Delirium in the Elderly

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Learning Objectives

- Identify the symptoms of delirium in the elderly
- Differentiate the most common causes of delirium in the elderly
- Demonstrate a treatment plan for delirium that combines environmental and pharmacologic modalities
Delirium

- **Latin roots**
  - *de* – meaning “away from”
  - *lira* – meaning “furrow in a field”
  - *ium* – meaning singular
  - Literally means “a going off the ploughed track, a madness”
DSM IV-TR Criteria for Delirium

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 pre-existing, 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. There is evidence from the history, physical examination, or laboratory findings that the disturbance is caused by the direct physiological consequences of general medical condition.
DSM-V Proposed Criteria for Delirium

A. *Disturbance in level of awareness and reduced ability to direct, focus, sustain, and shift attention.*

B. A change in cognition, (such as deficits in orientation, executive ability, language, visuoperception, learning and memory)

C. There is evidence from the history, physical examination or laboratory findings that the disturbance is caused by the direct physiologic consequences of a general medical condition.

D. The disturbance develops over a short period of time (usually hours to a few days) and tends to fluctuate *in severity* during the course of a day.
Delirium: Consciousness

- Normal wakefulness
- Confusion
- Stupor
- Coma

**delirium**
Delirium is Acute

cognition

delirium

dementia

time
Delirium Fluctuates

- acute onset
- lucid interval
- "sundowning"

conscious awareness

v
Associated Symptoms

- visual hallucinosis
- motor agitation
- paranoid delusions
- combative behaviors
- reversed sleep/wake cycle
Delirium Subtypes

- **Hyperactive delirium (30%)**
  - agitated, combative, assaultive
  - withdrawal states, toxic-metabolic

- **Hypoactive delirium (24%)**
  - apathetic, depressed, lethargic
  - infectious causes

- **Mixed delirium (46%)**
  - classic “waxing and waning” pattern
  - wide differential of etiologies
Prevalence

- Elderly patients on admission: 15%
- Elderly patients during admission: 40%
- Post hip fracture repair: 50%
- Nursing home: 60%
- Terminally ill: 80%
Risk Factors - Patient Characteristics

- Hospitalized elderly
- Cognitive impairment
- Lower education level (<8th grade)
- Decreased functional status
- Comorbid medical conditions
- Malnutrition
- Depression
Perioperative Risk Factors

- Orthopedic (16-62%) > vascular (29-42%) > cardiac (8-42%)
- Urgent or emergent procedure
- Delayed surgery after hip fracture
- Preoperative hemodynamic instability
- Hypoxemia
- Electrolyte disturbances
- Transfusion requirement
Perioperative Risk Factors

- Sleep deprivation
- Urinary catheter
- Immobility
- Poorly controlled pain
- Polypharmacy (esp. benzos/anticholinergics)
- Meperidine
Risk Factors - Medical Conditions

- Dementia
- Burns
- Abrupt discontinuation of alcohol or drugs
- Malnourishment
- Chronic hepatic disease
- Dialysis
- Parkinson's disease
- HIV infection
- Post-stroke status
Delirium Risk Factors

Visual Impairment (3.51)
Severe Illness (3.49)
Cognitive Impairment (2.82)
Inc. BUN/Cr (2.02)

Relative Risk
Inouye 1993
Rate of Delirium

Rate (%)

No. of Risk Factors

Modified from Francis, 1992
Pathogenesis

- Cholinergic deficiency
- Abnormalities in serotonin and melatonin
- Noradrenergic hyperactivity
- Neuronal damage - inflammation-induced edema → hypoxia → reduced synthesis of acetylcholine
- Global brain dysfunction - generalized slowing on EEG
Figure 1. Factors Contributing to Changes in Neurotransmitters, Leading to Delirium

↓ACH = Neuronal Excitability
- Anticholinergic drugs
- Age/dementia
- Hypoxia
- Anemia
- Hypotension
- Poor nutrition
- Infection
- Surgery
- Alzheimer’s disease

↑DA = ↓Release of ACH
- Drugs: dopamine agonists
- Infection
- Surgery
- Age/dementia

Mechanisms of Delirium Neurotransmitters

↑Cortisol & Beta-Endorphins
- Exogenous glucocorticoids
- Disruption of circadian rhythm

↓GABA = Neuronal Excitability
- Benzodiazepines
- Alcohol withdrawal

↑Serotonin
- Antidepressants
- Infection
- Hepatic encephalopathy

ACHE: acetylcholine; DA: dopamine; GABA: gamma-aminobutyric acid.
Source: References 1, 7-11.
Tip of the Iceberg

- Change in consciousness
- Low MMSE
- Hallucinations

pneumonia
cardiac dysrhythmia
silent MI
Life Threatening Causes of Delirium

- Wernicke-Korsakoff syndrome
- Hypoxia
- Hypoglycemia
- Hypertensive encephalopathy
- Hyperthermia or hypothermia
- Intracerebral hemorrhage
- Meningitis/encephalitis
- Poisoning
- Status epilepticus

