be discontinued or reduced in dosage. If a sedative is needed, haloperidol is the drug of choice. Because of the prevalence and seriousness of alcohol withdrawal, all delirious patients should receive intravenous thiamine to reduce the risk of Wernicke's encephalopathy.
- **CONCLUSIONS** An organized, systematic approach with early diagnosis and treatment may prove to be life-saving in many patients.

■ **INDEX TERMS:** DELIRIUM; AGED; HOSPITALIZATION
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DELIRIUM, the most common acute transient organic brain syndrome encountered in the hospital, can occur at any age. However, delirium is much more likely in elderly patients. Depending on the population, 11% to 33% of elderly patients become delirious during their hospital stay.¹⁻⁶ Delirium in the elderly often portends an underlying or impending medical disease such as congestive heart failure or pneumonia.⁷ Delirious patients stay in the hospital longer¹ and have a higher 2-year mortality rate than patients who are not delirious.⁸ Despite its prevalence and clinical importance, delirium in the elderly is often misdiagnosed and frequently evokes little interest among physicians and nurses.^{9,10}

This review focuses on the clinical features, etiology, diagnosis, and management of delirium in elderly hospitalized patients.

CLINICAL FEATURES

Alterations in cognition, attention, the sleep-wake cycle, and psychomotor behavior characterize the delirium syndrome.¹¹⁻¹³ Perception, thinking, and memory, the three aspects of cognition, are all

abnormal to some extent. As a result, the patient is less capable of acquiring, processing, storing, and retrieving information about self, body, and the environment.¹⁴ Delirious patients are always at least mildly disoriented in time but rarely lose their sense of personal identity. Visual hallucinations are very common and tend to be experienced as vivid, colorful, three-dimensional objects.

Disruption in the normal state of consciousness, the cardinal feature of delirium, results in attention deficits that fluctuate in severity during the course of the day. At one moment a patient may be lethargic, responding to questions slowly; the condition is easily overlooked or misdiagnosed as depression. Several hours later the same patient may be restless and agitated, speaking as if under pressure and moving about frequently. This agitation is usually associated with overactivity of the sympathetic nervous system and typically is seen in patients withdrawing from alcohol or sedatives.

Disordered wakefulness and abnormalities in the sleep-wake cycle are also classic features of delirium.¹¹⁻¹³ Wakefulness is typically reduced during the day—the patient is drowsy and tends to nap. At night, wakefulness is increased, and the patient's sleep is shortened and fragmented. A typical elderly delirious patient is agitated, restless, and bewildered at night, oscillating between sleeping and waking and between dreaming and hallucinating.¹³

Psychomotor activity in a delirious elderly patient is manifested by shouting, wandering, or pacing. Typical movement disorders may be present. Patients with metabolic encephalopathy commonly have asterixis; those withdrawing from ethanol or sedative-hypnotic agents have a coarse tremor. Because delirium may present with diverse clinical features, physicians should suspect it in any elderly individual with a change in mental status, personality, or behavior.

ETIOLOGY

Delirium results from widespread cerebral dysfunction caused by factors that can be classified into four major categories: primary intracranial disease; systemic diseases secondarily affecting the brain; exogenous toxic agents; and withdrawal from alcohol or sedative-hypnotic agents.¹³

Intracranial diseases

Virtually any intracranial process can cause delirium,

including meningitis, neoplasm, trauma, epilepsy, or stroke. Delirium may be the presenting feature of a subdural hematoma in an elderly patient. A recently recognized cause of delirium is infarction of the right middle cerebral artery,¹⁵ which also can cause visual neglect, anosognosia, and left-sided motor, sensory, and visual field deficits.

Systemic diseases

A large variety of systemic diseases can produce delirium, most commonly congestive heart failure, pneumonia, urinary tract infection, cancer, uremia, malnutrition, electrolyte disorder, myocardial infarction, or hypoglycemia.^{2,3,11,13} Another cause, which may be missed because of its insidious onset, is thyroid disease, either hypothyroidism or hyperthyroidism.

Delirium often follows surgery in the elderly.¹⁶ Elderly patients who suffer a fracture of the femoral neck are particularly vulnerable: in one study the incidence of delirium after hip fracture approached 50%.¹⁷ In this study, confused patients had significantly more postoperative complications and stayed in the hospital almost four times longer than alert and oriented patients. Factors associated with postoperative delirium included underlying depression or dementia, anticholinergic agents, and a bed without a window.

