Delirium in the Hospitalized Patient

Marsha Wittink, MD MBE  
Director, IMIP  
Assistant Professor Family Medicine and Psychiatry  
Kim Trombly, NP  
IMIP Medical Provider  
Greg Sherman, MD  
Geriatric Psychiatry Fellow  
Department of Psychiatry URMC

Delirium

- Derived from Latin ‘deviate from a strait line’
- AC Celsus (Roman 25 BCE-50 ACE): “transient and related to fever, poising or trauma”
- UR history: Engel and Romano
  - Reduction in brain metabolic rate
  - (EEG findings)

> Sharon Inouye Harvard

Definition

Delirium is a syndrome of acute confusion marked by periods of waxing and waning levels of consciousness, altered psychomotor behavior, and perceptual impairment.
Delirium is not
- Just a symptom of dementia or other neurocognitive disorder
- A psychiatric disease or diagnosis

Why should all medical providers worry about delirium?
- Incidence is high
- Increased mortality
- Increased morbidity
- Significant burden on family, patient and medical care team
- Increased cost
  #1 consult psych consult team
  #1 reason for transfer to 19200

Incidence is higher than you might think
- 1/3 of patients presenting to ER
- 1/3 of inpatients aged 70+ on general med units
- 85% experience at end of life
- 25-40% of inpatient cancer patients
- Incidence ranges 5.1% to 52.2% after noncardiac surgery (Dasgupta M et al. J Am Geriatr Soc 2006;54:1578-89)
  Highest rates after hip fracture and aortic surgeries

Increased Mortality
- One-year mortality: 35-40%
- Independent predictor of higher mortality up to 1 year after occurrence

Increased morbidity
- Functional decline
- New nursing home placement
- Persistent cognitive decline:
  - Only 18-22% have complete resolution 6-12 months after discharge
  - Many subjects may have had preexisting cognitive impairment previously unrecognized

But what exactly is Delirium?
- A fluctuating change in MS, associated with change in alertness
- An underlying precipitant (infection, medication, toxic substance etc)
- Assume it’s delirium until proven otherwise
- Then rule out other causes (psychiatric, neurologic)

Subtypes
- HYPERACTIVE
  - Confusion
  - Agitation
  - Hallucinations
  - Myoclonus
- HYPOACTIVE
  - Confusion
  - Somnolence
  - Withdrawn
- MIXED
  - Less likely to be recognized
  - More likely to get Psych consult or transfer to IMIPS

Delirium vs. Dementia
<table>
<thead>
<tr>
<th>Features</th>
<th>Delirium</th>
<th>Dementia</th>
</tr>
</thead>
<tbody>
<tr>
<td>Onset</td>
<td>Acute</td>
<td>Insidious</td>
</tr>
<tr>
<td>Course</td>
<td>Fluctuating</td>
<td>Progressive</td>
</tr>
<tr>
<td>Duration</td>
<td>Days – weeks</td>
<td>Months - years</td>
</tr>
<tr>
<td>Consciousness</td>
<td>Altered</td>
<td>Clear</td>
</tr>
<tr>
<td>Attention</td>
<td>Impaired</td>
<td>Normal (unless severe)</td>
</tr>
<tr>
<td>Psychomotor changes</td>
<td>Increased or decreased</td>
<td>Often normal</td>
</tr>
<tr>
<td>Reversibility</td>
<td>Usually</td>
<td>Rarely</td>
</tr>
</tbody>
</table>
**BUT… dementia is most consistent risk factor**

- Underlying dementia in 25-50%
- Presence of dementia increases risk of delirium by 2-3 times

**Pathophysiology**

- Main theory = reversible impairment of cerebral oxidative metabolism + neurotransmitter abnormalities
  - HYPOXIA ISCHEMIA PAIN
  - decreased Ach — (indirect evidence: anticholinergics induce and Alzheimers more susceptible, animal models)
  - Increased DA
  - Increased Serotonin
  - Decreased GABA
  - Inflammatory mechanism – cytokines eg interleukin-1 release from cells, destruction of BBB
  - Stress reaction (increased cortisol) + sleep deprivation

**Etiology**

A multifactorial syndrome that arises from an interrelationship between:

- **Predisposing factors** → a patient’s underlying vulnerability

  AND

- **Precipitating factors** → noxious insults
Predisposing Factors (vulnerability)

- Baseline cognitive impairment
- 2.5 fold increased risk of delirium in dementia patients
- 25-31% of delirious patients have underlying dementia
- Medical comorbidities:
  - Any medical illness
  - Visual impairment
  - Hearing impairment
  - Functional impairment
  - Depression
  - Advanced age
  - History of ETOH abuse
  - Male gender

Precipitating Factors (insults)

