

# Diagnosis and Management of Delirium in the Elderly

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## Introduction

Delirium (ie, acute confusional state, reversible dementia, pseudosenility, and acute brain syndrome)<sup>1</sup> manifests as transient impaired cognition and decreased ability to maintain function, orientation, and attention.<sup>2,3</sup> Impairment of cognitive function is common. Between 2 million and 4 million Americans have some form of dementia or dementing illness,<sup>4</sup> and the number of patients who experience delirium increases steadily after the fourth decade of life.<sup>5</sup> An estimated 10% of all hospitalized patients experience delirium.<sup>6</sup> In elderly patients, delirium affects at least 20% of patients age 65 years or older<sup>7</sup> and between 25% and 35% of patients age 85 years or older.<sup>8</sup>

The high incidence of delirium is particularly notable in hospitalized elderly patients.<sup>9</sup> Delirium occurs in 33% to 41% of hospitalized elderly patients.<sup>10,11</sup> Approximately 18% of elderly patients in medical units and 38% of elderly patients in surgical units are afflicted with delirium.<sup>1,12</sup> Another study reported that an astounding 61% of patients who underwent surgery for femoral neck fracture experienced delirium.<sup>13</sup> An estimated 15% of elderly patients with delirium die because of the underlying etiology of this disorder.<sup>14</sup>

Risk factors associated with delirium include prior cognitive impairment, an age of 80 years or greater, symptomatic infection, male gender, and use of neuroleptics or narcotics.<sup>10</sup> Appropriate assessment of patients with risk factors for delirium is important because these patients are associated with increased morbidity, greater lengths of inpatient hospitalization, higher patient care costs,<sup>15-17</sup> increased mortality, and higher probability of nursing home placement.<sup>15,18</sup>

During delirium assessment, healthcare providers must be cognizant that elderly patients who appear depressed may in fact be delirious.<sup>19</sup> This emphasis is particularly relevant because both delirium and

depression are underdiagnosed as well as undertreated in the elderly.<sup>20-22</sup> The type of patient care setting is an important consideration during delirium assessment; for example, one study reported that whereas 40.5% of patients in long-term care facilities experienced delirium, only 26.7% of cases were recognized by staff nurses.<sup>1</sup> However, when physicians and nurses combined their efforts, they identified 75% of cases of patient delirium.<sup>23</sup>

Thus, the primary care physician must be vigilant when assessing any elderly patient who presents with some form of acute impairment in memory or attention. Exogenous factors (ie, alcohol intoxication or withdrawal, medication) and endogenous disease (ie, infection; metabolic abnormality; thyroid disease; hepatic, renal, respiratory, or congestive heart failure) should be investigated to determine potential etiologies for delirium. In addition, endogenous disease may present or be exacerbated by exogenous factors.<sup>24</sup> As in this case study, an abbreviated mental status examination in combination with appropriate history and physical examination can be extremely helpful in patient assessment in the office setting.

Overall, in circumstances of acute cognitive deficit, the diagnosis of delirium should always be considered in elderly patients. Vigilance is important; if left untreated, patients with delirium may be hospitalized and the health care delivery system may incur high costs associated with treatment or potential misdiagnosis. More importantly, patients with delirium can benefit from assessment of the underlying disorder in the office setting. A primary care provider with a high

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index of suspicion can successfully keep an elderly patient with delirium out of the hospital, maximize the patient's functional status, and minimize the costs to the health care delivery system.

## **CASE PRESENTATION**

### **Initial Presentation**

A 74-year-old woman is brought by her son to her primary care physician. The son is concerned about his mother's sudden increased confusion in the past week.

### **History**

The physician first addresses the patient, who says she is doing well and denies any problems. When asked about the recent history of confusion, she is unable to provide details. The patient's behavior is in contrast to past visits with her physician, during which she has always been chipper and eager to give her history and to share recent gossip.

The physician then turns to the son for further information. The son notes that his mother has not called him in more than 1 week, whereas she used to call him daily. Three days before presentation he went to visit his mother at her home and found her to be unusually quiet as well as confused about where she was. After talking to her for a while, he noticed that she was slightly drowsy. In addition, he found that the house was uncharacteristically dirty and there was a slight odor of urine in his mother's bedroom.

The patient's medical history is notable for hypertension and diabetes of many years' duration, which have been controlled with medication. For the past 3 to 4 years, the patient has also suffered from insomnia and anxiety, which have been difficult to treat. In addition, she has reported chronic headaches and back pain, the causes for which have not been revealed by work-ups. These symptoms have been troubling in the past, and at times the patient has taken significant quantities of nonprescription analgesics (nonsteroidal anti-inflammatory drugs [NSAIDs], aspirin, acetaminophen) to control the pain. Current medications include hydrochlorothiazide (20 mg/day), glyburide (5 mg/day), alprazolam (1 mg at bedtime), and diazepam (5 mg at bedtime). She has taken the latter two medicines for years. When the physician asks for the exact doses, the patient is unable to state them.

The patient smokes one pack of cigarettes per day, a habit she has had for years. In the past she has also revealed to her physician that she drinks 2 to 3 glasses of wine per day. However, she has no history of alcohol dependence.

The patient is a retired school teacher who has been widowed for 3 years and currently lives alone in her house. She has two children; her son lives in the same neighborhood as she, and her daughter lives out of town. Prior to the past week, the patient was fully independent in her housekeeping and activities of daily living, and she had been leading a moderately active social life. Her son notes that approximately 1 year before her current presentation she had trouble doing her taxes and soon after he took over management of her finances.

