I Get Delirious-
Tackling a Common, Under-diagnosed, Even Deadly Hospital Problem

Andrew C. Bernard, MD
Associate Professor
Paul A. Kearney, MD Endowed Chair in Trauma Surgery
Director, Acute Care Surgery, Trauma and Surgical Critical Care
Department of Surgery
UK College of Medicine

Grand Rounds 4-11-12
Objectives

1. Describe delirium
2. List ways to prevent it
3. Outline a plan to address it when it occurs
..the most common psychiatric syndrome found in the general hospital setting...
DELIRIUM: SHOULD “NEVER” OCCUR, BUT IF IT DOES …

With increasing evidence linking delirium to serious sequelae, many intensive care units (ICUs) are adopting delirium screening in daily practice. In addition, government officials are wondering whether delirium should be deemed a “never” event in the hospital, prompting a close look at the identification, treatment and prevention of delirium among critically ill patients.

Delirium as the Next “Never” Event: Is That Realistic? Pratik P. Pandharipande, MD, MSCI
Definition

- acute or subacute
- organic mental syndrome
- disturbance of consciousness
- global cognitive impairment
- disorientation
- perceptual disturbance
- attention deficits
- disordered sleep-wake cycle
- fluctuation in presentation (e.g., waxing and waning)
- changes in psychomotor activity
Disturbance of consciousness accompanied by a change in cognition.
Incidence

• Survey of CC providers: 25-50%
  – Patel. *CCM* 2009

• In reality: 60-80%
Why haven’t I noticed?

1. Hyperactive (only 5%)
2. Hypoactive
3. Mixed

Delirium Can Vary Over Time
Another Reason....Measurement

• 41%----No objective measure
• 37%----’Clinical Assessment’
• 14%----CAM-ICU
  – Confusion Assessment Method in ICU
• 2%-----MMSE or Delirium Rating Scale
Confusion Assessment Method for the ICU (CAM-ICU)

Feature 1: Acute change or fluctuating course of mental status

and

Feature 2: Inattention

and

Feature 3: Altered level of consciousness

or

Feature 4: Disorganized thinking

‘Squeeze my hand when I say the letter A.’
≥ 3 of 10 = inattention

4 simple ‘yes/no’ questions
+ 1 command
Who gets delirium?
Delirium is Multifactorial

• Age
  – Fewer acetylcholine-producing cells
  – 2% ↑ per year after 65
  – eg, after simple outpatient surgery
Delirium is Multifactorial

• **Baseline cognitive impairment**
  - In THR patients:
    • 30% overall
    • 100% if demented preop
  - Even subtle preop attention deficits ↑ risk 4-5x
Delirium is Multifactorial

- Gender

2/3

1/3
Delirium is Multifactorial

- Sensory impairment
  - Visual impairment ↑ risk 3.5x
Delirium is Multifactorial

**Drugs**

1. Sedative hypnotics (e.g., benzodiazepines)
2. Antihypertensives (b-blockers)
3. Muscle relaxants
4. Narcotics
5. Antihistamines (first generation, e.g., hydroxyzine)
6. GI agents (Antispasmodics, H2-blockers)
7. Anti-nauseants (Scopolamine)
8. Anticonvulsants (e.g., barbiturates)
9. Fluoroquinolones
10. Psychotropic medications (TCA, Lithium)
11. Cardiac medications (Antiarrhythmics)
Ativan (last 24h) and Delirium

![Graph showing the probability of transitioning to delirium against lorazepam dose. The graph is labeled as follows: Probability of transitioning to delirium on the y-axis, Lorazepam dose in mg on the x-axis, and the p-value is 0.003.](image)

Versed and Delirium in SICU/TICU

![Graph showing the effect of Midazolam on delirium in Surgical and Trauma patients.](image)

Delirium is Multifactorial

- **Wise drug choices**
  1. Benzo’s are bad
  2. Avoid muscle relaxants
  3. Avoid antihistamines (benadryl for sleep)
  4. Use PPIs
Delirium is Multifactorial

• **Immobility and physical restraints**
  – endotracheal tubes
  – soft and leather restraints
  – IV lines
  – bladder catheters
  – SCD’s
  – casts
  – traction
Delirium is Multifactorial