Medication intoxication

The most common cause of delirium in the elderly is medication intoxication or adverse effects.¹³ The elderly are more likely than younger people to experience an adverse drug reaction because they are more likely to have multiple concurrent diseases requiring multiple medications and because of age-related changes in drug pharmacokinetics.¹⁸ With age, hepatic and renal function decline, total body water and extracellular fluid decrease, and the proportion of body fat increases.¹⁸ As a result, drugs metabolized or excreted by the liver or kidney are more likely to accumulate, resulting in toxic reactions. Water-soluble drugs such as digoxin and cimetidine have a smaller volume of distribution in the elderly, resulting in increased initial concentrations and greater risk for toxic reactions. Increases in total body fat in the elderly provide larger volumes of distribution for fat-soluble drugs such as diazepam. Such agents tend to accumulate, resulting in long half-lives, which predispose to toxic reactions.

Almost any drug can cause delirium in the elderly.

TABLE 1
DRUGS THAT CAN CAUSE DELIRIUM
OR COGNITIVE IMPAIRMENT

Agents with anticholinergic effects
Antihistamines
Disopyramide
Haloperidol
Opiate analgesics
Over-the-counter cold remedies
Phenothiazines
Propantheline
Tricyclic antidepressants
Other agents
Alcohol
Amantadine
Benzodiazepines
Beta blockers
Bromocriptine
Cimetidine
Clonidine
Corticosteroids
Digoxin
Levodopa
Lithium
Nonsteroidal anti-inflammatory drugs
Penicillin
Phenobarbital
Phenytoin
Quinidine

erly, but anticholinergic agents are most commonly implicated.¹¹ Memory, learning, attention, and wakefulness rely on adequate functioning of the cholinergic system. Because aging adversely alters the central cholinergic system, the elderly are particularly sensitive to anticholinergic medications.¹⁹ Antihistamines, narcotics, and some antidepressants (tricyclics, doxepin) have anticholinergic properties and should be used with great care in the elderly.

Drugs likely to cause confusion in the elderly are listed in *Table 1*. Elderly patients receive a disproportionately large share of all psychotropic medications prescribed. All classes of psychotropic drugs should be used only with well-defined therapeutic goals and in their smallest effective doses, and their use should be reassessed on a regular basis. In general, one should prescribe these medications at doses 30% to 50% lower than for younger patients. "Start low and go slow" is the rule.

Alcohol withdrawal

Withdrawal from substances of abuse is another common cause of delirium in the elderly. Alcoholism, though common, often goes unrecognized in the hospitalized elderly because clinicians do not

TABLE 2
DIFFERENTIAL DIAGNOSIS
OF DELIRIUM AND DEMENTIA

Feature	Delirium	Dementia
Onset	Acute	Chronic
Course	Fluctuating	Stable
Duration	Hours to weeks	Months to years
Alertness	Low or high	Usually normal
Thinking	Disorganized	Impoverished
Speech	Incoherent, slow or rapid	Difficulty with words
Physical illness or drug toxicity	Usually present	Usually absent

suspect it. Anxiety, insomnia, nausea, tremors, and even seizures may be mistakenly ascribed to other disorders that appear more frequently among the elderly than does alcoholism.

Delirium in the elderly is typically multifactorial: several causative factors are often implicated, and their potential to cause delirium is frequently enhanced by psychosocial stresses such as bereavement, transfer to an unfamiliar environment, or excessive or deficient sensory inputs. Sleep loss and fatigue may play a contributory role.

DIAGNOSIS AND DIFFERENTIAL DIAGNOSIS

In diagnosing delirium, one must distinguish it from dementia (*Table 2*) and from pseudodelirium (psychosis) (*Table 3*). The physician must recognize the clinical characteristics of the delirium syndrome and identify its causes. This process begins with a history and physical examination that includes a thorough neurologic examination. Rapid bedside screening tools such as the Folstein Mini Mental Test²⁰ or the Confusion Assessment Method²¹ can be used to measure a patient's neurologic impairment. This is especially helpful in patients with mild, early delirium whose ability to compensate minimizes their apparent deficiencies. Additional laboratory and diagnostic tests are then ordered as directed by the history and the physical findings (*Table 4*).

It is important to distinguish delirium from dementia because the two syndromes carry different prognostic implications. Making this distinction, however, may be very difficult because delirium in the elderly is often superimposed on dementia. As a general rule, a patient who has been functioning well intellectually and then suddenly acquires a cog-

TABLE 3
DIFFERENTIAL DIAGNOSIS OF DELIRIUM
AND ACUTE FUNCTIONAL PSYCHOSIS

Feature	Delirium	Acute functional psychosis
Onset	Sudden	Sudden
Course	Fluctuating	Stable
Consciousness	Reduced	Clear
Cognition	Globally disordered	May be selectively impaired
Hallucinations	Visual or visual and auditory	Auditory
Involuntary movements	Asterixis or tremor	Usually absent
Physical illness or drug toxicity	Usually present	Usually absent

nitive-attention disorder that fluctuates in character and severity during the day and becomes most marked at night is suffering from delirium unless proven otherwise.