- Medications
- Bed rest
- Indwelling bladder catheters
- Physical restraints
- Iatrogenic events
- Uncontrolled pain
- Fluid/electrolyte abnormalities
- Infections
- Medical illnesses
- Urinary retention and fecal impaction
- ETOH/drug withdrawal
- Environmental influences (e.g. noise)
- Infections (pneumonia, UTI)
- Withdrawal (alcohol, opiate)
- Acute metabolic (acidosis, renal failure)
- Trauma (acute severe pain)
- CNS pathology (epilepsy, cerebral haemorrhage)
- Hypoxia
- Deficiencies (B12, thiamine)
- Endocrine (thyroid, PTH, hypo/hyperglycaemia)
- Acute vascular (stroke, MI, PE, heart failure)
- Toxins/drugs (prescribed tramadol, dig toxicity, antidepressants, anticholinergics, corticosteroids) recreational
- Heavy metals

I WATCH DEATH mnemonic

- Infections
- Withdrawal
- Acute metabolic
- Trauma
- CNS pathology
- Hypoxia
- Deficiencies
- Endocrine
- Acute vascular
- Toxins/drugs
- Heavy metals
Prevention, Screening and Assessment of Delirium
Kim Trombly NP

Prevention, Screening and Assessment of Delirium
Patient experience
Precipitating factors
Prevention Methods (nursing)
Screening: ICU-CAM

Patient Experience: Video
Anthony Russo Sutter Health Conference: Patient recalls ICU experience (had H1N1 was intubated and sedated, talks about the very real “nightmares” confusion and continued memories)

https://youtu.be/ZYhooW0YHJg

Other testimonials and further information for patients/families: Vanderbilt University ICU delirium site:
http://www.icudelirium.org/testimonials.html

- Description of Delirium: 3:56-5:59
- What health care providers could have done: 18:55-20:25
Patient Testimonials from icudelirium.org

- I just hope one day I will be normal again, and this is temporary.
- I was hospitalized for 9 days with respiratory problems. In the FR and ICU, I could not remember all family members that were there. I also told the medical staff to call "Rick" (my husband who passed away 11 years ago). Once hospitalized, one night I believed that I was in Florida and people outside were trying to break in. I tried to get up and call 911 but my daughter stopped me.
- I felt better and returned to work but was fired 10 weeks later.
- It is seven years ago and I still trying to sort out what was real and what wasn’t. I still think about it several times a week and continue to ask questions of my family. I have a compelling need to know what happened to me. The final diagnosis was ARDS and Encephalopathy, however, they never determined the cause.
- I nearly ended my life a few times.
- When I returned to work, the work I did before seemed foreign and unfamiliar. I became isolated and excluded from everyone. No one wanted to be around me. My wife of more than 36 years told me that I was just feeling sorry for myself, and I just needed to get on with my life. I nearly ended my life a few times. My family believed that I was just faking it all.

Precipitating Factors (insults)

- Medications
- Bedrest
- Indwelling bladder catheters
- Physical restraints
- Iatrogenic events
- Uncontrolled pain
- Fluid/electrolyte abnormalities
- Infections
- Medical illnesses
- Urinary retention and fecal impaction
- ETOH/drug withdrawal
- Environmental influences

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**Prevention:**
Promote Healthy Sleep Patterns

1. Lights on & curtains open during the day, off at night
2. Decrease noise, distractions and interruptions
3. TV off at night
4. Offer ear plugs and eye mask
5. NO VITALS WHILE ASLEEP?!?!?
6. NO BLOOD DRAWS UNTIL 6 AM?!?!?
7. AVOID sleeping medications!!

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**TABLE 1: 2012 AGS Beers Criteria for Potentially Inappropriate Medication Use in Older Adults**