• **Sleep deprivation**
  – average amount of sleep in ICU patients: 1:51/24 hr
  – frequent therapeutic interventions/procedures
  – pain
  – fear
  – noise

• may cause or aggravate/perpetuate delirium

• dyssynchronization of the melatonin secretion
Delirium is Multifactorial

- **Oversedation**
  - most are GABA-ergic
  1) interfere with sleep patterns
  2) cause acetylcholine-deficient state
  3) disrupt the circadian rhythm of **melatonin** release

(appplies to opioids too!)
Delirium is Multifactorial

- **Psychiatric Disorders**
  - Alcohol and substance abuse
  - Depression
  - Schizophrenia
  - Bipolar disorder
Delirium is Multifactorial

- **Pain**
  - postop pain is independent predictor
  - and pain meds (opioids)
  - opioids cause 60% of delirium in advanced cancer
Delirium is Multifactorial

- Severity of comorbidities
  - each additional point in APACHE II score
  - high medical comorbidity is an independent risk factor
Central Baptist starting program to reduce elderly patient delirium

When older adults are hospitalized, they can become confused and disoriented. This is often due to a temporary delirium, which is different than the more persistent symptoms we see in dementia, such as Alzheimer's disease.

A diagnosis of delirium is based on four factors: sudden onset of symptoms that fluctuate in severity; inattention; disorganized thinking and an altered level of consciousness. Generally, delirium clears within a few days, but may persist for several weeks or months.

A recent study places the incidence of delirium in post-operative hip-replacement patients at 11.6 percent. Other studies estimate incidence rates as high as 33 percent.

Delirium is independently associated with increased length of hospital stay, serious illness and death, long-term cognitive and functional deterioration and higher rates of institutionalization. Delirium constitutes an economic burden to the health care system estimated at $60,000 per patient per year.

Risk factors for delirium include being 65 or older, having a prior or current cognitive impairment, current hip fracture and/or another severe illness. Medications, metabolic disorders, infection, surgical procedures and neurological disorders also increase the risk.

A program designed to help prevent or properly treat delirium among hospitalized patients has shown to be effective. Central Baptist Hospital plans to begin the Hospital Elder Life Program (HELP), developed by Dr. Sharon Inouye of Yale University, by January. As part of HELP, select patients are screened for delirium risk factors. If present, a prevention program is prescribed for each patient. Many program interventions are designed to be performed by non-medical volunteers or family members.

The program's components include a sleep-enhancement protocol of back rubs and herbal tea, getting the patient up and walking early and often; insuring patients have access to clean and working visual and/or hearing aids; therapeutic activities such as knitting or reading; and a plan to ensure adequate fluid intake.

Though the interventions are simple, HELP has been shown to be surprisingly effective. The New England Journal of Medicine reported a 34 percent reduction in delirium patients using the program.

Dr. Gregory Cooper is a neurologist with Baptist Neurology Center at Central Baptist Hospital.

---

**Health Tip**

Many symptoms of delirium in hospitalized patients can be reversed when the cause is identified quickly. Treatment is aimed at determining and correcting the underlying problem.
Delirium Kills

- Delirium incidence in ICU: 80%
- Mortality:
  - 8% vs 1%
    - Francis J. JAMA 1990; 263:1097–1101
  - (6-month) mortality 34% vs 15%
    - Ely EW. JAMA 2004; 291:1753–1762
  - 90-day mortality 11% vs 3% among elderly
Cost

- Prolonged stays (5–10 days longer)
- Cardiac surgery: postop delirium costs $6,150 per patient (55)
- Doubled cost of valve replacement (i.e., $6,763 vs $12,965)
- Step-down critical care unit: 14% of patients developed delirium, representing 22% of ALL hospital days (54)
- Patients with delirium remained hospitalized an average of 9.2 days longer than their counterparts without delirium average cost of $28,000 per patient
- costs 31% higher if delirium (i.e., $41,836 versus $27,106 per patient) (56

Hospitalized Elderly Patients

1. delirium common
2. higher costs
3. shorter survival
4. average costs/day were 2.5-fold greater
5. total cost attributable to delirium ranged from $16,303 to $64,421 per patient

Delirium → Outcome

What’s the connection?