The son reports a possible family history of memory loss in the patient's mother who died at age 84 years in a nursing home. There is no other known family psychiatric or neurologic history.

### **Physical Examination**

Physical examination reveals an elderly woman with slightly soiled clothes and a blank expression on her face. Her speech is slightly slurred. She is mildly overweight at 185 lb, with a height of 5'6". Vital signs are normal. Head, eyes, ears, nose, throat, neck, heart, lung, abdomen, and extremities are normal. Stool guaiac is negative.

### **Neurologic Examination**

Neurologic examination is notable for a mild, bilateral, resting tremor. Gait is normal. Cranial nerves are grossly intact. Strength and tone are normal. Coordination is normal to finger-nose-finger testing. Reflexes are symmetrical, and Babinski's sign is absent bilaterally.

### **Mental Status Examination**

Mental status examination reveals a minimally blunted affect with distractibility during the examination, as if the patient were not paying attention to the questions. She is very quiet, with minimally reactive affect. However, the patient does not feel sad and denies self-deprecatory thoughts; she also has a normal energy level and feels that her body is strong and healthy. She has no delusions or hallucinations, although she notes that at night her eyes "play tricks" on her and she sees faces on the bedroom curtain. She is poorly oriented to time and place. The patient's score on the Mini-Mental State Examination (MMSE) is 16 points (of a possible 30 points): she loses 4 points on orientation, 3 points on recall, 5 points on attention/calculation, and 2 points on the three-step command.

### **QUESTION**

- **What conditions are associated with a presentation of altered mental state in an elderly patient?**

**Table 1.** Comparative Features of Delirium, Dementia, and Major Depression

Feature	Delirium	Dementia	Major Depression
Definition	Impaired sensorium (reduced level of consciousness)	Global decline in cognitive capacity in clear consciousness	Disturbance in mood, with associated low vital sense and low self-attitude
Core symptoms	Inattention, distractibility, drowsiness, befuddlement	Amnesia, aphasia, agnosia, apraxia, disturbed executive functioning	Sadness, anhedonia, crying
Common associated symptoms	Cognitive impairment, hallucinations, mood lability	Depression, delusions, hallucinations, irritability	Fatigue, insomnia, anorexia, guilt, self-blame, hopelessness, helplessness
Temporal features	Acute or subacute onset	Chronic onset, usually gradual	Episodic, subacute onset
Diurnal features	Usually worse in the evening and night	No clear pattern	Usually worse in the morning

## DISCUSSION

### Conditions Associated with Altered Mental State

The patient in this case study presents with a mental status change that is occurring against a background of a possible family history of dementia as well as a personal history of several chronic health conditions, use of multiple medications, nicotine dependence, and possible overuse of alcohol. The patient's history also includes evidence of recent urinary incontinence. The clinician's first task is to classify the patient's presenting mental state. The most likely possibilities are delirium, dementia, and depression, the major features of which are shown in **Table 1**.

The predominant features of this patient's presentation are subacute onset and moderate cognitive impairment, with prominent deficits in attention, orientation, and engageability. The latter three features indicate that the patient has an impairment in sensorium (level of consciousness). Impaired sensorium is best determined by history, clinical observation, and direct examination of the mental state. Historical information might reveal occasional drowsiness, fluctuations in alertness, distractibility, or periods of agitation during which the patient is "mixed-up." Clinical observation during the course of history-taking or physical examination might reveal inattention, trouble following questions, blunted reactivity, fearfulness, losing track of thoughts, drowsiness, or confusion. Quantification of cognitive status, such as with the MMSE (**Figure 1**), might reveal global cognitive deficits accounted for by inattention, trouble with directions, disorientation, and memory loss.<sup>25</sup>

The MMSE in this patient revealed a total score of 16 points—in the moderately impaired range. Her impairment in sensorium is not dramatic, as she is not impressively drowsy or hard to arouse. However, there clearly is impairment, as reflected in the history, clinical observation, and examination. Thus, based on the

features listed in **Table 1**, it is best to classify her mental status change as a delirium.

The diagnosis of dementia (ie, a global decline in cognitive capacity occurring in clear consciousness) requires the presence of a normal sensorium. Therefore, the patient's impairment in sensorium at this point prohibits ascribing her mental state entirely to dementia. Also, dementia is usually much more insidious and chronic in its presentation and accompanied by more chronic functional impairments. Of note, among elderly patients, delirium often is superimposed on dementia; therefore, after the patient's delirium resolves, her physician must reconsider whether or not she has dementia.

The differential diagnosis also includes major depression, as many elderly persons with severe depression present in a manner similar to the patient in this case study. However, although this patient has affective blunting, she does not feel sad or depressed, she has no clear decrease in vital sense (eg, fatigue, anorexia, insomnia), and she does not have a decrease in self-attitude (eg, guilt, hopelessness, helplessness, feeling a burden). Major depression is often subacute in onset; however, major depression usually takes longer than 1 week to lead to a similar degree of functional impairment. In addition, the absence of a family or personal history of depressive illness makes major depression less likely in this patient.

## QUESTION

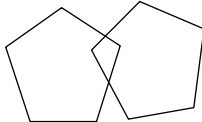
- **How is delirium distinguished clinically from other conditions that alter mental state?**

## DISCUSSION

### Clinical Features of Delirium

Delirium is a mental syndrome defined entirely by clinical presentation. The syndrome includes a core clinical component and several associated (supportive) clinical features.

