NEW DEVELOPMENTS IN
DELIRIUM

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WHAT IS DELIRIUM?
(Acute Confusional State)

Definition:
• acute decline in attention and cognition

Pearl: Delirium is an important preventable syndrome for older patients
• common problem
• serious complications
• often unrecognized
• up to 40% cases preventable
Delirium is common

Delirium Rates

Hospital:
• Prevalence (on admission) 14-24%
• Incidence (in hospital) 6-56%

Postoperative: 15-53%

Intensive care unit: 70-87%

Nursing home/post-acute care: 20-60%

Palliative care: up to 80%

Ref: Inouye SK, NEJM 2006;354:1157-65
Delirium has serious complications

• Delirium associated with:
  – Increased morbidity and mortality
  – Functional and cognitive decline
  – Increased rates of dementia
  – Institutionalization
  – Increased healthcare utilization and costs
  – Post-traumatic stress disorder
  – Caregiver burden
Adverse Outcomes of Delirium

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Rate When Delirium:</th>
<th>No. Studies</th>
<th>Risk (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Present n/N (%)</td>
<td>Absent n/N (%)</td>
<td></td>
</tr>
<tr>
<td>Mortality</td>
<td>217/714 (30%)</td>
<td>616/2243 (27%)</td>
<td>7</td>
</tr>
<tr>
<td>Institutionalization</td>
<td>176/527 (33%)</td>
<td>219/2052 (11%)</td>
<td>9</td>
</tr>
<tr>
<td>Dementia</td>
<td>35/56 (63%)</td>
<td>15/185 (8%)</td>
<td>2</td>
</tr>
</tbody>
</table>

Ref: Witlox J et al. JAMA 2010;304:443-51
Impact of Delirium
(N=225 cardiac surgery patients)

Impact of Delirium (cont)

• Delirium occurred in 46% patients following cardiac surgery
• Cognitive trajectory characterized by abrupt initial decline followed by gradual recovery over 6 months
• Patients did not get fully back to baseline even at one year follow-up
• Implications for rehab and management of delirium; importance of prevention of delirium.
## Adverse Outcomes Associated with Delirium in Persons with Alzheimer’s Disease (N=771)

<table>
<thead>
<tr>
<th>Adverse Outcome</th>
<th>Adjusted Relative Risk (95% CI)</th>
<th>Attributable Risk %</th>
<th>Risk Attributable to Delirium</th>
</tr>
</thead>
<tbody>
<tr>
<td>Death</td>
<td>5.4 (2.3-12.5)</td>
<td>6.2</td>
<td>1 in 16</td>
</tr>
<tr>
<td>Institutionalization</td>
<td>9.3 (5.5-15.7)</td>
<td>15.2</td>
<td>1 in 7</td>
</tr>
<tr>
<td>Cognitive Decline</td>
<td>1.6 (1.2-2.3)</td>
<td>20.6</td>
<td>1 in 5</td>
</tr>
<tr>
<td>Any Adverse Outcome</td>
<td>2.2 (1.8-2.7)</td>
<td>12.4</td>
<td>1 in 8</td>
</tr>
</tbody>
</table>

Delirium Alters Cognitive Trajectory in Dementia

Gross AL et al. Arch Intern Med 2012; on-line
Delirium is expensive

Hospital costs (> $8 billion/year)
Post-hospital costs (> $100 billion/year)
  • Rehospitalization, ER visits
  • Institutionalization
  • Rehabilitation
  • Home care
  • Caregiver burden

Aging of U.S. population

Delirium is often unrecognized

Previous studies: 32-66% cases unrecognized by physicians

Pearl: We cannot manage delirium or decrease its complications unless we recognize it
CONFUSION ASSESSMENT METHOD (CAM) ALGORITHM

[rate based on cognitive testing]

(1) acute onset and fluctuating course  
   -and-  

(2) inattention  
   -and either-  

(3) disorganized thinking  
   -or-  

(4) altered level of consciousness

KEY CAM FEATURES

• Acute onset and fluctuating course: symptoms tend to come on abruptly and wax/wane over the course of a day
  – History is essential (family member, caregiver)

• Inattention: inability to maintain attention on external stimuli or shift attention to new stimuli
  – Tests: Digit span (>5F, >3B), days of week backwards (0 errors), months of year backwards (1 error allowed)
• Disorganized thinking: symptoms reveal disorganization of thought (disconnected or nonsensical speech, illogical thinking, unpredictable switching of subject), or severe degrees of cognitive impairment.
  – Outside range of normal
  – Tests: orientation, memory, abstraction
• Altered level of consciousness:
  – Typically reduced
CAM PERFORMANCE AND USE

• Most widely used standard tool for delirium used nationally and internationally
• Validated in over 1000 patients with sensitivity 94% and specificity of 89%
• Translated into > 20 languages
• Used in over 4000 original published studies to date

Ref: Wei LA et al. JAGS 2008;56:823-30
SPECTRUM OF DELIRIUM

Ranging from:

Hypoactive delirium (lethargy, excess somnolence) -- often missed to:

Hyperactive delirium (agitated, hallucinating, inappropriate)