Etiologies

- **systemic disease**
  - infection
  - metabolic derangement
  - cardiovascular
  - collagen/vascular

- **toxicity**
  - medications
  - drugs of abuse
  - poisons

- **withdrawal states**
- **post-operative states**
  - hip fracture repair
  - cardiac surgery

- **primary brain disease**
  - stroke
  - trauma
  - infection
  - neoplasm
  - vasculitis
# Etiology in the Elderly

<table>
<thead>
<tr>
<th>Etiology</th>
<th>Definite</th>
<th>Probable</th>
<th>Possible</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>fluid imbalance</td>
<td>4</td>
<td>1</td>
<td>15</td>
<td>20</td>
</tr>
<tr>
<td>infection</td>
<td>4</td>
<td>6</td>
<td>10</td>
<td>20</td>
</tr>
<tr>
<td>drug toxicity</td>
<td>7</td>
<td>0</td>
<td>8</td>
<td>15</td>
</tr>
<tr>
<td>metabolic</td>
<td>0</td>
<td>1</td>
<td>12</td>
<td>13</td>
</tr>
<tr>
<td>sensory</td>
<td>0</td>
<td>1</td>
<td>11</td>
<td>12</td>
</tr>
<tr>
<td>low perfusion</td>
<td>2</td>
<td>0</td>
<td>5</td>
<td>7</td>
</tr>
<tr>
<td>withdrawal</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>intracranial</td>
<td>1</td>
<td>1</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>18</td>
<td>10</td>
<td>62</td>
<td>90</td>
</tr>
</tbody>
</table>

Modified from Francis 1992
## Length of Stay

<table>
<thead>
<tr>
<th>Patients</th>
<th>Length of Stay Mean (SD)</th>
<th>Excessive Hospital Stay (days)</th>
<th>Paired-comparison t Tests (P)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Actual (days)</td>
<td>Predicted (days)</td>
<td></td>
</tr>
<tr>
<td>Entire cohort</td>
<td>12.3 (13.5)</td>
<td>7.5 (3.3)</td>
<td>4.8</td>
</tr>
<tr>
<td>Non-delirious</td>
<td>10.6 (10.1)</td>
<td>7.3 (3.4)</td>
<td>3.3</td>
</tr>
<tr>
<td>Delirious</td>
<td>21.6 (23.7)</td>
<td>8.6 (2.3)</td>
<td>13.0</td>
</tr>
</tbody>
</table>

Thomas 1988
Morbidity

**Medical complications**
- pneumonia
- dehydration
- decubiti

**Unsafe behaviors**
- falls
- self-extubation
- noncompliance
Significance

- Increased morbidity
- Increased mortality
- Longer hospital stays
- NH placement
Mortality

0% 10% 20% 30% 40%

in hospital 1 month 6 months

22-76% 15% 25%
Treatment of Delirium

Symptomatic Treatment

Definitive Treatment
Symptomatic Treatment

- sensory aids
- education & reassurance
- orientation
- hydration & nourishment
- activity
- pharmacologic
Prevention of Delirium:

- **cognitive impairment**
  - orientation board
  - frequent re-orientation
  - cognitively-stimulating activities

- **sleep deprivation**
  - warm drink at bedtime
  - relaxation tapes or music
  - back massage
  - noise reduction on the unit
  - schedule adjustment to permit sleep

Inouye 1999
Prevention of Delirium

- **immobility**
  - ambulation or active ROM tid
  - minimal use of catheters or restraints

- **visual impairment**
  - glasses or magnifying lenses
  - large-print books
  - large phone keypads
  - fluorescent tape on call bell

Inouye 1999
Prevention of Delirium

- **hearing impairment**
  - earwax disimpaction
  - hearing aids
  - portable amplifying devices
  - other communication techniques

- **dehydration**
  - early recognition and rehydration

Inouye 1999
## Prevention of Delirium

<table>
<thead>
<tr>
<th>N=852 pts</th>
<th>specialized delirium protocol</th>
<th>usual care group</th>
<th>significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>1st episode delirium</td>
<td>42 (9.9)</td>
<td>64 (15.0)</td>
<td>p=0.02</td>
</tr>
<tr>
<td>total days delirium</td>
<td>105</td>
<td>161</td>
<td>p=0.02</td>
</tr>
<tr>
<td># episodes delirium</td>
<td>62</td>
<td>90</td>
<td>p=0.03</td>
</tr>
<tr>
<td>delirium severity</td>
<td>3.85 (1.27)</td>
<td>3.52 (1.44)</td>
<td>p=0.25</td>
</tr>
</tbody>
</table>

Inouye 1999
Avoid Restraint Use

- Physical restraints are associated with developing delirium.
- Restraint use may actually increase fall risk.
- Restraint reduction was not associated with an increase in falls.
- Restraint use within delirium tremens associated with higher mortality.
Pharmacologic Interventions

haloperidol (Haldol)

- **Geriatric dose:** 0.25 to 1 mg IV q 8 hrs standing and 0.25 to 1 mg IV q 6 hrs prn.