Functional psychosis or pseudodelirium may be mistaken for delirium. This term describes a delirium-like transient state for which there is no demonstrable organic cause. A patient with pseudodelirium is likely to have inconsistent results on cognitive testing, a history of psychiatric illness, markedly depressive or manic behavior, systematized rather than fleeting delusions, and no characteristic fluctuation and nocturnal worsening of symptoms. Auditory hallucinations are more typical of psychosis than of delirium. In patients with functional psychosis, the electroencephalogram is usually normal, whereas in delirium it reveals diffuse slow-wave activity.

TREATMENT

If a patient has become delirious, causative factors must be sought in order to treat or remove them. All drugs taken are suspect and should be discontinued or reduced in dosage. Adequate fluid, electrolyte, and nutritional support must be maintained. A sensory environment that protects the patient from both extremes of sensory inputs is essential. A quiet, well-lit room with several familiar objects and photographs both orients and calms patients.

When sedation is required, haloperidol is the drug of choice for most patients.^{16,21,22} It is effective, has limited anticholinergic side effects, and usually

TABLE 4
DIAGNOSIS OF DELIRIUM

History and physical examination
Laboratory tests
Serum electrolyte concentrations
Blood and urinary glucose concentrations
Blood urea nitrogen and serum creatinine concentrations, urinalysis
Hepatic enzyme concentrations
Arterial blood gases
Complete blood count
Calcium, phosphorus, magnesium
Thyroid function tests
Vitamin B ₁₂
Drug and alcohol screen
Other
Electrocardiography
Electroencephalography
Computed tomography
Lumbar puncture
Blood culture

does not cause severe orthostatic hypotension. Dose-related, reversible extrapyramidal symptoms are the most frequent side effects. Rarer but more troublesome side effects include tardive dyskinesia (a potentially irreversible syndrome of involuntary dyskinetic movements) and the neuroleptic malignant syndrome (a potentially lethal condition with hyperpyrexia, muscle rigidity, mental status changes, and autonomic instability). The initial dosage should be low (0.5 mg twice daily orally or intravenously) and titrated upward as needed.

Because of the prevalence and seriousness of alcohol withdrawal, all delirious patients should receive intravenous thiamine to reduce the risk of Wernicke's encephalopathy. When alcohol, benzodiazepine, or barbiturate withdrawal is suspected, benzodiazepines are the drugs of choice for agitation. Because of age-associated changes in hepatic metabolism, short-acting agents such as oxazepam and lorazepam should be used.

OUTCOME AND PROGNOSIS

Delirium traditionally has been considered a transitory state that subsides with appropriate treatment. Recent evidence, however, shows that complete resolution of symptoms may actually occur in only a minority of patients. Levkoff et al⁴ prospectively studied 125 elderly hospitalized patients who had delirium. Only five patients (4%) experienced resolution of all new symptoms before hospital discharge, 20.8% did by 3 months, and 17.7% did by 6

months. Although several studies failed to show that delirious patients had a higher mortality rate at 6 months than controls,^{2,4} a higher mortality rate appears to emerge with longer follow-up. Francis and Kapoor⁸ studied elderly patients for 2 years after an episode of delirium and found they had a higher mortality rate and a higher risk for loss of independence than similar patients without delirium. This study also suggested that delirium may serve as a marker for future cognitive decline.

A likely explanation for these findings is that patients who become delirious tend to be frail and elderly and have multiple concomitant medical problems. Interestingly, simple historical screening upon admission can identify patients at high risk for becoming delirious. Schor et al⁵ showed that delirium in hospitalized elderly patients is most closely associated with certain factors present on admission, including previous cognitive impairment, age over 80, symptomatic infection, male sex, and neuroleptic

or narcotic use. Although these investigators used a standardized instrument to identify risk factors for delirium, they did not validate those risk factors in an independent sample. To date, only the predictive model of Inouge et al^{21,23} (impaired vision, severe illness, cognitive impairment, and a high ratio of blood urea nitrogen to creatinine) has been validated in an independent sample.

SUMMARY

The hallmark of aged individuals is a reduced capacity for homeostatic regulation and reduced resistance to stress. When such a person becomes ill, delirium may result. Even with early recognition of the delirium syndrome and prompt initiation of therapy, elderly delirious patients may succumb to the underlying disorder. An organized systematic approach with early diagnosis and treatment may prove life-saving in many individuals.

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