

## Delirium

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Delirium, or acute confusional state, represents a serious and often unrecognized neuropsychiatric disturbance of cognition and attention that is common in the elderly and chronically ill patients. Delirium is a constellation of symptoms caused by an underlying **medical condition** and often **polypharmacy**. Postoperatively, delirium is a common complication in older people, occurring after 15-25% of elective procedures and 25-65% of emergency procedures such as hip fracture repair.<sup>1</sup> Failure to recognize delirium can have grave consequences. It should be considered a medical emergency warranting prompt diagnosis and treatment.<sup>5</sup> Mortality rates among hospitalized patients with delirium range from 2 to 20 times higher than those without delirium and may be sustained for 6 – 24 months following hospital discharge.<sup>2</sup> Overall, delirium is associated with increased morbidity, longer hospitalizations and increased rates of nursing home placement. The tremendous personal and financial impact of delirium cannot be ignored. Each year, delirium complicates hospital stays for more than 2.3 million older individuals (17.5 million inpatient days) and an estimated cost of \$8 billion annually.<sup>3,4</sup> The key to management of delirium is **prevention!** Early detection followed by aggressive treatment and management of the underlying cause and the associated neuropsychiatric symptoms result in a reduction in morbidity and mortality.

### Pathophysiology

Although the pathophysiology is not completely understood *functional disorders* of the brain rather than structural abnormalities are characteristic of delirium. Evidence suggests the involvement of multiple neurotransmitters and both cortical and subcortical areas of the brain.<sup>5</sup> Cholinergic function is critical to normal cognition. Delirium is associated with cholinergic inhibition through use of medications with a high anticholinergic effect (Table1) as well as cerebral hypoxia and hypoglycemia (which interfere with acetylcholine synthesis leading to a hypocholinergic state).<sup>4</sup> Other neurotransmitters implicated in delirium include dopamine, serotonin, noradrenergic, opiate agonists and histaminergic systems and Gamma-aminobutyric acid (GABA is decreased in benzodiazepine withdraw or administration of certain antibiotics such as, penicillin, beta-lactam analogues and fluoroquinolones).<sup>4</sup> Cytokines associated with delirium include alpha-interferon and interleukin- 1

and 2 levels which are elevated in the brain during stress, inflammation, trauma, and tumor growth.

### **Risk Factors for Delirium**

Those more likely to experience delirium include older people with multiple medical conditions, on numerous medications and a high level of physical disability.

**Table 1: Risk Factors for Delirium**

Advanced age	Polypharmacy (anticholinergic drugs – see table 2, opioids, sedative hypnotics, withdrawal)
Electrolyte abnormalities (dehydration, sodium, glucose)	Gastrointestinal (constipation, ulcer)
Genitourinary (urinary infection, urinary retention)	Hypoalbuminemia (cytokines suppress albumin synthesis in liver)
Infections (urine, pulmonary, wound)	Trauma ( fall, fracture, pain)
Cardiopulmonary (MI, hypotension, hypoxia)	CNS (CVA,dementia, substance abuse)
Vitamin deficiency (thiamin due to alcohol or malnutrition)	Immobility (during hospitalization due to foley, IV restraints and not getting out of bed)

### **Approach to the patient with Delirium**

The diagnosis of delirium should be considered in any person, regardless of age, who exhibits an acute or subacute change in cognition, level of arousal, and behaviors that fluctuate over the course of the day. Once recognized, the foundation of the diagnosis of delirium involves knowledge of the patient’s baseline mental and functional status along with a complete history and physical, including medication review.

