

DELIRIUM

AGS Geriatrics Evaluation and Management Tools (Geriatrics E&M Tools) support clinicians and systems that are caring for older adults with common geriatric conditions.

From the AMERICAN GERIATRICS SOCIETY

Geriatrics Evaluation & Management Tools

BACKGROUND

- Delirium- clinical phenomenon described in DSM5, Acute encephalopathy neurobiological process. Other synonyms like acute confusional state, altered mental status (among many), should not be used
- Predictor for future cognitive and functional decline as well as shortened lifespan
- Found in 1/3 of hospitalized medical patients older than age 70
- Found in 15% of patients older than age 70 presenting to emergency departments
- Under-recognized: less than 50% of all cases recognized in routine care
- Failure to diagnose/manage delirium leads to costly, life-threatening complications; loss of function and independence; and increased risk of death.

DIFFERENTIAL DIAGNOSIS

- **NOTE: The concept of "differential diagnosis of delirium/dementia/depression/cognitive decline" can be misleading—conditions may coexist and are risk factors for one another.**
- To distinguish between delirium, dementia, and depression, the clinician must ascertain the patient's baseline status and the timeframe of cognitive changes. Information from family members and caregivers can be essential.

HISTORY OF PRESENT ILLNESS (Diagnosis of Delirium)

- DSM-5 criteria for delirium highlight that it is an acute and fluctuating syndrome of impaired attention and awareness.
- Patients at risk for delirium should be screened at least daily.
- Time course of the changes in mental status and their association with other symptoms or events (eg, fever, shortness of breath, medication change) should be documented.
- Systematic reviews recommend the Confusion Assessment Method (CAM) as the most useful bedside assessment tool for delirium.
- 3D-CAM is a brief diagnostic tool that is highly sensitive and specific for diagnosing delirium in hospitalized patients.
 - UB-CAM is an adaptive version of the 3D-CAM that can be completed in slightly over one minute on average.
- The CAM-ICU is an adaptation for intubated patients only that does not require verbal responses.
- The CAM-S is a validated delirium severity measure that does not diagnose delirium but can be used in conjunction with a CAM diagnostic tool to quantify the intensity of delirium symptoms.

Confusion Assessment Method (CAM): Diagnosis requires #1 and #2 and either #3 or #4.

1. Acute change in mental status and fluctuating course:

- Is there evidence of an acute change in cognition from the patient's baseline?
- Does the abnormal behavior fluctuate during the day (tend to come and go, or increase or decrease in severity)?

2. Inattention: Does the patient have difficulty focusing attention? Can use one of the following tests for attention:

- Digit span up to 5 forward, 4 backward
- Days of the week backward, months of the year backwards
- "World" backward
- Continuous performance task such as "Vigilance A"

3. Disorganized thinking: Is the patient's thinking disorganized or incoherent (rambling or irrelevant conversation, unclear or illogical flow of ideas, unpredictable switching from subject to subject)?

4. Altered level of consciousness: Is the patient's mental status anything other than alert (vigilant, lethargic, stuporous, comatose)?

Confusion Assessment Method. Copyright 2003, Hospital Elder Life Program, LLC. Not to be reproduced without permission. No responsibility is assumed by the AGS or the Hospital Elder Life Program, LLC for any injury and/or damage to persons or property arising out of the application of any of the content at help. agscocare.org.

Inouye SK, vanDyck CH, Alessi CA, et al. Clarifying confusion: the confusion assessment method. A new method for detection of delirium. *Ann Intern Med.* 1990;113(12):941-948.

Marcantonio ER, Ngo LH, O'Connor M, et al. 3D-CAM: derivation and validation of a 3-minute diagnostic interview for CAM-defined delirium: a cross-sectional diagnostic test study [published correction appears in *Ann Intern Med.* 2014 Nov 18;161(10):764]. *Ann Intern Med.* 2014;161(8):554-561. doi:10.7326/M14-0865

EVALUATION OF DELIRIUM

- As the number or severity of predisposing factors for delirium increase, a decreased number or reduced severity of precipitating factors are required to initiate delirium.
- Predisposing factors:** advanced age, dementia, prior delirium, dependency in activities of daily living (ADLs), medical comorbidities, history of alcohol abuse, male gender, diminished vision and/or hearing

