

Delirium in the hospital: Emphasis on the management of geriatric patients

Prevention, early diagnosis, comprehensive treatment are the cornerstone of care

Although delirium has many descriptive terms (*Table 1, page 36*), a common unifying term is “acute global cognitive dysfunction,” now recognized as delirium; a consensus supported by DSM-5¹ and ICD-10² (*Table 2, page 37*). According to DSM-5, the essential feature is a disturbance of attention or awareness that is accompanied by a change in baseline cognition that cannot be explained by another preexisting, established, or evolving neurocognitive disorder (the newly named DSM-5 entity for dementia syndromes).¹ Because delirium affects the cortex diffusely, psychiatric symptoms can include cognitive, mood, anxiety, or psychotic symptoms. Because many systemic illnesses can induce delirium, the differential diagnosis spans all organ systems.

Three subtypes

Delirium can be classified, based on symptoms,^{3,4} into 3 subtypes: hyperactive-hyperalert, hypoactive-hypoalert, and mixed delirium. Hyperactive patients present with restlessness and agitation. Hypoactive patients are lethargic, confused, slow to respond to questions, and often appear depressed. The differential prognostic significance of these subtypes has been examined in the literature, with conflicting results. Rabinowitz⁵ reported that hypoactive delirium has the worst prognosis, while Marcantonio et al⁶ indicated that the hyperactive subtype is associated with the highest mortality rate. Mixed delirium, with periods of both hyperactivity and hypoactivity, is the most common type of delirium.⁷

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Delirium

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Terminal delirium often is unrecognized and can interfere with assessment of other clinical issues

Table 1

Terms for delirium

Acute confusional state
Acute brain failure
Agitation
Altered mental status
Confusion
Encephalopathy
ICU psychosis
Mental status changes
Sundowning
Terminal restlessness (eg, in palliative care)

A prodromal phase, characterized by anxiety, frequent requests for nursing and medical assistance, decreased attention, restlessness, vivid dreams, disorientation immediately after awakening, and hallucinations, can occur before an episode of full-spectrum delirium; this prodromal state often is identified retrospectively—after the patient is in an episode of delirium.^{8,9}

Evidence-based guidelines aim to improve recognition and clinical management.¹⁰⁻¹³ Disruptive behavior is the main reason for psychiatric referral in delirium.^{14,15} Delayed psychiatric consultation because of non-recognition of delirium is related to variables such as older age; history of a pre-existing, comorbid neurocognitive disorder; and the clinical appearance of hypoactive delirium.¹⁴

The case of Mr. D (*Box, page 38*),¹⁶ illustrates how the emergence of antipsychotic-associated neuroleptic malignant syndrome (NMS) can complicate antipsychotic treatment of delirium in a geriatric medical patient, although delirium also is a common presentation in NMS.¹⁷ Delirium developed after an increase in carbidopa/levodopa, which has central dopaminergic effects that can precipitate delirium, particularly in a geriatric patient with preexisting comorbid neurocognitive disorder. Further complicating Mr. D's delirium presentation was the development of NMS, which had a multifactorial causation, such as the use of dopamine antagonists (ie, quetiapine, metoclopramide), and an abrupt decrease of a dopaminergic agent (ie, carbidopa/levodopa), all inducing a central dopamine relative hypoactivity.

Epidemiology

Delirium is more common in older patients,¹⁵ and is seen in 30% to 40% of hospitalized geriatric patients.¹⁸ Delirium in older patients, compared with other adults, is associated with more severe cognitive impairment.¹⁹ It is common among geriatric surgical patients (15% to 62%)²⁰ with a peak 2 to 5 days postoperatively for hip fracture,²¹ and often is seen in ICU patients (70% to 87%).²⁰ However, Spronk et al²² found that delirium is significantly under-recognized in the ICU. Nearly 90% of terminally ill patients become delirious before death.²³ Terminal delirium often is unrecognized and can interfere with assessment of other clinical problems.²⁴ A preexisting history of comorbid neurocognitive disorder was evident in as many as two-thirds of delirium cases.²⁵

Pathophysiology and risk factors

The pathophysiology of delirium has been characterized as an imbalance of CNS metabolism, including decreased blood flow in various regions of the brain that may normalize once delirium resolves.²⁶ Studies describe the simultaneous decrease of cholinergic transmission and dopaminergic excess.^{27,28} Predisposing and precipitating factors for delirium that are of particular importance in geriatric patients include:

- advanced age
- CNS disease
- infection
- cognitive impairment
- male sex
- poor nutrition
- dehydration and other metabolic abnormalities
- cardiovascular events
- substance use
- medication
- sensory deprivation (eg, impaired vision or hearing)
- sleep deprivation
- low level of physical activity.^{27,29,30}

Table 3 (page 39) lists the most common delirium-provocative medications.²⁷

Evaluation and psychometric scales

The EEG can be useful in evaluating delirium, especially in clinically ambiguous



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Table 2

DSM-5 and ICD-10 criteria for delirium

DSM-5 criteria	ICD-10 criteria
A. Disturbance in attention (ie, reduced ability to direct, focus, sustain, and shift attention) and awareness (reduced orientation to the environment)	A. Impairment of consciousness and attention (reduced ability to focus, sustain, and shift attention)
B. Disturbance develops over a short period of time (usually hours to a few days), represents a change from baseline attention and awareness, and tends to fluctuate in severity during the course of a day	B. Global disturbance of cognition (perceptual disturbance, impaired abstract thinking and comprehension, impaired immediate recall and recent memory, disorientation)
C. An additional change disturbance in cognition (eg, memory deficit, disorientation, language, visuospatial ability, or perception)	C. Psychomotor disturbances (hypoactivity or hyperactivity, increased reaction time, increased or decreased flow of speech, enhanced startle reaction)
D. Disturbances in Criteria A and C are not better explained by another preexisting, established, or evolving neurocognitive disorder and do not occur in the context of a severely reduced level of arousal, such as coma	D. Disturbance of the sleep-wake cycle (insomnia, reversal of the sleep-wake cycle, nocturnal worsening of symptoms, disturbing dreams or nightmares)
E. Disturbance is a direct physiological consequence of another medical condition, substance intoxication or withdrawal, or exposure to a toxin, or is due to multiple etiologies	E. Emotional disturbances, (eg depression, anxiety or fear, irritability, euphoria, apathy, or wondering perplexity)

Source: References 1,2

cases. EEG findings may indicate generalized slowing or dropout of the posterior dominant rhythm, and generalized slow theta and delta waves, findings that are more common in delirium than in other neurocognitive disorders and other psychiatric illnesses. The EEG must be interpreted in the context of the delirium diagnostic workup, because abnormalities seen in other neurocognitive disorders can overlap with those of delirium.³¹

The EEG referral should specify the clinical suspicion of delirium to help interpret the results. Delirium cases in which the patient's previous cognitive status is unknown may benefit from EEG evaluation, such as:

- in possible status epilepticus
- when delirium improvement has reached a plateau at a lower level of cognitive function than before onset of delirium
- when the patient is unable or unwilling to complete a psychiatric interview.²⁷

Assessment instruments are available to diagnose and monitor delirium (*Table 4, page 40*). Typically, delirium assessment includes examining levels of arousal, psychomotor activity, cognition (ie, orientation, attention, and memory), and perceptual disturbances.

Psychometrically, a review of *Table 4 (page 40)* suggests that validity appeared stable with adequate specificity (64% to 99%) but more variable sensitivity (36% to 100%). These reliability parameters also will be affected by the classification system (ie, DSM vs ICD) and the cut-off score employed.³² Most measures (eg, Confusion Assessment Method [CAM], CAM-ICU) provide an adequate sample of behavioral (ie, level of alertness), motor (ie, psychomotor activity), and cognitive (ie, orientation, attention, memory, and receptive language) function, with the exception of the Global Attentiveness Rating, which is a 2-minute open conversation protocol between physician and patient.

Some measures are stand-alone instruments, such as the Memorial Delirium Assessment Scale, whereas the CAM requires administration of separate cognitive screens, including the Mini-Mental State Examination (MMSE) and Digit Span.³³ Instruments to detect delirium in critically ill patients are a more recent development. Wong et al³⁴ reported that the most widely studied tool was the CAM. Obtaining collateral information from family, caregivers, and

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Delirium assessment includes examining levels of arousal, psychomotor activity, cognition, and perceptual disturbances



Delirium

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Considering the medication profile for patients with complex systemic illness may be crucial in preventing delirium

Box

Case: Delirium after medication change

Mr. D, age 78, has Parkinson's disease and associated mild neurocognitive disorder. His family brings him to the hospital for acute onset of confusion, persecutory delusions, visual hallucinations, agitation, and aggressive behavior after his carbidopa/levodopa dosage is increased. His psychiatric and family history are unremarkable. Medications include metoclopramide, 30 mg/d, for its antiemetic effect.