<table>
<thead>
<tr>
<th>Organ System/Therapeutic Category/Drug(s)</th>
<th>Recommendation, Rational, Quality of Evidence (QoE) &amp; Strength of Recommendation (SR)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anticholinergics (includes TCA's)</td>
<td>Avoid. Highly anticholinergic; clearance reduced with advanced age, and tolerance develops when used as hypnotic; increased risk of confusion, dry mouth, constipation, and other anticholinergic effects/lability.</td>
</tr>
<tr>
<td>First-generation antihistamines (in single agent or as part of combination products)</td>
<td>Avoid. Use of diphenhydramine in special situations such as acute treatment of urticaria; allergic reaction may be appropriate.</td>
</tr>
<tr>
<td>Brompheniramine</td>
<td>QE = High (Hydroxyzine and Promethazine); Moderate (All others); SR = Strong</td>
</tr>
<tr>
<td>Chlorpheniramine</td>
<td>QE = High (Hydroxyzine and Promethazine); Moderate (All others); SR = Strong</td>
</tr>
<tr>
<td>Cetirizine</td>
<td>QE = High (Hydroxyzine and Promethazine); Moderate (All others); SR = Strong</td>
</tr>
<tr>
<td>Diphenhydramine</td>
<td>QE = High (Hydroxyzine and Promethazine); Moderate (All others); SR = Strong</td>
</tr>
<tr>
<td>Doxylamine</td>
<td>QE = Moderate; SR = Strong</td>
</tr>
<tr>
<td>Hydroxyzine</td>
<td>QE = Moderate; SR = Strong</td>
</tr>
<tr>
<td>Promethazine</td>
<td>QE = Moderate; SR = Strong</td>
</tr>
<tr>
<td>Triptoreline</td>
<td>QE = Moderate; SR = Strong</td>
</tr>
<tr>
<td>Antiparkinson agents</td>
<td>Avoid. Not recommended for prevention of extrapyramidal symptoms with antipsychotics; more effective agents available for treatment of Parkinson disease.</td>
</tr>
<tr>
<td>Benztropine (oral)</td>
<td>QE = Moderate; SR = Strong</td>
</tr>
<tr>
<td>Trihexyphenidyl</td>
<td>QE = Moderate; SR = Strong</td>
</tr>
<tr>
<td>Antipsychotics</td>
<td>Avoid except in short-term palliative care to decrease oral secretions.</td>
</tr>
<tr>
<td>Haloperidol</td>
<td>Highly anticholinergic; uncertain effectiveness.</td>
</tr>
<tr>
<td>Clozapine</td>
<td>QE = Moderate; SR = Strong</td>
</tr>
<tr>
<td>Olanzapine</td>
<td>QE = Moderate; SR = Strong</td>
</tr>
<tr>
<td>Quetiapine</td>
<td>QE = Moderate; SR = Strong</td>
</tr>
<tr>
<td>Ziprasidone</td>
<td>QE = Moderate; SR = Strong</td>
</tr>
</tbody>
</table>

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25
Prevention: Promote Physical Activity

1. Ambulate throughout the day
2. AVOID RESTRAINTS!
3. Provide safe exercises
4. Have patient out of bed for meals

Prevention: Mental Stimulation

1. Games, puzzles, reading
2. Engage them in conversation with staff
3. Encourage memorabilia from home

Prevention: Promote Healthy Eating and Bodily Functions

1. Identify patients that need assistance with meals
2. Keep fluids at bedside if appropriate
3. Avoid constipation
4. Avoid urinary retention

Prevention: Promote Healthy Hearing and Vision

1. Make sure patient is wearing hearing aids
2. Make sure eye glasses are available and being worn
3. Use proper lighting
Screening: Early Identification is Key!

1. Create a culture of delirium awareness
2. Standardize screening
3. Find nursing and provider champions

PICKING A SCREENING TOOL?
- Multiple screening tools available
- Most importantly, pick an assessment tool and adopt delirium monitoring as a standard of care on the unit.
- CAM-ICU—Confusional Assessment Method for ICU
  - Non-proprietary—permission to use not needed.
  - Derived from the original CAM—S.Inouye/HELP
  - Easy to use—takes about 2 minutes to complete
  - ~89% sensitive/86% specific on med/surg units
  - bCAM—similar to CAM-ICU but for non ventilated patients.

CAM SCREENING PROCESS

INCLUSION CRITERIA
- ALL Pts. >65 OR WITH DX. OF DELIRIUM, ENCEPHALOPATHY, MENTAL STATUS CHANGES, AMS, ETC.
- OR WITH ANY CHANGE IN MENTAL STATUS AFTER ADM.

CAM SCREENINGS
- PERFORM CAM SCREENS EVERY 24 HRS ON ALL Pts.
- IF ANY CAM+—PT. LIKELY NOT DELIRIOUS
- IF ANY CAM+—PT. LIKELY DELIRIOUS—ASK PROVIDER

ALL POS CAMS
- REPORT IMMEDIATELY TO PROVIDER ON SITE
- IF NOT PROGRESS, INFORM NURSE LEADER
- PHONE CONSULT TO ORDER EVALUATION REQUESTED
SCREENING PROCESS

1) Assess level of consciousness:
   - RASS (Richmond Agitation-Sedation Scale)**
   - SAS (Sedation Agitation Scale)
2) Proceed to CAM-ICU assessment tool
   - Q shift or every 8 hours
   - Part of the nursing/provider handoff
   - Pos. CAM's discussed daily at multidisciplinary team rounds.
   - Pharmacist consultation for all positive patients.
   - Patient family education.
Delirium Screening Demonstration

Also several youtube videos:
https://www.youtube.com/watch?v=6WyJ0zL7VkI
https://www.youtube.com/watch?v=yEwBzKTbJEk

Delirium Management
Gregory Sherman

So You’ve Identified Delirium
- New onset
- Inattention
- Waxing and waning cognition, disorientation
- Disrupted circadian cycles
- Agitation, impulsivity, paranoia, hallucinations (Hyperactive Delirium)
- Somnolent, lethargic (Hypoactive Delirium)

Now What?