Patient Falls

CORTRAK®

UTI
Prevention is Key
Haloperidol prophylaxis decreases delirium incidence in elderly patients after noncardiac surgery: A randomized controlled trial*

Wei Wang, MD; Hong-Liang Li, MD; Dong-Xin Wang, MD, PhD; Xi Zhu, MD; Shuang-Ling Li, MD; Gai-Qi Yao, MD; Kai-Sheng Chen, MD; Xiu-E Gu, RN, BSN; Sai-Nan Zhu, MS

- 0.5mg loading dose
- 0.1mg/hr for 12 hours
Spontaneous Awakening

Dexmedetomidine and the Reduction of Postoperative Delirium after Cardiac Surgery

José R. Maldonado, M.D., Ashley Wysong, M.S.
Pieter J.A. van der Starre, M.D., Thaddeus Block, M.D.
Craig Miller, M.D., Bruce A. Reitz, M.D.

(Psychosomatics 2009; 50:206–217)

<table>
<thead>
<tr>
<th>Group A: Dexmedetomidine</th>
<th>Group B: Propofol</th>
<th>Group C: Midazolam</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dexmedetomidine loading dose: 0.4 µg/kg, infusion: 0.2-0.7 µg/kg/hr</td>
<td>Propofol: 25-50 µg/kg/min</td>
<td>Midazolam: 0.5-2 mg/hr</td>
</tr>
</tbody>
</table>

**TABLE 5. Selected Postoperative Outcome Variables for Cardiac Patients With Cardiopulmonary Bypass × Intervention Group**

<table>
<thead>
<tr>
<th></th>
<th>Dexmedetomidine (N=30)</th>
<th>Propofol (N=30)</th>
<th>Midazolam (N=30)</th>
<th>Overall p</th>
<th>Dexmedetomidine vs. Propofol</th>
<th>Dexmedetomidine vs. Midazolam</th>
</tr>
</thead>
<tbody>
<tr>
<td>Delirium</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Incidence of delirium (per protocol)</td>
<td>1/30 (3%)</td>
<td>15/30 (50%)</td>
<td>15/30 (50%)</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Incidence of delirium (ITT)</td>
<td>4/40 (10%)</td>
<td>16/36 (44%)</td>
<td>17/40 (44%)</td>
<td>&lt;0.001</td>
<td>0.001</td>
<td>0.002</td>
</tr>
<tr>
<td>Delirium, number of days</td>
<td>2/216 (1%)</td>
<td>45/276 (16%)</td>
<td>75/259 (29%)</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Mean length of delirium, days</td>
<td>2.0 (0)</td>
<td>3.0 (3.1)</td>
<td>5.4 (6.6)</td>
<td>0.82</td>
<td>0.93</td>
<td>0.63</td>
</tr>
</tbody>
</table>
Why is Precedex good in ICU?

- GABA-ergics produce delirium.
- Improved outcomes with dexmedetomidine
- Less delirium with dex
- Delirium clears faster with dex
- Less overall cost
- May even be better than haldol
Specific Quality Indicators

Leentjens et al. Academy of Psychosomatic Medicine (APM) and the European Association for Consultation-Liaison Psychiatry and Psychosomatics (EACLPP)

1. institutional protocol for delirium
2. professionals with expertise in delirium 24/7
3. % of patients over 65 screened for delirium risk factors on admission or pre-operatively
4. % of patients at high-risk screened during the first few days
5. When delirium present:
   1. treat with antipsychotic, unless medically contraindicated
   2. benzodiazepines are avoided unless a clear reason for using them (e.g., alcohol withdrawal)
Key Points

1. Delirium is organ dysfunction.
2. It’s not ‘OK’ (even though it’s 60-80% of patients).
3. We cause it with our drugs, but it’s not benign.
4. Inattention and disorganized thinking are abnormal.
5. We should be monitoring.
6. We should be documenting.
7. Neurocognitive function should be presented on rounds.
   1. RASS target
   2. RASS actual
   3. CAM-ICU
   4. Drugs
8. Seconds (only) are required to assess the above.
9. You can make it better.
assessments resources for ICU Delirium

The current clinical practice guidelines of the Society of Critical Care Medicine (SCCM) for the sustained use of analgesics and sedatives are geared toward the maintenance of optimal comfort in critically ill patients by focusing on 3 central components - pain, anxiety and delirium. The SCCM guidelines recommended that the emergence and/or persistence of delirium be regularly monitored in critically ill patients. Two of the validated tools for assessing delirium in ICU patients are the CAM-ICU and ICDSC.