Shortly after admission, Mr. D's carbidopa/levodopa dose of 1.5 tablets of 25/100 mg 3 times a day is abruptly decreased to the previous dosage of one-half tablet of 25/100 mg 3 times a day and he is started on quetiapine, 50 mg/d, to address the psychiatric symptoms. Agitation improves after titrating quetiapine to 100 mg/d, although his medical condition deteriorates, with ongoing confusion.

One week later, lethargy, diaphoresis, and hyperthermia of 39°C are noted. Mr. D exhibits fluctuating vital signs and severe muscle rigidity in all extremities.

Lab values reveal an elevated level of

serum creatine kinase, leukocytosis, and a normal troponin value. EEG shows generalized slow waves without a seizure focus. CT of head, cerebrospinal fluid studies, and chest radiograph are unremarkable.

The Confusion Assessment Method¹⁶ algorithm is performed once a day. An initial diagnosis of hyperactive delirium, progressing to hypoactive, neuroleptic malignant syndrome-associated delirium is made.

Quetiapine and metoclopramide are discontinued, carbidopa/levodopa is optimized, hydration is maintained, and serial monitoring of the complete blood count, renal function, and creatine kinase levels are performed, with gradual normalization of the creatine kinase level. Judicious, as-needed use of lorazepam controls occasional agitation.

Hospital staff watch Mr. D for unsafe behaviors; clear instructions, adequate lighting, and minimal noise level were implemented. Delirium symptoms resolve by week 2 and he is transferred to a rehabilitation unit to address physical deconditioning.

hospital staff is essential, particularly given the fluctuating nature of delirium.

Management

Prevention. Identify patients at high risk of delirium so that preventive strategies can be employed. Multi-component, nonpharmacotherapeutic interventions are used in clinical settings but few randomized trials have been conducted. The contributing effectiveness of individual components is not well-studied, but most include staff education to increase awareness of delirium. Of 3 multi-component intervention randomized trials, 2 reported a significantly lower incidence of delirium in the intervention group.³⁵⁻³⁷ Implementation of a multi-component protocol in medical/surgical units was associated with a significant reduction in use of restraints.³⁸

As in Mr. D's case, complex drug regimens, particularly for CNS illness, can increase the risk of delirium. Considering the medication profile for patients with complex systemic illness—in particular, minimizing the use of anticholinergics and dopamine agonists—may be crucial in preventing delirium.

Prophylactic administration of anti-psychotics may reduce the risk of developing postoperative delirium.³⁹ Studies of the use of these agents were characterized by small sample sizes and selected groups of patient populations. Of the 4 randomized studies evaluating prophylactic anti-psychotics (vs placebo), 3 found a lower incidence of delirium in the intervention groups.³⁹⁻⁴¹

A study of haloperidol in post-GI surgery patients showed a reduced occurrence of delirium,⁴⁰ whereas its prophylactic use in patients undergoing hip surgery⁴² did not reduce the incidence of delirium compared with placebo, but did decrease severity when delirium occurred.⁴²

Risperidone³⁹ in post-cardiac surgery and olanzapine⁴¹ perioperatively in patients undergoing total knee or hip replacement have been shown to decrease delirium severity and duration. Targeted prophylaxis with risperidone⁴³ in post-cardiac surgery patients who showed disturbed cognition but did not meet criteria for delirium reduced the number of patients requiring medication, compared with placebo.⁴³

Dexmedetomidine, an α -2 adrenergic receptor agonist, compared with propofol or midazolam in post-cardiac valve surgery patients, resulted in a decreased incidence of delirium but no difference in delirium duration, hospital length of stay, or use of other medications.⁴⁴ However, other studies have shown that dexmedetomidine reduces ICU length of stay and duration of mechanical ventilation.⁴⁵