Precipitating Factors (Mnemonic for Some Causes of Delirium)	
Drugs	<ul style="list-style-type: none"> Any new additions, increased dosages, or interactions Consider over-the-counter drugs and alcohol Consider especially high-risk drugs (see "Medications," next page)
Electrolyte disturbances	<ul style="list-style-type: none"> Especially dehydration, sodium imbalance Thyroid abnormalities
Lack of drugs	<ul style="list-style-type: none"> Withdrawal from chronically used sedatives, including alcohol and sleeping pills Uncontrolled pain
Infection	<ul style="list-style-type: none"> Especially respiratory, skin, and urinary tract infections
Reduced sensory input or mobility	<ul style="list-style-type: none"> Poor vision, poor hearing Use of restraints, bedbound status
Intracranial	<ul style="list-style-type: none"> Rare: consider only if new focal neurologic findings or suggestive history, or diagnostic evaluation is otherwise negative Infection, hemorrhage, tumor, stroke
Urinary, fecal	<ul style="list-style-type: none"> Urinary retention ("cystocerebral syndrome") Urinary catheterization Fecal impaction
Myocardial, pulmonary	<ul style="list-style-type: none"> Myocardial infarction, arrhythmia, exacerbations of congestive heart failure or COPD, hypoxia
Surgery	<ul style="list-style-type: none"> Incidence of delirium: <ul style="list-style-type: none"> 15-25% after elective noncardiac surgery Up to 50% after cardiac bypass, abdominal aortic aneurysm or hip fracture repair

PHYSICAL EXAMINATION

- Vital signs, including oxygen saturation
- Thorough physical examination with focus on neurologic and mental status examination; both hyperactive and hypoactive subtypes are described.

MEDICATIONS

Alcohol, anticholinergics (oxybutynin, benztropine), anticonvulsants (primidone, phenobarbital, phenytoin), antidepressants (amitriptyline, imipramine, doxepin), antihistamines (diphenhydramine), anti-inflammatory agents (prednisone), antiparkinsonian agents (levodopa-carbidopa, dopamine agonists, amantadine), antipsychotics, barbiturates, benzodiazepines (triazolam, alprazolam, diazepam, flurazepam, chlordiazepoxide), H₂-antagonists (cimetidine, ranitidine), opioid analgesics (especially meperidine)

DIAGNOSTIC TESTS (BASED ON HISTORY AND PHYSICAL)

- Complete blood count
- Thyroid function test
- Serum drug levels
- Chest radiograph
- Cerebral imaging rarely helpful, except with head trauma or new focal neurologic findings.
- EEG and CSF analysis rarely helpful, except with associated seizure activity or signs of meningitis.
- Complete metabolic panel
- Urinalysis
- Arterial blood gases
- ECG
- Serum calcium
- Blood cultures
- Ammonia
- Blood alcohol levels

PREVENTION/MANAGEMENT STRATEGIES

- Strategies to prevent and manage delirium are often the same, but prevention of delirium leads to better patient outcomes than management once delirium has occurred.
- Two 2019 systematic reviews found no evidence that antipsychotics were helpful in either the prevention or treatment of delirium. Use of these agents should be limited to the indications listed below.
- Multifactorial approach to management is most successful because multiple factors contribute to delirium; thus, multiple interventions, even if individually small, can yield marked clinical improvement:

Step	Key Issues	Proposed Treatment
1. Identify and treat reversible contributors	<ul style="list-style-type: none"> Medications Infections Fluid balance disorders Impaired CNS oxygenation Severe pain Sensory deprivation Elimination problems 	<ul style="list-style-type: none"> Reduce or eliminate offending medications, or substitute less psychoactive medications. Treat common infections: urinary, respiratory, soft tissue. Assess and treat dehydration, heart failure, electrolyte disorders. Treat severe anemia (transfusion), hypoxia, hypotension. Assess and treat; use local measures and scheduled pain regimens that minimize opioids; avoid meperidine. Use eyeglasses, hearing aid, portable amplifier; clear cerumen. Assess and treat urinary retention and fecal impaction. Prevent constipation.
2. Maintain behavioral control	<ul style="list-style-type: none"> Behavioral interventions Pharmacologic interventions 	<ul style="list-style-type: none"> Teach hospital staff appropriate interaction with delirious patients; encourage family visitations. Teach de-escalation strategies to reduce agitation. See Pharmacologic Therapy of Agitated Delirium.
3. Anticipate and prevent or manage complications	<ul style="list-style-type: none"> Urinary incontinence Immobility and falls Pressure ulcers Sleep disturbance Feeding disorders 	<ul style="list-style-type: none"> Implement scheduled toileting program. Avoid physical restraints; mobilize with assistance; use physical therapy. Mobilize; reposition immobilized patient frequently and monitor pressure points. Implement a nonpharmacologic sleep protocol; avoid sedatives. Assist with feeding; use aspiration precautions; provide nutritional supplementation as necessary.
4. Restore function in delirious patients	<ul style="list-style-type: none"> Hospital environment Cognitive reconditioning Ability to perform ADLs Family education/support/participation Discharge 	<ul style="list-style-type: none"> Reduce clutter and noise (especially at night); provide adequate lighting; have familiar objects brought from home. Have staff reorient patient to time, place, person at least three times daily. As delirium clears, match performance to ability. Provide education about delirium, its causes and reversibility, how to interact, and family's role in restoring function. Because delirium can persist, provide for increased ADL support; follow mental status changes as "barometer" of recovery.