**MINI-MENTAL STATE EXAMINATION**

		Patient's Score	Maximum Score
<b>Orientation</b> (Give one point for each correct answer.)			
Time:	Ask the patient to identify the current:		
	Year	_____	1
	Season	_____	1
	Date	_____	1
	Day	_____	1
	Month	_____	1
Place:	Ask the patient to identify the:		
	State he/she is in	_____	1
	Country he/she is in	_____	1
	Town or city he/she is in	_____	1
	Nature or purpose of building he/she is in	_____	1
	Floor of building he/she is in	_____	1
<b>Registration</b>			
	Name three objects, taking one second to say each. Then, ask the patient to repeat all three objects. Give one point for each correct answer. Then repeat the objects until the patient learns all three. Count trials and record.		
	Trials _____	_____	3
<b>Attention and calculation</b>			
Serial sevens:	Ask the patient to count backward from 100 by sevens (93, 86, 79, 72, 65). Stop after five answers. Give one point for each correct answer.		
Alternative:	Ask the patient to spell "world" backward.	_____	5
<b>Recall</b> (Give one point for each correct answer.)			
	Ask the patient to name the three objects repeated above.	_____	3
<b>Language</b> (Give one point for each correct response.)			
Naming:	Point to a pencil and to a watch. Ask the patient to name each as you point.	_____	2
Repetition:	Ask the patient to repeat, "No ifs, ands, or buts."	_____	1
Three-stage command:	Ask the patient to follow a three-stage command, such as, "Take this paper in your right hand. Fold the paper in half. Put the paper on the floor."	_____	3
Reading:	On a blank piece of paper print the sentence, "Close your eyes," in letters large enough to see clearly. Ask the patient to read and obey the command.	_____	1
Writing:	Ask the patient to write a sentence of his or her choice. The sentence should contain a subject, a verb, and an object and should make sense. Ignore spelling errors.	_____	1
Copying:	Ask the patient to copy the design shown. Give one point if all sides and angles are preserved and if the intersecting sides form a quadrangle.		
		_____	1
<b>Total</b>		_____	30

**Figure 1.** The Mini-Mental State Examination (MMSE) is a useful tool for the clinical examination of patients who present with cognitive impairment. The MMSE is simple and easy to administer in the primary care setting and, because it is objectively scored, can be used to document progression of a patient's illness over time. Of a possible 30 points, a total score of 20–24 points generally indicates mild impairment, 18–19 points indicates moderate impairment, and 15 points or less indicates a severe deficit. Adapted with permission from Folstein MF, Folstein SE, McHugh PR: Mini-mental state. A practical method for grading the cognitive state of patients for the clinician. *J Psychiatr Res* 1975;12:189.

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**Core symptoms.** At the core of delirium is impairment in sensorium (level of consciousness). Clinically, an impaired sensorium manifests in different ways. In severe cases, patients are drowsy, somnolent, in twilight states, or even comatose. However, most cases of impaired sensorium are milder.<sup>26</sup> In mild cases, patients may be difficult to engage mentally. In ordinary conversation, patients may have trouble paying attention, be easily distracted, or give confused responses. Other patients may feel groggy or act as if they are not thinking properly, and patients may be disoriented and unable to maintain a task for more than 10 to 15 seconds.

**Common associated symptoms.** In general, any mental symptom and several abnormal behaviors can occur in the context of delirium. The most common symptoms are noted in **Table 2**. Prominent symptoms include disorientation, memory disturbance, mood lability, fearfulness, anxiety, sadness, hallucinations (especially visual), and persecutory delusions. Delirious patients might exhibit physical aggression, pacing, and repetitive calling out. Patients often have impairments in sleep or appetite. In some cases, inappropriate hypersexuality may be exhibited.

**Diurnal features.** Time is an important variable in understanding delirium. The impairment in sensorium fluctuates diurnally and is usually worse late in the day or during the night. Thus, it is possible for patients with delirium to have long periods of time during which their level of consciousness is fully intact and when other associated symptoms are absent. Delirium is often missed by clinicians who rely exclusively on a patient's self-reported history and a brief cross-sectional examination to ascertain the presence or absence of the syndrome.

**Temporal features.** Time course is another important feature of the clinical presentation of delirium. In most cases, delirium is acute in onset and evolves over days. However, some patients with delirium experience a subacute onset of days to weeks, as illustrated in this case study. In addition, although delirium is generally reversible, it can be chronic. An extreme example of chronic delirium is coma. Also, patients with certain dementias (eg, senile dementia of the Lewy body type, vascular dementia) appear to be in a chronic state of delirium.

#### Clinical Subclassification

Several studies have attempted to classify delirium based on clinical presentation (phenomenology). Two subtypes have been proposed.<sup>26-28</sup> In the first subtype, patients are usually hypoactive, drowsy, or withdrawn (19%). In the second subtype, patients are hyperactive, aroused, agitated, and pacing (15%). The majority of

**Table 2.** Symptoms of Delirium

#### Core symptoms

Impaired level of consciousness  
 Impaired engageability  
 Distractibility  
 Inattention  
 Drowsiness  
 Twilight state  
 Coma

#### Common associated symptoms

Cognitive impairment  
 Poor memory  
 Disorientation  
 Aphasia/language disorder  
 Mood symptoms  
 Sadness  
 Lability  
 Anxiety  
 Apathy  
 Psychotic symptoms  
 Hallucinations, especially visual  
 Delusions, especially persecutory  
 Behavior  
 Physical or verbal aggression  
 Pacing  
 Calling out  
 Drives  
 Sleep impairment  
 Anorexia  
 Hypersexuality

patients with delirium (52%) alternate between hypoactive and hyperactive states; the remainder of patients (14%) cannot be classified using either of these categories.<sup>29</sup>