The Confusion Assessment Method for the ICU (CAM-ICU) was adapted for use in nonverbal ICU patients from the original Confusion Assessment Method (CAM) (Inouye, Ann Intern Med 1990). The CAM-ICU was designed to be a serial assessment tool for use by bedside clinicians (e.g. nurses, physicians, etc). Thus it is easy to use, taking less than 2 minutes to complete and requires minimal training.

The Intensive Care Delirium Screening Checklist is an eight item delirium checklist (Bergeron, Intensive Care Med 2001). This checklist is completed based on data from the previous 24 hours. The eight items are scored 1 (present) or 0 (absent), for a total of 8 points. A score of 4 or greater is a positive screen for delirium.

Education
Use the educational tools below, as well as the videos for delirium education (on the right).
The Whole Package

• Spontaneous awakening trial
• STEER protocol
  • (Screen. Test. Exercise. Evaluate. Report.)
• CAM-ICU
• Early mobilization
• Patient and family centered care

http://www.youtube.com/watch?v=ui_EjM-zk9w
Management

1. Timely diagnosis
2. Identify underlying medical contributors
3. Non-pharm treatment
4. Pharm treatment
Patient with Sepsis

Mechanical Ventilation
Weakness
Cognitive and Functional Impairment, Institutionalization, Mortality
Delirium
Sedation
- Duration of delirium predicts outcome
- Pisani Am J Resp care 2009

- Each day of delirium increases 1-year mortality by 10%
- Girard CCM 2010
• Dexmedetomidine vs midazolam for ventilated ICU patients.

Riker RR JAMA 2009.
Preventive Pharmacology

- Preop antipsychotics
- Acetylcholinesterase inhibitors
- Dramatic reduction in postop delirium (3% versus 50%) in cardiac patients with dexmedetomidine (avoidance of more conventional GABA-ergic agents)
Antipsychotics

- Haldol-D2 dopaminergic
- Ziprasidone—entirely serotonergic
- Olanzapine and risperidone—mostly serotonergic
- Quetiapine—adrenergic and histaminic

Which is best?
- Haldol or quetiapine
Delirium, Pain and Sedation in the ICU

- Dasta et al. Anesth and Analg 2010
CAM-ICU

http://www.youtube.com/watch?v=1hSDNOVHMs&feature=related
Confusion Assessment Method in the ICU

RASS is above - 4
(-3 through +4)
Proceed to next Step

If RASS is -4 or -5
Stop
Reassess patient at later time

Delirium Assessment (CAM-ICU): 1 AND 2 AND (Either 3 OR 4)

1. Acute Onset or Fluctuating Course
   An acute change from mental status baseline?
   Or Patient’s mental status fluctuating during the past 24hrs
   No
   Stop
   No delirium
   Yes

2. Inattention
   Please read the following ten letters: SAVEAHAART
   Scoring:
   Error: when patient fails to squeeze on the letter “A”
   Error: when the patient squeezes on any letter other than “A.”
   < 3 Errors
   Stop
   No delirium
   ≥ 3 Errors

3. Altered Level of Consciousness (“actual” RASS)
   If RASS is zero, Proceed to next step
   0
   RASS
   If RASS is other than zero
   Stop
   Patient is Delirious

4. Disorganized Thinking
   1. Will a stone float on water? (Or: Will a leaf float on water?)
   2. Are there fish in the sea? (Or: Are there elephants in the sea?)
   3. Does one pound weigh more than two pounds? (Or: Do two pounds weigh more than one?)
   4. Can you use a hammer to pound a nail? (Or: Can you use a hammer to cut wood?)
   5. Command:
      Say to patient: “Hold up this many fingers” (Examiner holds two fingers in front of patient)
      “Now do the same thing with the other hand” (Not repeating the number of fingers).
      If patient is unable to move both arms for the second part, ask patient “add one more finger”
   ≥ 2 Errors
   Patient is Delirious
   < 2 Errors
   Stop
   No delirium
I. Timely Diagnosis