Pearl: Hypoactive form is more common in older persons (75%) and associated with higher mortality.
## COMPARATIVE FEATURES OF DELIRIUM AND DEMENTIA

<table>
<thead>
<tr>
<th>Feature</th>
<th>Delirium</th>
<th>vs.</th>
<th>Dementia</th>
</tr>
</thead>
<tbody>
<tr>
<td>Onset</td>
<td>Abrupt</td>
<td>vs.</td>
<td>Insidious</td>
</tr>
<tr>
<td>Duration</td>
<td>Hours to days</td>
<td>vs.</td>
<td>Months to years</td>
</tr>
<tr>
<td>Attention</td>
<td>Impaired</td>
<td>vs.</td>
<td>Normal unless severe</td>
</tr>
<tr>
<td>Consciousness</td>
<td>Fluctuating, reduced</td>
<td>vs.</td>
<td>Clear</td>
</tr>
<tr>
<td>Speech</td>
<td>Incoherent, disorganized</td>
<td>vs.</td>
<td>Ordered, anomic/aphasic</td>
</tr>
</tbody>
</table>
PATHOPHYSIOLOGY OF DELIRIUM

• Poorly understood
• Functional rather than structural lesion
• Characteristic EEG findings (generalized slowing)
• Hypothesis: final common pathway of many pathogenic mechanisms
MULTIFACTORIAL MODEL OF DELIRIUM IN OLDER PERSONS

Ref: Inouye SK et al. JAMA 1996; 275:852-857
## Risk Factors from Predictive Models

<table>
<thead>
<tr>
<th>Predisposing Factors</th>
<th>General Medicine</th>
<th>Surgery</th>
<th>ICU</th>
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<tbody>
<tr>
<td></td>
<td></td>
<td>Non-cardiac</td>
<td>Cardiac</td>
</tr>
<tr>
<td>Dementia</td>
<td>2.3-4.7</td>
<td>2.8</td>
<td></td>
</tr>
<tr>
<td>Cognitive impairment</td>
<td>2.1-2.8</td>
<td>3.5-4.2</td>
<td>1.3</td>
</tr>
<tr>
<td>History of delirium</td>
<td></td>
<td>3.0</td>
<td></td>
</tr>
<tr>
<td>Functional impairment</td>
<td>4.0</td>
<td>2.5-3.5</td>
<td></td>
</tr>
<tr>
<td>Vision impairment</td>
<td>2.1-3.5</td>
<td>1.1-3.0</td>
<td></td>
</tr>
<tr>
<td>Hearing impairment</td>
<td></td>
<td>1.3</td>
<td></td>
</tr>
<tr>
<td>Comorbidity/severity of illness</td>
<td>1.3-5.6</td>
<td>4.3</td>
<td>1.1</td>
</tr>
<tr>
<td>Depression</td>
<td>3.2</td>
<td></td>
<td>1.2</td>
</tr>
<tr>
<td>History of transient ischemia/ stroke</td>
<td></td>
<td></td>
<td>1.6</td>
</tr>
<tr>
<td>Alcohol abuse</td>
<td>5.7</td>
<td>1.4-3.3</td>
<td></td>
</tr>
<tr>
<td>Older age</td>
<td>4.0</td>
<td>3.3-6.6</td>
<td>1.1</td>
</tr>
</tbody>
</table>
## Risk Factors from Predictive Models

<table>
<thead>
<tr>
<th>Precipitating Factors</th>
<th>Medicine</th>
<th>Surgery</th>
<th>ICU</th>
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<tbody>
<tr>
<td></td>
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</tr>
<tr>
<td><strong>Medications</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Multiple medications added</td>
<td>2.9</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Psychoactive medication use</td>
<td>4.5</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sedative-hypnotics</td>
<td></td>
<td></td>
<td>4.5</td>
</tr>
<tr>
<td><strong>Use of physical restraints</strong></td>
<td>3.2-4.4</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Use of bladder catheter</strong></td>
<td>2.4</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Physiologic</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Elevated BUN/creatinine ratio</td>
<td>2.0-5.1</td>
<td>2.9</td>
<td></td>
</tr>
<tr>
<td>Abnormal serum albumin</td>
<td></td>
<td>1.4</td>
<td></td>
</tr>
<tr>
<td>Abnormal sodium, glucose, potassium</td>
<td></td>
<td>3.4</td>
<td>1.4</td>
</tr>
<tr>
<td>Metabolic acidosis</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Infection</strong></td>
<td></td>
<td></td>
<td>3.1</td>
</tr>
<tr>
<td><strong>Any iatrogenic event</strong></td>
<td>1.9</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Surgery</strong></td>
<td></td>
<td>3.5-8.3</td>
<td></td>
</tr>
<tr>
<td>Urgent or trauma admission</td>
<td></td>
<td>1.5-3.4</td>
<td></td>
</tr>
<tr>
<td>Coma</td>
<td></td>
<td>1.8-21.3</td>
<td></td>
</tr>
</tbody>
</table>
ETIOLOGY

Dementia
Electrolytes
Lungs, liver, heart, kidney, brain
Infection
Rx—Treatment and withdrawal (ETOH, benzos)
Injury, pain, stress
Unfamiliar environment
Metabolic

Pearl: Addressing the multifactorial etiology is key to managing delirium.