#### QUESTION

- **How is the diagnosis of delirium made?**

#### DISCUSSION

##### Diagnostic Criteria for Delirium

Because delirium is a clinical syndrome, consensus criteria have been developed for delirium diagnosis. Currently, the most widely used criteria are those of the American Psychiatric Association (Washington, DC),

**Table 3.** DSM-IV Diagnostic Criteria for Delirium Caused by a General Medical Condition

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- A. A disturbance of consciousness (ie, reduced clarity of awareness of the environment) with reduced ability to focus, sustain, or shift attention
  - B. A change in cognition (such as memory deficit, disorientation, language disturbance) or the development of a perceptual disturbance that is not better accounted for by a preexisting, established, or evolving dementia
  - C. The disturbance develops over a short period of time (usually hours to days) and tends to fluctuate during the course of the day
  - D. Evidence from the history, physical examination, or laboratory findings that the disturbance is caused by the direct physiological consequences of a general medical condition
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Adapted with permission from American Psychiatric Association: Delirium, dementia, and amnesic and other cognitive disorders. In *Diagnostic and Statistical Manual of Mental Disorders*, 4th ed. Washington, DC: American Psychiatric Association; 1994:129.

which are published in the *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV)*.<sup>30</sup> The DSM-IV criteria for diagnosis of delirium vary depending on the clinical presentation and the cause of delirium. **Table 3** lists the DSM-IV criteria for the diagnosis of delirium caused by a general medical condition. Similar criteria are provided in the DSM-IV for delirium that is substance induced, related to substance withdrawal, or caused by multiple etiologies. The DSM-IV criteria are useful clinical tools for determining the presence or absence of delirium. However, although widely accepted and highly useful, these criteria are also arbitrary; thus, some patients with delirium do not meet the DSM-IV diagnostic criteria.

#### Scales to Assist with the Diagnosis of Delirium

Several scales have been developed to assist in diagnosing or quantifying the severity of delirium. The confusion assessment method (CAM)<sup>31</sup> was designed to assist nonpsychiatric physicians in the diagnosis of delirium in the general hospital. CAM uses a checklist (**Table 4**) and a diagnostic algorithm (**Table 5**) to decide whether a patient is delirious. CAM is easy to use and requires minimal training. The 10-item delirium rating scale (DRS)<sup>32</sup> was developed for use by physicians in quantifying the severity of delirium. The DRS is particularly useful for predicting prognosis, because patients who score above 18 points (of a possible 32 points) typically require more than 1 week to recover. Scores of 12 points or more on the DRS are strongly predictive of a diagnosis of delirium by psychiatric examination. Both the CAM and the DRS are confounded in diagnosing or quantifying the severity of delirium in a patient with concurrent dementia.

#### QUESTION

- **Is delirium a major problem in the primary care community?**

#### DISCUSSION

##### Epidemiology

There have been few population studies of delirium. The only community-based study to date reported that the overall prevalence of delirium in the general population is 0.4% and that the prevalence in persons older than age 54 years is 1.1%.<sup>33</sup> Studies from general hospitals suggest that 10% to 30% of patients are delirious on admission and that 4% to 53% of patients develop delirium during their admission.<sup>26-28</sup> There are no published studies of the prevalence of delirium in primary care office practice or in the nursing home. In an informal study of 36 randomly selected residents of a nursing home for patients with dementia, the prevalence of delirium in the past week was 2.8% (one out of 36 patients).

##### Underrecognition of Delirium

Delirium is underrecognized in all clinical settings: the general hospital, the emergency room, the primary care setting, and the nursing home.<sup>26</sup> Generalists most often miss the hypoactive forms of delirium. Generalists are more likely to identify the hyperactive forms as being a clinical problem, although they may not make a precise diagnosis of delirium.<sup>29</sup> It is estimated that primary care physicians detect only 25% to 40% of all cases of delirium.<sup>26,28</sup>

##### Consequences of Delirium

The consequences of delirium can be substantial. Studies have shown that, compared with hospitalized patients without delirium, hospitalized patients with delirium have increased functional decline after discharge from the hospital, persistent or progressive cognitive impairment 6 months later, loss of independent community living, and increased mortality, even after adjustment for other critical variables.<sup>26,28</sup> Among patients admitted to the hospital with delirium, 27%

**Table 4.** The Confusion Assessment Method (CAM) Instrument

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**Acute onset**

1. Is there evidence of an acute change in mental status from the patient's baseline?

**Inattention\***

2. A. Did the patient have difficulty focusing attention? For example, was the patient easily distracted or did he or she have difficulty keeping track of what was being said?
- Not present at any time during interview
  - Present at some time during interview, in mild form
  - Present at some time during interview, in marked form
  - Uncertain
- B. (If present or abnormal) Did this behavior fluctuate during the interview, that is, tend to come and go or increase and decrease in severity?
- Yes
  - No
  - Uncertain
  - Not applicable
- C. (If present or abnormal) Please describe this behavior:

**Disorganized thinking**

3. Was the patient's thinking disorganized or incoherent? For example, did the patient demonstrate rambling or irrelevant conversation, unclear or illogical flow of ideas, or unpredictable switching from subject to subject?