PHARMA- COLOGIC THERAPY OF AGITATED DELIRIUM

- Evidence suggests a very limited role for pharmacologic intervention in delirium, used specifically only for symptoms that are a threat to safety or disrupt needed medical care and that cannot be adequately managed with nonpharmacologic interventions; low-dose, high-potency antipsychotics are usually the treatment of choice.
 - The lowest dose of the least toxic pharmacologic agent should be used for the shortest possible time and discontinued when target symptoms are no longer present.
 - Indications for pharmacologic interventions should be clearly identified and documented, and need for ongoing use should be reassessed daily with in-person examination of patients.
- Cholinesterase inhibitors should not be newly prescribed to prevent or treat delirium.

Agent	Class	Dosage	Benefits	Adverse Events	Comments
First-line					
Risperidone ^{OL}	Second-generation antipsychotic	0.25–0.5 mg po or ODT, or solution q4h prn Max dose ^a : 2 mg/24h	Relatively nonsedating	Slightly fewer EPS than haloperidol; less cardiac toxicity	Small trials ^b Black box warnings ^c
Olanzapine ^{OL}	Second-generation antipsychotic	2.5–5 mg po, ODT, or IM q12h (cannot be given IV) Max dose ^a : 20 mg/24h	Fewer EPS than risperidone	More sedating than risperidone	Small trials ^b ; oral formulations less effective for acute management Black box warnings ^c
Quetiapine ^{OL}	Second-generation antipsychotic	12.5–25 po q12h Max dose ^a : 50 mg/24h	Fewer EPS than risperidone; can be used in patients with parkinsonism	More sedating than risperidone; hypotension	Small trials ^b Often used as a sedative-hypnotic Black box warnings ^c
Ziprasidone ^{OL}	Second-generation antipsychotic	5–10 mg IM, 20 mg capsule po Max dose ^a : 20 mg/24h	Fewer EPS than haloperidol; moderate sedation	Risk of cardiac arrhythmia, heart failure, agranulocytosis	Large 2018 trial in ICU ^d Because of risks, used primarily in ICU Black box warnings ^c
Second-line (higher risk of adverse effects)					
Haloperidol ^{OL}	First-generation antipsychotic	0.25–0.5 mg po, IM, or IV q4h prn; Max dose ^a : 3 mg/24h	Relatively nonsedating	EPS, especially if >3 mg/d	Large 2018 trial in ICU ^d Black box warnings ^c
Lorazepam ^{OL}	Benzodiazepine	0.25–0.5 mg po or IV q8h prn for agitation	Use in sedative and alcohol withdrawal; history of neuroleptic malignant syndrome	More paradoxical excitation and respiratory depression than haloperidol	Generally should not be used except for specific listed "benefits"

NOTE: ODT = oral disintegrating tablet, EPS = extrapyramidal symptoms

Based on meta-analyses, use of these drugs should be limited to severe delusions and hallucinations or disruptive behavior that is a danger to the patient or others and after nonpharmacologic strategies have been tried and been unsuccessful.

^a Maximum dose per 24 hours is the recommended total cumulative dose threshold to minimize risk of adverse events in frail older adults. Younger patients may be able to tolerate somewhat higher doses.

^b Second-generation antipsychotics have been tested primarily in small equivalency trials with haloperidol and in placebo-controlled trials in the ICU.

^c The FDA requires a "black box" warning for all second-generation antipsychotics because of the increased risk of stroke and mortality in patients with dementia. First-generation antipsychotic agents also have a black box warning regarding an increase in all-cause mortality among patients with dementia.

^d In a 2018 randomized trial comparing haloperidol, ziprasidone, and placebo in 566 ICU patients, there was no difference between arms in the primary outcome, median number of days alive without delirium or coma in the 2 weeks after randomization, or in secondary outcomes (30-day and 90-day survival, time to freedom from mechanical ventilation, and time to ICU and hospital discharge).

FOLLOW-UP

- Symptoms of delirium may persist for weeks to months in a substantial portion of affected individuals.
- Patients admitted to SNFs with delirium are at high risk for being misdiagnosed with dementia; delirium should be clearly documented in the hospital discharge paperwork.
- A history of delirium is a risk factor for dementia: education and follow-up are important.