Medications Associated with Delirium

[2012 AGS Beers Criteria: Potentially Inappropriate Medications for Elderly]

- All tricyclic antidepressants
- Anticholinergics (eg, diphenhydramine)
- Benzodiazepines
- Corticosteroids
- H2-receptor antagonists
- Meperidine
- Sedative hypnotics
- Thioridazine/chlorpromazine
MINIMIZE PSYCHOACTIVE MEDICATIONS

Pearl: Evaluating drug usage is a high-yield intervention for delirium in the hospital

1) Frequently review medication list
2) Minimize psychoactive medications
   • Avoid PRN’s
   • Use nonpharmacological approaches
   • Substitute less toxic alternatives
     (e.g. antacid or sucralfate for H\textsubscript{2} blocker; Psyllium + kaolin/pectin for diarrhea instead of loperamide)
   • Reduce dosage
3) Re-evaluate chronic medication usage
   • Hospital ideal time to make changes
   • Substrate is not the same
EVALUATION AND MANAGEMENT OF DELIRIUM

1. Cognitive Evaluation:
   
   Cognitive Screening and Confusion Assessment Method

   **Pearl:** You may need to use detective work to determine if acute change (e.g., family member, previous nurse)

2. Search for underlying etiology:
   
   Physical examination (including neurological exam) and vital signs
   Review medication list (current and preadmission), alcohol history
   Targeted metabolic work-up: CBC, lytes, BUN/Cr, Glucose, LFT’s, Calcium, p02, EKG
   Search for occult infection
   Neuroimaging in < 5% cases
DELIRIUM PREVENTION: NONPHARMACOLOGIC APPROACHES

• Should be applied in all at-risk older persons.

• Strategies:
  – Address delirium risk factors (e.g., Hospital Elder Life Program): mobility, orientation
  – Apply nonpharmacologic approaches for sleep and anxiety
  – Avoid psychoactive medications; review med lists each day

DELIRIUM MANAGEMENT: PHARMACOLOGIC

- Evidence limited: few RCTs, small size, no placebo controls
- Hypoactive delirium: no evidence of benefit
- Overall: Low-dose, high-potency antipsychotics preferred (haloperidol)
  - Atypicals equivalent to haloperidol
  - Reduces agitation, but may prolong cognitive deficits

Lacasse 2006 Ann Pharm; Cochrane reviews
DELIRIUM MANAGEMENT: PHARMACOLOGIC

Pearl: Reserve for patients with severe agitation which will:
1. cause interruption of essential medical therapies (e.g., intubation)
2. pose safety hazard to patient or staff
3. severe distressing hallucinations or delusions

Recommended Approach:
• Haloperidol 0.25-0.50 mg po or IM (IV short acting, risk of torsades)
• Repeat dose Q 30 minutes until patient manageable (maximum haloperidol dose 3-5 mg/24 hours)
• Maintenance: 50% loading dose in divided doses over next 24 hours
• Taper dose over next few days
## CURRENT TREATMENTS FOR DELIRIUM

<table>
<thead>
<tr>
<th>Drug/Dose</th>
<th>Adverse Effects</th>
<th>Comments</th>
</tr>
</thead>
</table>
| Haloperidol 0.5-1.0 mg po/IM BID; repeat Q4h PRN | - Extrapyramidal symptoms  
- Prolonged QT interval  
- Avoid in: withdrawal, Parkinson’s, hepatic insufficiency, neuroleptic malignant syndrome | Recommended treatment choice from RCTs  
Evidence for prevention remains equivocal |
| Atypical antipsychotics  
Risperidone 0.5 mg BID  
Olanzapine 2.5-5.0 mg QD  
Quetiapine 25 mg BID | - Extrapyramidal symptoms (EPS)  
- Prolonged QT interval  
- Increased mortality in elderly with dementia | Not well-tested; efficacy equivalent or less than haloperidol, but less EPS; no RCTs of Quetiapine |
| Lorazepam 0.5-1.0 mg po/IM; repeat Q4h PRN | - Respiratory depression  
- Oversedation  
- Paradoxical excitation | Reserve for ETOH or benzo withdrawal  
Results in worsening of delirium |

- No evidence for beneficial effects of acetylcholinesterase inhibitors  
- Trials of melatonin underway

Inouye SK, NEJM 2006;354:1157-65; Fong TG, Nat Rev Neurol. 2009;5:210-20; Grover S, Pharmacopsychiatry 2011;44:43-54
TAKE HOME MESSAGES: WHAT WE CAN DO

1. Cognitive Assessment: Cognitive Screening and CAM. Get the history/timecourse of cognitive changes
2. "Brown Bag" test: Know all your patients’ meds
3. Use of nonpharmacologic approaches to management of sleep, anxiety, agitation
4. Avoid bedrest orders
5. Make sure glasses, hearing aids, dentures available
6. Let patients know their schedule (tests, etc.) Keep them and their families involved in their care.