**Altered level of consciousness**

4. Overall, how would you rate this patient's level of consciousness?
- Alert (normal)
  - Vigilant (hyperalert, overly sensitive to environmental stimuli, startled very easily)
  - Lethargic (drowsy, easily aroused)
  - Stupor (difficult to arouse)
  - Coma (unarousable)
  - Uncertain

**Disorientation**

5. Was the patient disoriented at any time during the interview? For example, did the patient think that he or she was somewhere other than the hospital, using the wrong bed, or misjudging the time of day?

**Memory impairment**

6. Did the patient demonstrate any memory problems during the interview, such as inability to remember events in the hospital or difficulty remembering instructions?

**Perceptual disturbances**

7. Did the patient have any evidence of perceptual disturbances, for example, hallucinations, illusions, or misinterpretations (such as thinking something was moving when it was not)?

**Psychomotor agitation**

8. Part 1
- At any time during the interview, did the patient have an unusually increased level of motor activity, such as restlessness, picking at bedclothes, tapping fingers, or making frequent sudden changes of position?

**Psychomotor retardation**

8. Part 2
- At any time during the interview, did the patient have an unusually decreased level of motor activity, such as sluggishness, staring into space, staying in one position for a long time, or moving very slowly?

**Altered sleep-wake cycle**

9. Did the patient have evidence of disturbance of the sleep-wake cycle, such as excessive daytime sleepiness and insomnia at night?
- 

\*The questions listed under this topic were repeated for each topic where applicable.

Adapted with permission from Inouye SK, van Dyck CH, Alessi CA, et al: Clarifying confusion: the confusion assessment method. A new method for detection of delirium. *Ann Intern Med* 1990;113:946.

**Table 5.** The Confusion Assessment Method (CAM) Diagnostic Algorithm

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NOTE: The diagnosis of delirium by CAM requires the presence of features 1 and 2 and either 3 or 4.

**Feature 1: Acute onset and fluctuating course**

This feature is usually obtained from a family member or nurse and is shown by positive responses to the following questions: Is there evidence of an acute change in mental status from the patient's baseline? Did the (abnormal) behavior fluctuate during the day, that is, tend to come and go or increase and decrease in severity?

**Feature 2: Inattention**

This feature is shown by a positive response to the following question: Did the patient have difficulty focusing attention? For example, was the patient easily distracted or did he or she have difficulty keeping track of what was being said?

**Feature 3: Disorganized thinking**

This feature is shown by a positive response to the following question: Was the patient's thinking disorganized or incoherent? For example, did the patient demonstrate rambling or irrelevant conversation, unclear or illogical flow of ideas, or unpredictable switching from subject to subject?

**Feature 4: Altered level of consciousness**

This feature is shown by any answer other than "alert" to the following question: Overall, how would you rate this patient's level of consciousness?

Alert (normal)

Lethargic (drowsy, easily aroused)

Coma (unarousable)

Vigilant (hyperalert)

Stupor (difficult to arouse)

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Adapted with permission from Inouye SK, van Dyck CH, Alessi CA, et al: Clarifying confusion: the confusion assessment method. A new method for detection of delirium. *Ann Intern Med* 1990;113:947.

die in the first 6 months after admission and 39% die in the first year. Additionally, delirium has been shown to increase length of stay in the general hospital and to increase in-hospital mortality.<sup>26</sup> The consequences of delirium occurring in the primary care setting are not known but are likely to be significant, given the available data on underrecognition of the syndrome and the generally poorer outcomes for patients who are hospitalized with delirium than for patients who are hospitalized without delirium.

**DIAGNOSIS AND INITIAL MANAGEMENT**

The physician concludes that the patient is suffering from delirium. He discusses this diagnosis with the patient and her son. He explains that delirium has many causes and he will need to order tests to determine the cause. Because of the patient's recent confusion, the physician recommends that she not stay at home alone because she may fall, have trouble with daily living activities, misuse her medicines, or be unable to respond to an emergency. He states that 24-hour supervision is needed for the next few days until the patient's delirium improves or resolves. He mentions the possibility of hospitalization to provide a safe environment while the patient undergoes testing, but the son offers to have his mother stay at his house

for a few days instead. He and his family can provide the necessary supervision.

The physician orders a set of tests and makes a referral to a home health agency. He requests a daily home visit from a nurse to monitor the patient (vital signs, MMSE, neurologic evaluation, oral intake, medication use) and to educate the patient and her family about the potential risks of overusing NSAIDs and other nonprescription drugs. The physician arranges for daily telephone contact with the home health agency nurse and schedules a follow-up visit with the patient for 1 week later.

**QUESTIONS**

- **What are the major causes of delirium?**
- **Which of these causes are possible factors in this patient?**

**DISCUSSION**

**Common Causes of Delirium**

Many medications, metabolic derangements, and medical disorders can cause delirium (**Table 6**). In the majority of patients the cause of delirium is multifactorial, and this patient would seem to be no exception. Several possible causes of delirium must be considered in this case.