Treatment. Management of hospitalized medically ill geriatric patients with delirium is challenging and requires a comprehensive approach. The first step in delirium management is prompt identification and management of systemic medical disturbances associated with the delirium episode. First-line, nonpharmacotherapeutic strategies for patients with delirium include:

- reorientation
- behavioral interventions (eg, use of clear instructions and frequent eye contact with patients)
- environmental interventions (eg, minimal noise, adequate lighting, and limited room and staff changes)
- avoidance of physical restraints.⁴⁶

Consider employing family members or hospital staff sitters to stay with the patient and to reassure, reorient, and watch for agitation and other unsafe behaviors (eg, attempted elopement). Psychoeducation for the patient and family on the phenomenology of delirium can be helpful.

The use of drug treatment strategies should be integrated into a comprehensive approach that includes the routine use of nondrug measures.⁴⁶ Using medications for treating hypoactive delirium, formerly controversial, now has wider acceptance.^{47,48} A few high-quality randomized trials have been performed.^{25,49,50}

Pharmacotherapy, especially in frail patients, should be initiated at the lowest starting dosage and titrated cautiously to clinical effect and for the shortest period of time necessary. Antipsychotics are preferred agents for treating all subtypes of delirium; haloperidol is widely used.^{46,51,52} However, antipsychotics, including haloperidol, can be associated with adverse neurologic effects such as extrapyramidal symptoms (EPS) and NMS.

Table 3

Deliriogenic or psychotoxic medications

α -adrenergic and β -adrenergic blockers
Antiarrhythmics
Anticonvulsants
Antidepressants (eg, tricyclic antidepressants)
Corticosteroids
Digoxin
GABAergics (including benzodiazepines)
Immunomodulators
Lithium
Nonsteroidal anti-inflammatory drugs
Sedatives

Source: Adapted from Reference 27

Although reported less frequently than with haloperidol, other agents have been implicated in development of EPS and NMS, including atypical antipsychotics and antiemetic dopamine antagonists, particularly in parkinsonism-prone patients.⁵³ Strategies that can minimize such risks in geriatric inpatients with delirium include oral, rather than parenteral, use of antipsychotics—preferential use of atypical over typical antipsychotics—and lowest effective dosages.⁵⁴

In controlled trials, atypical antipsychotics for delirium showed efficacy compared with haloperidol.^{52,55} However, there is no research that demonstrates any advantage of one atypical over another.²⁵

In Mr. D's case, the most important intervention for managing delirium caused by NMS is to discontinue all dopamine antagonists and treat agitation with judicious doses of a benzodiazepine, with supportive care.¹⁷ In cases of sudden discontinuation or a dosage decrease of dopamine agonists, these medications should be resumed or optimized to minimize the risk of NMS-associated rhabdomyolysis and subsequent renal failure.¹⁷ Antipsychotics carry an increased risk of stroke and mortality in older patients with established or evolving neurocognitive disorders^{56,57} and can cause prolongation of the QTc interval.⁵⁷

Other medications that could be used for delirium include cholinesterase inhibitors^{58,59} (although larger trials and a systematic

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Atypical antipsychotics showed efficacy compared with haloperidol; no research demonstrates any advantage of one atypical over another



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Benzodiazepines are first-line treatment for delirium associated with seizures or withdrawal from alcohol and other substances

Table 4

Common measures of delirium

Tests	Number of items	Sensitivity	Specificity	Alternate version
Clinical Assessment of Confusion-A ^a	25	36%	95%	No
Confusion Assessment Method ^b	9	86%	93%	No
Confusion Assessment Method-Intensive Care Unit ^c	4*	92% to 100%	88% to 100%	No
Confusion Assessment Protocol ^d	7	71%	64%	No
Cognitive Test for Delirium ^e	15	100%	95%	Yes
Delirium Assessment Scale ^f	8	80%	90%	No
Delirium Index ^g	7	95%	95%	No
Delirium Observation Screening Scale ^h	13	92%	82%	No
Delirium Rating Scale – Revised ⁱ	13 + 3	92%	93%	No
Delirium Symptom Interview ^j	109	90%	80%	No
Global Attentiveness Rating ^k	1	94%	99%	No
Nursing Delirium Screening Scale ^l	5	95%	98%	No
Memorial Delirium Assessment Scale ^m	10	92%	92%	No

* Four features used in the assessment; 1-acute or fluctuating course of mental status, 2-inattention, 3-altered level of consciousness, 4-disorganized thinking

Source: See this article at CurrentPsychiatry.com for references

review did not support this use⁶⁰), and 5-HT receptor antagonists,⁶¹ such as trazodone. Benzodiazepines, such as lorazepam, are first-line treatment for delirium associated with seizures or withdrawal from alcohol, sedatives, hypnotics, and anxiolytics and for delirium caused by NMS. Be cautious about using benzodiazepines in geriatric patients because of a risk of respiratory depression, falls, sedation, and amnesia.