History: Understanding a patient’s baseline cognition and functional status is crucial to be able to interpret the significance of their present change in status. When a patient is unable to provide this needed information, one should seek out those who are well acquainted with the patient; including close family members, caregivers (friends, nursing staff) and the patient’s continuing care providers (physicians and nurse practitioners).<sup>7</sup> Various tools to assess cognition are available such as the Mini Mental

Status exam (MMSE) and the Confusion Assessment Method.<sup>2,5</sup> The CAM requires the patient demonstrate an acute change in mental status with a fluctuating course, inattention, and either disorganized thinking or an altered level of consciousness.<sup>2,5</sup> Specifically assess alcohol history. Review all medications as they represent a common reversible cause of delirium accounting for 22-39% of all cases.<sup>4</sup> Those containing anticholinergic properties are the biggest culprits.

**Table 2**  
**Anticholinergic Effects of Common Drugs**

Atropine	1.00 (most anticholenergic)
Cimetidine	0.86
Prednisone	0.55
Benadryl	~0.50
Elavil	~0.50
Theophylline	0.44
Digoxin	0.25
Ranitidine	0.22
Lasix	0.22
Isordil dinitrate	0.15
Warfarin	0.12
Codeine	0.11

Adapted from Tune, et al.<sup>4</sup>

Benzodiazepines, because of loss of oxidative pathway functions in the elderly, and therefore decrease rate of clearance, can have side effects, which last long beyond their original use. The list is exhaustive and the more medications a patient is on, the more possible the interactions, and therefore the greater the likelihood that one or more may be contributing to delirium.<sup>6,7</sup>

**Physical Exam:** The physical exam should be complete, including a neurologic exam, skin assessment and check for urinary retention or fecal impaction. Special attention should be paid to seek out potential sources of infection (urine, lung, intra-abdominal, skin, blood and sinuses), which may present without fever or focal signs and symptoms. Review vital signs, including pulse oximetry to look for abnormalities and changes from baseline values. Looking for sources of pain (musculoskeletal system) may point to evidence of underlying fracture, although uncontrolled pain from a chronic diagnosis can also contribute to delirium.

#### Initial Work –Up:

Simple bedside testing can often confirm a suspected cause of delirium and can be particularly helpful when no obvious cause is identified from either history or physical exam. Workup should, however, be targeted to clues obtained during history and physical.

- Vital sign, pulse ox, finger stick glucose
- Labs: BMP, Calcium, CBC, and urine
- CXR and EKG
- Additional evaluation guided by patient needs. (i.e.: TSH, drug levels, toxicology screens, liver function tests, lumbar puncture, blood cultures, EEG, CT/MRI)

One can usually uncover most causes of delirium and avoid subjecting a patient to multiple, costly test which in turn, (by virtue of the need to take the patient out of a familiar surrounding and provide sedation) may further contribute to delirium. Clinical suspicion based on history and physical should be the examiner's guide when ordering studies.<sup>7</sup>

#### **Management**

##### Identify and treat the underlying medical causes:

Attend to function and consult physical and occupational therapy and remove in-dwelling catheters, NGT, and IV's as soon as possible. For unmet pain needs begin a fixed schedule (not PRN) of acetaminophen and/or opioids.<sup>6</sup> AVOID Demerol, as the metabolite produces CNS excitation. Avoid medications with anticholinergic properties. Treat hypoxemia, fluid and electrolyte imbalances, and underlying infections

##### Non-pharmacologic measures:

- 1) Recruit family to stay with patient and participate with care.
- 2) Provide memory clues by having a clock, calendar, and familiar items, such as family photos within visible range of the patient.
- 3) Cognitive-emotional supportive measures include providing reorientation and reassurance.
- 4) Make sure patients are wearing eyeglasses, hearing aides.
- 5) Maintain regular sleep/wake cycles by promoting good sleep hygiene. Avoid taking vital signs, drawing labs and giving medications during the night when possible.
- 6) Get patients up and out of bed, and increase socialization and stimulation during the day to

avoid boredom, and thus prevent daytime napping.

- 7) Keep rooms well lit during wakeful hours.
- 8) Avoid/remove physical restraints including posey vests, wrist restraints, IV lines, indwelling catheters and nasogastric tubes.
- 9) Provide food that the patient likes, is able to chew, and swallow appropriately. Feed and provide oral fluids to patients who cannot feed themselves.
- 10) Maintaining bladder and bowel program with regular toileting. Avoid constipation by providing adequate hydration and prescribing stimulant laxative with all narcotic orders.