**Table 6.** The Most Common Causes of Delirium

Medications	Infections	Primary cerebral diseases	Toxins
Antidepressants	Urinary tract infection	Subdural hematoma	Alcohol
Antipsychotics	Upper respiratory tract infection	Trauma	Illicit drugs
Lithium	Pneumonia	Subarachnoid hemorrhage	Occupational exposures
Anticonvulsants	Cellulitis	Stroke	<b>Substance withdrawal</b>
Disulfiram	Sepsis	Vasculitis	Alcohol
Sedative/hypnotics	<b>Metabolic derangements</b>	Status epilepticus	Sedative/hypnotics
H <sub>2</sub> -receptor antagonists	Disorders related to surgery and other procedures	Alzheimer's disease	Opioids
Cytotoxic agents	Fever	Lewy body disease	
Antiemetics	Anemia	<b>Cardiovascular diseases</b>	
Opioid analgesics	Dehydration	Congestive heart failure	
Anticholinergics	Fluid/electrolyte disorder	Myocardial infarction	
Corticosteroids	Hepatic failure	Cardiac arrhythmia	
Diuretics	Hyper- or hypoglycemia	Hypertensive crisis	
Antiarrhythmics	Hyper- or hypothyroidism	Hypotension	
Antihypertensives	Hypoxia/hypercapnia	<b>Pulmonary diseases</b>	
Anti-infectives		Pulmonary embolism	
Salicylates		Chronic obstructive pulmonary disease	
Nonsteroidal anti-inflammatory drugs			

**Dementia.** If the patient in this case study suffered from a dementia (eg, Alzheimer's disease or senile dementia of the Lewy body type) she would be at an increased risk for developing delirium. However, her history provides little evidence for a dementia. Prior to the present illness she did not demonstrate any cognitive decline, and the only evidence of a chronic functional decline is that earlier in the year she turned over management of her finances to her son.

**Medications and metabolic factors.** This patient's delirium might be explained entirely by the combined effects of metabolic stressors acting on a 74-year-old brain. For example, the patient's plasma glucose level could be somewhat elevated (eg, between 200 to 300 mg/dL) and she could have been over-medicating with analgesics and benzodiazepines for recurring headache and insomnia. The combination of these two factors could have contributed to a sufficient perturbation of brain activity to cause delirium.

**Medical conditions.** New medical conditions must also be considered as possible causes of this patient's delirium. The history includes evidence of recent urinary incontinence, which raises the possibility of a urinary tract infection. Dehydration must also be ruled out because the patient has been living alone and her

oral intake has been unmonitored. No record of recent bowel movements is available, but moderate to severe constipation without pain or abdominal tenderness could be the cause of the patient's delirium. In addition, the patient could have severe anemia caused by occult gastrointestinal bleeding related to her chronic use of aspirin and NSAIDs. Previously undiagnosed hypothyroidism might also account for the patient's delirium.

#### QUESTION

- **What tests should be ordered to evaluate for possible causes of delirium in this patient?**

#### DISCUSSION

##### Laboratory Tests

The selection of laboratory studies should be hypothesis-driven to investigate for suspected contributing causes of delirium in a given patient. In this patient, an electrolyte panel and blood chemistries (glucose, calcium, magnesium, creatinine, blood urea nitrogen [BUN], liver enzymes) should be obtained to rule out an electrolyte imbalance, hyperglycemia, renal insufficiency, dehydration, malnutrition, or hepatic failure as the cause of the delirium. A complete blood count

(CBC) should also be obtained to rule out severe anemia or an infection (elevated leukocyte count). A urinalysis and possibly a urine culture with sensitivity should also be performed. In general, a urinalysis should be obtained in any older woman with delirium given the high likelihood of a urinary tract infection (UTI) as a contributing cause. If not done in the recent past, a thyroid panel should also be ordered.

Given this patient's history of excessive nonprescription medication use, a urine toxicology screen should be considered to look for medicines not known to be taken. A serum salicylate level might also be considered for the same reason.

### Imaging Studies

Given that this patient developed an acute mental status change while living alone, computed tomography of the head without contrast may be ordered to rule out an occult subdural hematoma (especially if the patient had a recent fall) or other acute central nervous system disease. If the initial history and physical examination had revealed evidence of cough, fever, shortness of breath, or chest pain, a chest radiograph and an electrocardiogram would be warranted.

### Electroencephalography

If the delirium is subtle or the diagnosis is uncertain, an electroencephalogram (EEG) may be useful to confirm the diagnosis of delirium and follow the disease course. Patients with delirium develop generalized background slowing in the EEG. Either absolute slowing (ie, reduction of the background rhythm below 6 Hz) or relative slowing (ie, reduction in the person's specific background rhythm by 3 to 4 Hz) may be evident. Because most patients assessed with delirium do not have prior EEG records, their specific background rhythm might not be known. In addition, as many as 20% of patients with delirium have normal EEGs<sup>26</sup> and many patients with dementia, particularly those in advanced stages, have slowed EEGs in the absence of delirium. Therefore, because of inadequate specificity and sensitivity, the EEG is no more than an ancillary test for delirium.

### QUESTION

- **What is known about the pathophysiology of delirium?**

### DISCUSSION

#### Pathophysiology of Delirium

Delirium is most likely to occur in individuals with limited brain reserve, such as patients who are brain damaged (because of Alzheimer's disease, stroke, multiple

sclerosis, traumatic brain injury, HIV/AIDS, or other neurologic conditions) and patients with mental retardation. Delirium is also likely to occur if a patient's brain is subjected to a series of concurrent metabolic demands, any one of which occurring alone might not cause delirium. Risk factors for delirium include advanced age; dementia or cognitive impairment; brain injury of any type; multiple, severe, or unstable general medical conditions; polypharmacy; social isolation; visual impairment; metabolic disturbance; bone fracture; fever or hyperthermia; low serum albumin; and psychoactive drug use.<sup>26-28</sup>

Symptoms of delirium develop when demands on the brain are greater than the brain's reserve. An analogy may be drawn to congestive heart failure, in which demands on the heart that exceed the heart's reserve lead to pump failure, with resultant symptoms (eg, shortness of breath, edema). Once the threshold for heart failure is crossed, built-in physiologic changes lead to rapid worsening of the heart failure followed by pulmonary edema and, ultimately, death. The same is true for delirium. If demands on the brain exceed the brain's reserve, level of consciousness becomes impaired and a series of associated symptoms can result.