Initial Steps
- Review their current medications (Hospital and Home)
- Stop deliriogenic agents (safely, please)
- Appropriate Laboratory Workup
  - CBC, BMP, Hepatic Function Panel
  - Urinalysis
  - TSH, B12, folate, prealbumin, mag, phos, U.Tox, levels of medications if available/appropriate
- Other screening tests
  - CT vs MRI
  - EEG
  - CXR, KUB
Initial Steps

- Collateral Contacts
  - Assessment of baseline function, onset of symptoms, recent changes.
  - PCP, family, living facility
- Cognitive Assessment
  - SLUMS, MOCA, MMSE
  - Can be useful in trending their cognition during and after resolution of delirium.

Safety and Communication

- Minimization of risks
  - Removing potentially dangerous objects
  - Reducing fall risk
    - Avoid intermittent pneumatic compression, telemetry, constant IV tubing if possible
  - May require additional assistance and redirection
    - 1:1, GPS
- Communicate with staff, request documentation about behaviors/confusion/agitation
- Communicate with family members

Environmental Interventions

- Glasses, hearing aides, dentures
- Cueing with clocks, calendar (or date on whiteboard), family pictures, etc
- Restore circadian rhythm with natural light and appropriate timing of lights
- Reduce sleep disturbances (vitals, blood draws, etc)
- Reorientation with reassurance
- Attempt to limit restraints

Somatic Interventions

- STOP medications that may be perpetuating delirium
- Treat any withdrawal syndromes (EtOH, benzo [esp after prolonged ICU stay])
- Treat underlying conditions
- Appropriate pain management
- Antipsychotics remain the mainstay of acute intervention for delirium
Somatic Interventions

- Haloperidol
  - High-potency (binds tightly to dopa receptors)
  - More likely to cause EPS, less anticholinergic effects
  - Has demonstrated reduction in severity and duration of agitation
  - Can be given IV (2:1 dose equivalent IV:PO)
  - Metabolized by CYP450 2D6, lower dose for hepatic impairment
  - Lower doses required with dementia or neurocognitive DO's
  - 2-5 mg IV for mild-moderate agitation, 7.5–10 mg IV for severe agitation. Repeat q30 minutes until calm, q2-6 hours as needed once improved
  - (In elderly, trial doses 1/3 of what is usually prescribed. The APA guidelines recommend 0.25–0.5 mg every 4 hours)

- Risperidone
  - High potency (dopamine, serotonin) second generation
  - Not available IV/IM, is available in dissolvable (M-tab) formulation
  - 0.25-4 mg BID

- Olanzapine, quetiapine
  - Can be acutely sedating, less potent dopamine blockade
  - Carry anticholinergic SE's
  - Neither available IV. Olanzapine has a dissolvable form

  Olanzapine can be given IM but NOT with benzos due to hypotension

Somatic Interventions

- Antipsychotic Management Considerations
  - Please use the lowest effective dose and taper down as able
  - If you start an antipsychotic for delirium and their delirium resolves, PLEASE taper and D/C

The Warning Slides

- NMS
  - muscle rigidity, fever, autonomic instability, delirium, markedly elevated CK.
  - Typically with rapid dose changes

- EPS
  - Parkinsonism: masked facial appearance, stooped/shuffling gait, tremor, rigidity, cogwheeling, gait instability
  - AIMS, Modified Simpson Angus

- Akathisia
  - Uncontrollable sense of restlessness (skin crawling), psychomotor agitation
The Warning Slides

- Acute Dystonia
  - Manage with IM benadryl.
  - Stop antipsychotic.

- QTc
  - Prolonged QTc interval (>450 ms in men, >470 ms in women)
  - Hodges Formula: \( QTc = QT + 1.75 \times (\text{heart rate} - 60) \)
  - Risk of torsades/ventricular arrhythmias
    - Other risks for torsades: MI, CHF, age, bradycardia, medical conversion from a/fib, hepatic/renal dysfunction

The Warning Slides

- FDA Black Box Warning
  - U.S. Boxed Warning: Elderly patients with dementia-related psychosis treated with antipsychotics are at an increased risk of sudden death compared to placebo.

- Risk: Benefit Ratio

Somatic Interventions

- Cholinergics
  - Donepezil: theorized that acetylcholinesterase inhibition may reduce the burden of delirium in patient’s whose AMS is caused by anticholinergic effects
  - Could be beneficial in those who need ongoing management with anticholinergics (urinary meds, respiratory meds)