Pharmacologic Management:

Delusions and hallucinations are common in delirium (90%) and usually worse at night (sundowning). Hallucinations are usually visual (40-90%) and behaviors of fear and agitation are seen. Delusions when present are typically of persecution and usually linked to the environment. These sensory features of delirium (delusions and hallucinations) are less common in the elderly. The elderly tend to exhibit more somatic features such as incontinence, gait impairment, and tremor and language disorders. The preferred management is non-pharmacologic. If non-pharmacologic measures alone are inadequate or the patient is at risk to harm self then targeted pharmacologic therapy may be added.

Neuroleptics: to control delusions, paranoia and hallucinations; neuroleptics are the most effective.<sup>2,6,7</sup> Haldol (Haloperidol) has few anticholinergic side effects, few active metabolites, low likelihood of sedation and hypotension.

**START LOW GO SLOW –**

- Haldol 0.25mg BID (PO, IM, IV)  
Or
- Risperdal 0.25mg BID (PO)

Diphenhydramine (Benadryl): Given its highly anticholinergic properties, NO BENADRYL.

Short-acting benzodiazepines: for withdrawal or if sedation is needed. Agitation is often seen in response to the delusions or hallucinations and treatment of these symptoms alone may decrease agitation. Long acting agents such as diazepam (Valium) should be avoided. Potential negative side effects of any benzodiazepine use include further cognitive impairment, precipitation of agitation, and disinhibition in those with underlying dementia.<sup>2</sup>

**START LOW GO SLOW**

- Ativan 0.25mg bid (PO,IM,IV)

**Summary**

Delirium occurs frequently in older and chronically ill patients and is a predictor of poor prognosis. Functional outcomes are adversely affected when a delirium occurs. Prevention is key. Begin an evaluation for delirium by considering the most common causes such as medications, infection, alcohol withdraw or a sudden change in metabolic state due to a medical condition. Finally, the management of delirium is threefold: 1) identify and treat the underlying medical cause, 2) consider nonpharmacologic interventions, and 3) consider pharmacologic therapies to manage symptoms of delirium.

**References**

1. Marcantonio,E.R., Flacker,J.M.,Michaels,M and Resnick,N. Delirium Is Independently Associated with Poor functional Recovery After Hip Fracture. JAGS. 2000;48:618-24.
2. Bair BD. Delirium. Part III, p 111-115. In: Cobbs EL, Duthie EH, Murphy JB, eds., Geriatrics Review Syllabus: A Core Curriculum in Geriatric Medicine. 4<sup>th</sup> ed. Dubuque, Iowa: Kendall/Hunt Publishing Company for the American Geriatrics Society; 1999.
3. Inouye SK, Bogardus ST, Charpentier PA, Leo-Summers L, Acampora D, Holford TR, Cooney LM. A multicomponent intervention to prevent delirium in hospitalized older patients. N Engl J Med. 1999;340:669-76.
4. Tune, Larry E., Delirium. Chapter 93. In Hazzard, W.R., Blass, J.P., Ettinger,Jr, W.H. et al. Principles of Geriatric Medicine and Gerontology. 4<sup>th</sup> Ed. New York: McGraw-Hill, 1999.
5. Chan D, Brennan NJ. Delirium: Making the diagnosis, improving the prognosis. Geriatrics. 1999;54:28-30, 36, 39-42.
6. Reuben DB, Grossberg GT, Mion LC, et al. Delirium, p18-19. Geriatrics At Your Fingertips 1998/1999 Edition. Belle Mead, NJ: Excerpta Medica, Inc: 1998
7. Boling PA. Geriatric Quick Consult Chapter 1: Delirium. <http://www.virginia geriatics.org/>. VCU Health Systems, Richmond VA. 2002