The specific pathophysiologic defect of delirium is unknown. Recent studies and functional brain imaging have suggested that particular brain areas are involved in the pathogenesis of delirium.<sup>26,34</sup> These brain areas include the prefrontal cortex, the right cerebral hemisphere, the right thalamus, and the right caudate nucleus. How injury or malfunction in these regions of the brain and their associated circuits leads to the clinical syndrome of delirium is not understood. In the past, a cholinergic hypothesis was proposed, according to which delirium is caused by a reduction in brain cholinergic neurotransmission.<sup>26</sup> However, delirium may involve disruption of several neurotransmitter systems, including imbalances of cholinergic, dopaminergic, serotonergic, and GABAergic ( $\gamma$ -aminobutyric acid-transmitting) systems.<sup>26,34</sup> Other neurotransmitter systems that might be involved are the noradrenergic, glutaminergic, opiate, and histaminergic systems.

### LABORATORY TEST RESULTS AND DIRECTED THERAPY

The following tests are performed the same day and sent to the laboratory for evaluation: urinalysis, CBC, serum electrolyte levels, serum metabolic panel, thyroid panel, serum salicylate level, and urine toxicology screen. The patient goes home with her son as planned. The next day, the physician reviews the patient's test results. Results on the metabolic panel are as follows: glucose, 231 mg/dL; leukocyte count, 11,000/mm<sup>3</sup>, with a left shift; BUN, 64 mg/dL; creatinine, 2.8 mg/dL;

and hemoglobin, 12.8 g/dL; all other findings are normal. The urinalysis reveals leukocytes that are "too numerous to count" and moderate bacteriuria. The serum salicylate level, urine toxicology screen, and thyroid panel are normal.

The physician concludes that a UTI is the cause of the patient's delirium, exacerbated by dehydration and hyperglycemia. The physician calls the home health nurse and orders that 1 L of normal saline be given intravenously and that fluids be pushed orally (8 oz every 2 to 3 hours). He also orders a urine culture and sensitivity, while starting the patient on a sulfonamide antibiotic empirically for a UTI. The nurse informs the physician that the patient had trouble sleeping at night and has been having visual hallucinations. The physician orders haloperidol (0.5 mg at bedtime) and asks the nurse to review the drug's side effects with the patient and her son.

Two days later, the urine culture is positive for *Escherichia coli*, which is sensitive to sulfonamide antibiotics. The BUN level has dropped to 32 mg/dL, the creatinine level is 2.1 mg/dL, and the glucose level is 175 mg/dL. The nurse informs the physician that the patient is no longer experiencing hallucinations and is sleeping well.

#### QUESTION

- **Should there be any change in the treatment now that the patient shows improvement?**

#### DISCUSSION

After delirium has been diagnosed and a treatment plan has been developed, it is important to maintain therapy consistently until the delirium is relieved. Monitoring for resolution of the delirium might include clinical response, the use of a rating scale (for which the DRS is best suited), or EEG. In general, most delirium-associated symptoms resolve within days. However, some symptoms may persist for weeks or months, especially in elderly patients with coexisting dementia.

#### FOLLOW-UP VISIT TO THE PHYSICIAN

At the follow-up visit a few days later, the patient's mental state is back to baseline and her MMSE is 28 (of a possible 30 points). The patient is chipper and talkative and wants to tell the physician about her grandson who just finished kindergarten.

#### QUESTION

- **Now that this patient's delirium episode seems to have resolved, is further management needed?**

#### DISCUSSION

##### Appropriate Follow-Up for a Delirium Episode

The patient in this case study appears to have recovered well from the delirium. The haloperidol should be discontinued and the patient reassessed (ie, repeat vital signs and mental status examination) in the physician's office 1 week later. At this point, the physician should consider why this patient developed delirium and what can be done to prevent a recurrence. Is it possible that she suffers from a very early dementia? Although a score of 28 points on the MMSE is within the normal range, it is possible that for this patient this score represents a decline. To help search for evidence of memory, cognitive, and functional decline in this patient, the physician should obtain a more detailed history from the son and daughter as well as friends and, possibly, neighbors. Also, the MMSE should be repeated in 6 months and annually thereafter to watch for further decline.

In addition, the physician should educate the patient about UTI prevention and the appropriate use of non-prescription medications to prevent a possible recurrence of delirium. The patient should be tapered off the benzodiazepines and prescription analgesics and should be referred to a psychiatrist for the evaluation and management of recurrent insomnia and headaches.

#### QUESTIONS

- **What treatment approach should be taken to avoid major consequences of delirium?**
- **Is prevention of delirium possible?**

#### DISCUSSION

##### Specific Treatments

Specific treatments for delirium must be distinguished from supportive or nonspecific therapies. Specific treatments are directed at the fundamental etiology of the delirium. Given that most cases of delirium are multifactorial, effective treatment requires aggressive therapy for all underlying causes. In many instances, this means discontinuing all but essential medicines with close monitoring of the patient. Hospitalization should be considered to assure adequate 24-hour support and supervision.

##### Supportive Treatments

Given that the resolution of delirium symptoms can sometimes take several weeks, it is important to provide all elements of supportive care in a sustained, consistent fashion.