A. Be vigilant for the possibility

B. Obtain info on the patient’s baseline cognitive functioning (all available sources—spouse, family, or nursing staff)

C. Screen for delirium in high-risk groups.
   – objective delirium rating scales if possible [e.g., Delirium Rating Rating Scale-98 (73) or confusion assessment method (74)].
II. Identify Rx Underlying Medical Contributors

• Treatment of choice is timely discovery and correction of underlying medical causes of delirium:
  – infectious processes
  – electrolyte imbalances
  – correct vital signs and end-organ functioning
  – restore sleep-wake cycle
  – minimize fear, anxiety, and pain
  – manage extrinsic/environmental factors (lighting and noise)
III. Institute Non-pharmacological Treatment Strategies

1. Correct malnutrition, dehydration, and electrolyte abnormalities as quickly and safely as possible
2. Remove immobilizing lines and devices (i.e., IV lines, chest tubes, bladder catheters and physical restraints) as early as safely possible
3. Correct any sensory deficits (i.e., eyeglasses or hearing aids)
4. Promote as normal a circadian sleep pattern
   1. It is better if this can be achieved by environmental manipulations, such as light control (i.e., lights on and curtains drawn during the day and lights off at night) and noise control (i.e., provide ear plugs, turn off TVs, and minimize night staff chatter) rather than by the use of medications.
5. Provide adequate intellectual and environmental stimulation as early as possible (e.g., orient the patient to date, time, and circumstance regularly, provide a newspaper, or set the TV to a news broadcast).
IV. Pharmacological Treatment Strategies

• Stop agents known to cause delirium or that have high anticholinergic potential if possible
  – Avoid using GABA-ergic agents to control agitation, if possible. *Exception: In patients* undergoing CNS depressant withdrawal (i.e., alcohol, benzodiazepines, or barbiturates) or when more appropriate agents have failed and sedation is needed to prevent patient’s harming himself or herself.
  – Assess and treat pain
  – Avoid opioids for behavioral control
Management

1. Acetylcholinesterase inhibitor (e.g., rivastigmine, donepezil, physostigmine, or rivastigmine) for correction of central anticholinergic syndrome.

Serotonin antagonist (e.g., ondansetron), to control toxic elevations of serotonin usually associated with hypoactive delirium, although some studies have suggested use of a serotonin antagonist may be indicated in all types of delirium.

Rotate opioids (morphine to fentanyl to hydromorphone)

Melatonin to promote a more natural sleep

Adrenergic agonists (e.g., dexmedetomidine or clonidine) for protection against the acute release of norepinephrine due to hypoxia or ischemia, which leads to further neuronal injury and the development or worsening of delirium.
Management

The data to date are more robust for delirium prevention (69, 80), although data are emerging for treatment, especially delirium associated with massive norepinephrine discharges (i.e., alcohol withdrawal).

*N-methyl-D-aspartate receptor blocking* agents to minimize glutamine-induced neuronal injury (e.g., amantadine or memantine).

F. For hyperactive delirium:
Use low to moderate doses of haloperidol (e.g., 20 mg/24 hour), if the patient’s cardiac condition allows it and there are no significant electrolyte abnormalities.*

Before using haloperidol, obtain a 12-lead electrocardiogram and measure the corrected Q-T interval (QTc) and electrolyte levels. Correct potassium and magnesium levels, if needed.

If possible, avoid the use of other medications known to increase QTc and/or inhibitors of CYP3A4.

Discontinue use of haloperidol if QTc increases to 25% of baseline or 500msec.
Management

When the use of haloperidol is contraindicated or not desirable (i.e., prolonged QTc or history of severe extrapyramidal symptoms), atypical antipsychotics should be considered (1, 81):

• a. Evidence is better for risperidone and quetiapine.
• b. Limited data are available for olanzapine, aripiprazole, and perospirone.
• c. Avoid clozapine and ziprasidone.

*Note: antipsychotics should be used with caution and only short term for the management of delirium or agitation in patients suffering from dementia. Data suggest a twofold increase in mortality for patients with dementia after longterm treatment with antipsychotic agents

• G. For hypoactive delirium:
  • 1. Evidence suggests that dopamine antagonists may still have a place, given the excess dopamine theory.
  • a. If haloperidol is used, recommended doses are in the very low range (i.e., 0.25–1 mg/24 h).*