- Watch QTc (cut-off 460 msec)- Torsades

- Contraindicated: DLB, Parkinson’s dx, TD
Higher doses and intravenous administration of haloperidol appear to be associated with a higher risk of QT prolongation and Torsades de Pointes. (at least 28 cases now reported)

Because of this risk of Torsades de Pointes and QT prolongation, ECG monitoring is recommended if haloperidol is given intravenously.

Haloperidol is not approved for
Prophylaxis of Delirium w/ Meds

- Study of haloperidol 0.5mg three times per day prophylaxis before elderly hip surgery:
  - Reduced severity and duration of symptoms but not the incidence of delirium.

- Study of olanzepine 10mg vs placebo before elderly joint replacement patients
  - Incidence of delirium significantly lower in tx arm
  - However, delirium lasted longer/ more severe in tx arm

- Study of risperdone 1 mg upon awakening from elective cardiac surgery
  - 20.6% absolute risk reduction of delirium
Pharmacologic Interventions

Atypical Antipsychotics

- No controlled studies
- Anecdotal evidence
- Aripiprazole 2.5-10mg bid
- quetiapine 25-200 mg in bid - tid
- risperdone 0.5-2 mg bid
- olanzapine 2.5-10 mg hs
<table>
<thead>
<tr>
<th>Drug</th>
<th>Dose</th>
<th>Adverse effects</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Acute therapy</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Antipsychotics&lt;sup&gt;a&lt;/sup&gt;</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Haloperidol</td>
<td>0.5–1 mg PO or IM; can repeat every 4 h (PO) or every 60 min (IM)</td>
<td>Extrapyramidal syndrome, prolonged QT interval</td>
<td>Randomized, controlled trials demonstrate reduction in symptom severity and duration&lt;sup&gt;81,82&lt;/sup&gt;</td>
</tr>
<tr>
<td>Atypical antipsychotics&lt;sup&gt;a&lt;/sup&gt;</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Risperidone</td>
<td>0.5 mg BID</td>
<td>Extrapyramidal syndrome, prolonged QT interval</td>
<td>Randomized, controlled trials comparing efficacy against haloperidol showed comparable response rates&lt;sup&gt;82-84&lt;/sup&gt;</td>
</tr>
<tr>
<td>Olanzapine</td>
<td>2.5–5 mg daily</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Quetiapine</td>
<td>25 mg BID</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Benzodiazepines&lt;sup&gt;b&lt;/sup&gt;</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lorazepam</td>
<td>0.5–1 mg PO; can repeat every 4 h</td>
<td>Paradoxical excitation, respiratory depression, excessive sedation, confusion</td>
<td>Did not show improvement in condition; treatment limited by adverse effects&lt;sup&gt;81&lt;/sup&gt;</td>
</tr>
<tr>
<td>Cholinesterase inhibitors&lt;sup&gt;c&lt;/sup&gt;</td>
<td></td>
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<tr>
<td>Donepezil</td>
<td>5 mg QD</td>
<td>Nausea, vomiting, diarrhea</td>
<td>No randomized, controlled studies have been conducted; some case studies have indicated promise&lt;sup&gt;83-85&lt;/sup&gt;</td>
</tr>
<tr>
<td><strong>Prophylactic therapies (potential)</strong>&lt;sup&gt;e&lt;/sup&gt;</td>
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<td>Extrapyramidal syndrome, prolonged QT interval</td>
<td>Use in surgical cases may reduce delirium incidence,&lt;sup&gt;59&lt;/sup&gt; needs to be confirmed in additional studies</td>
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<td>5 mg QD</td>
<td>Nausea, vomiting, diarrhea</td>
<td>Prevention studies have not demonstrated efficacy&lt;sup&gt;81,82&lt;/sup&gt;</td>
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<sup>a</sup>Antipsychotics are the most widely used drugs for the treatment of delirium-related agitation but can have marked adverse effects.  
<sup>b</sup>Benzodiazepines should be reserved for treatment of drug withdrawal, diffuse Lewy body disease, or as second-line treatment following failure of antipsychotics.  
<sup>c</sup>Not currently accepted clinical therapies.  
Abbreviations: BID, twice daily; IM, intramuscularly; PO, per os (by mouth); QD, once daily.
Course of Delirium

prodromal
1-3 days

overt

resolving
days to months

Cognitive changes may persist 6 months
ADLS changes may persist 12+ months
Duration of Delirium: Elderly

21 days

Koponen 1989
Delirium Recall

% with Recall

severe  moderate  mild

16  55  100

Breitbart 2002