**Nursing support.** Delirious patients require aggressive nursing support for nutrition, hydration, elimination,

and fever reduction.<sup>26,28,35</sup> For example, patients should receive oral or intravenous hydration as clinically indicated. Temperatures above 38°C should be treated with antipyretics. Oral intake, vital signs, and food intake should be monitored daily. Caloric intake should be appropriate to the patient's body mass index and supported with nutritional supplements if necessary. Urinary and fecal output should be monitored closely; a good-sized bowel movement at least every other day should be pursued, with laxatives if necessary.

**Environmental manipulations.** Environmental manipulations are recommended to support patients through the mental status changes. Patients should be provided with strong cues as to day and night. During the day, lights should be kept on and an active environment should be created; during the night, lights should be dimmed and the room should be quiet and subdued, perhaps with soothing music. Activity should be provided and designed to simulate a day's schedule, with stimulation neither too limited nor too excessive. Patients should be encouraged to perform activities of daily living as much as possible and to engage in other simple activities that they can tolerate (eg, watching TV, listening to music, talking to friends on the telephone).

Patients should also have frequent encounters with other people and, if possible, not be left alone. Someone should always be visible or within earshot of the patient. When it is necessary for the caretaker or chaperon to leave the patient, the person should say where he or she is going and check back with the patient often.

Frequent reorientation should also be provided. The patient's room should have a current calendar and clock with the correct time situated in a visible place. In addition, people who interact with the patient should seek opportunities to remind the patient of where he or she is and of the correct date and time of day as part of casual conversation.

**Patient and family education.** Patients should receive education and reassurance. They should be told that they suffer from delirium, a condition in which the brain is overwhelmed and does not function well. Patients should be reminded that almost any emotion or mental symptom can occur during delirium, including fear, anxiety, and sadness, and that all these symptoms should go away with time and resolution of the delirium. Patients who experience distressing symptoms, such as delusions and hallucinations, should be reassured that their mind might be "playing tricks" on them and that this symptom will resolve. If

patients are fixated on their delusions or hallucinations and are fearful, every attempt should be made to distract them and focus their mind on an activity.

Spouses, family members, and visitors should also be educated about delirium. It is important to help these individuals understand the biologic basis of delirium, how it is diagnosed, and how it is treated. Most of the patients family and friends need help understanding how not to misinterpret what the patient is saying in the midst of the delirium episode. For example, spouses might see their loved one hallucinate and fear that the person is "losing their mind"; or, they might hear the patient express fearful paranoia and become scared themselves. Instead, spouses and family members should be taught to recognize unusual behavior as symptoms of the delirium and to help distract the patient from the symptoms. Family members and friends should be reminded of the transient nature of most cases of delirium and of the possibility of using psychotropic drugs to address some of the most distressing symptoms.

**Pharmacotherapy.** In rare instances, pharmacotherapy is indicated for the control of distressing symptoms, including delusions, hallucinations, overactive or aggressive behavior that is distressing or harmful to the patient or threatening to others, and severe anxiety or fearfulness. Pharmacotherapy is also indicated for sedating the patient when procedures are necessary. Most psychoactive medicines have some anticholinergic properties that may worsen or prolong the course of delirium. Low doses should be used initially for specific target symptoms, slowly titrating to the minimal dose necessary for the desired effect.

The preferred medications—by consensus and supported by clinical trials<sup>26-28,36</sup>—are high-potency antipsychotic agents such as haloperidol, fluphenazine, and thiothixene. Advantages of these agents include their relatively low anticholinergic activity and their availability in a liquid form for oral administration. Some antipsychotic agents are also available for intramuscular or intravenous administration. Haloperidol, starting at 0.25 mg/day and titrating up several times a day, is the preferred first-line agent, by any route possible. Parenteral administration is usually twice as potent as oral administration. Alternative medications include the newer antipsychotic agents such as risperidone (0.25 to 3 mg/day) and olanzapine (2.5 to 10 mg/day). For patients who are undergoing procedures, droperidol is a good alternative, given the drug's short duration of action and its parenteral availability. Doses of 0.5 to 2 mg per procedure might be necessary for acute sedation.

Benzodiazepines are best avoided as treatment for delirium for several reasons: these agents might lead to paradoxical disinhibition, might worsen cognitive impairment, and are less effective than clinical trials suggest.<sup>35</sup> One exception is if the delirium is caused by withdrawal from alcohol or a sedative/hypnotic drug (delirium tremens), intermediate-acting benzodiazepine lorazepam is the preferred treatment because it can be administered intramuscularly.

### Prevention

Several studies have investigated the possibility of preventing delirium in hospitalized patients.<sup>37</sup> Most of these studies involved patients undergoing surgery or elderly medical patients admitted to the hospital for a range of reasons. In some of the studies, preventive interventions (eg, education about surgery or delirium, supportive care during periods of highest risk) reduced the risk of delirium by as much as 81%. However, this risk reduction was smaller among elderly medical patients than among surgical patients, and, in some studies, patients who received preventive interventions actually had a worse outcome than patients who received standard care.

### CONCLUSION

Delirium is a common, serious, life-threatening medical condition that especially afflicts those who are elderly, suffer from coarse brain disease, or are taking multiple medications. Delirium can occur in any clinical setting and is most prevalent in the hospital and nursing home. In some cases, prevention of delirium may be possible. The management of delirium requires a high index of suspicion to diagnose it early, careful evaluation to identify and treat all contributing causes, and comprehensive supportive care. **HP**

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