Geriatric patients with alcoholism and those with malnutrition are prone to thiamine and vitamin B₁₂ deficiencies, which can induce delirium. Laboratory assessment and consideration of supplementation is recommended. Despite high occurrence of delirium in hospitalized older adults with preexisting comorbid neurocognitive disorders, there is no standard care for delirium comorbid with another neurocognitive disorder.⁶² Clinical practice guidelines for older patients receiving palliative care have been developed⁶³; the goal is to minimize suffering and discomfort in patients in palliative care.⁶⁴

Post-delirium prophylaxis. Medications for delirium usually can be tapered and discontinued once the episode has resolved and the patient is stable; it is common to discontinue medications when the patient

has been symptom-free for 1 week.⁶⁵ Some patients (eg, with end-stage liver disease, disseminated cancer) are prone to recurrent or to prolonged or chronic delirium. A period of post-recovery treatment with antipsychotics—even indefinite treatment in some cases—should be considered.

Post-delirium debriefing and aftercare.

The psychological complications of delirium are distressing for the patient and his (her) caregivers. Psychiatric complications associated with delirium, including acute stress disorder—which might predict posttraumatic stress disorder—have been explored; early recognition and treatment may improve long-term outcomes.⁶⁶ After recovery from acute delirium, cognitive assessment (eg, MMSE⁶⁷ or Montreal Cognitive Assessment⁶⁸) is recommended to validate current cognitive status because patients may have persistent decrement in cognitive function compared with pre-delirium condition, even after recovery from the acute episode.

Post-delirium debriefing may help patients who have recovered from a delirium episode. Patients may fear that their brief period of hallucinations might represent the onset of a chronic-relapsing psychotic disorder. Allow patients to communicate their

distress about the delirium episode and give them the opportunity to talk through the experience. Brief them on the possibility that delirium will recur and advise them to seek emergency medical care in case of recurrence. Advise patients to monitor and maintain a normal sleep-wake cycle.

Family members can watch for syndromal recurrence of delirium. They should be encouraged to discuss their reaction to having seen their relative in a delirious state.

Health care systems with integrated electronic medical records should list “delirium, resolved” on the patient’s illness profile or problem list and alert the patient’s primary care provider to the delirium history to avoid future exposure to delirium-provocative medications, and to prompt the provider to assume an active role in post-delirium care, including delirium recurrence surveillance, medication adjustment, risk factor management, and post-recovery cognitive assessment.

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continued

Bottom Line

Evaluation of delirium in geriatric patients includes clinical vigilance and screening, differentiating delirium from other neurocognitive disorders, and identifying and treating underlying causes. Perioperative use of antipsychotics may reduce the incidence of delirium, although hospital length of stay generally has not been reduced with prophylaxis. Management interventions include staff education, systematic screening, use of multicomponent interventions, and pharmacologic interventions.

Clinical Point

Allow patients to communicate their distress about the delirium episode and to talk through the experience



Delirium

Clinical Point

Health care systems should list 'delirium resolved' on a patient's illness profile and alert the patient's primary care provider

Related Resources

- Downing LJ, Caprio TV, Lyness JM. Geriatric psychiatry review: differential diagnosis and treatment of the 3 D's - delirium, dementia, and depression. *Curr Psychiatry Rep*. 2013;15(6):365.
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Drug Brand Names

Carbidopa/levodopa • Sinemet	Metoclopramide • Reglan
Dexmedetomidine • Precedex	Midazolam • Versed
Haloperidol • Haldol	Olanzapine • Zyprexa
Lithium • Eskalith, Lithobid	Propofol • Diprivan
Lorazepam • Ativan	Quetiapine • Seroquel
	Risperidone • Risperdal
	Trazodone • Desyrel

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