KEY REFERENCES – Laying the foundation for D of ABCDEF bundle

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- Dubois M. Intensive Care Med. 2001;27:1297-1304 (Risk Factors)
- Ely E. Intensive Care Med. 2001;27:1892-1900 (LOS and Risk Factors)
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- Needham D. Arch Phys Med Rehabil. 2010;91:536-542 (Delirium Reduction)
- Colombo R. Minerva Anestesiol. 2012;78:1026-1033 (Delirium Reduction)
- Balas M. Crit Care Med. 2013;42:1024-1036 (Delirium Reduction)
- Kamdar B. Crit Care Med. 2013;41:800-809 (Delirium Reduction)
Course Objectives

• Define delirium and manifestations
• Discuss the impact of delirium on patient outcomes
• Review tools to measure delirium
  • Confusion Assessment Method for the Intensive Care Unit (CAM-ICU), Intensive Care Delirium Screening Checklist (ICDSC)
• Identify strategies to build an ICU attentive to delirium
• Examine general principles, non-pharmacologic and pharmacologic interventions for the management of delirium
Creating a Standard Language

- Acute confusional state
- Confusion
- Acute brain syndrome
- Altered mental status
- Toxic or metabolic encephalopathy
- Sundowning
Clinical Practice Guidelines for the Management of Pain, Agitation, and Delirium in Adult Patients in the Intensive Care Unit

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Articles Published on Delirium

Number of Articles by Year (*2015 projected)

Slide: E Wes Ely, MD Vanderbilt University
Delirium: Key Features (DSM-V)

A. Disturbance in attention and awareness

B. Disturbance in cognition: e.g., memory, disorientation, language, perception

C. Develops over a short period of time and tends to fluctuate during the course of the day

D. Disturbances are NOT better explained by a preexisting, established or evolving neurocognitive disorder and do NOT occur in the context of a severely reduced level of arousal such as coma

E. There is evidence from the history and physical exam and/or labs that the disturbance is caused by a medical condition, substance intoxication or withdrawal, or medication/toxin side effect

Associated but Nondiagnostic Symptoms of ICU Delirium

- Hallucinations, delusions
- Abnormal psychometric activity (e.g., agitation, lethargy)
- Emotional disturbances (e.g., fear, anger, depression, apathy)
- Sleep disturbances
Delirium: Motoric Subtypes

- **Alert and Calm**
  - Lethargic
  - Sedated
  - Stupor

- **Hyperactive Delirium (~1%)**
  - Combative
  - Agitated
  - Restless

- **Hypoactive Delirium (35%)**

- **Mixed Delirium (64%)**

ICU Delirium: Pathophysiology

- Genetic predisposition
- Primed microglial cells
- GABA/NMDA receptor imbalance
- Cholinergic activity
- Dopaminergic activity
- Serotonergic activity

Delirium: Epidemiology and Short-Term Outcomes

• Prevalence
  • 50% to 80% of mechanically ventilated patients
  • 20% to 50% of lower severity patients

• Associated outcomes
  • Prolonged hospitalization
  • Increased mortality
  • Increased cost

Delirium: Long-Term Outcomes

• Mortality
  • Each day of delirium in the ICU increases the hazard of 1-year mortality by 10% ¹

• Cognitive Impairment
  • ICU delirium is an independent risk factor for long-term cognitive impairment ²,³
    34% with scores similar to moderate TBI
    24% with scores similar to mild Alzheimer disease

¹Pisani MA Am J Respir Crit Care Med. 2009;180:1092-1097.
PAD Delirium Assessment Recommendations

• Routinely monitor for delirium in all adult ICU patients (+1B)

• Use either:
  – Confusion Assessment Method for ICU (CAM-ICU)
  – Intensive Care Delirium Screening Checklist (ICDSC)

Assessment: Coma vs. Delirium

• Coma: defined by level of arousal
  • SAS 1 or 2, RASS = -4 or -5
    • Only responsive to physical or noxious stimulus, if at all
    • Unable to communicate

• Comatose patients should be reassessed over time to permit delirium scoring
  • Scoring is optimal during a patient’s maximal level of wakefulness

• Eligible for delirium when they arouse to verbal stimulus
  • RASS -3: brief eye opening to voice, no contact
  • SAS 3: awakens to verbal stimulus, but drifts off
Confusion Assessment Method (CAM, 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

CAM-ICU Flowsheet

Confusion Assessment Method for the ICU (CAM-ICU) Flowsheet

1. Acute Change or Fluctuating Course of Mental Status:
   - Is there an acute change from mental status baseline? **OR**
   - Has the patient’s mental status fluctuated during the past 24 hours?

   **NO** → CAM-ICU negative
   **YES** →  
   **> 2 Errors** → CAM-ICU negative

2. Inattention:
   - “Squeeze my hand when I say the letter ‘A’.”
   - Read the following sequence of letters: SAVE A H A R T
   - ERRORS: No squeeze with ‘A’ & Squeeze on letter other than ‘A’
   - If unable to complete Letters → Pictures

   **0 - 2 Errors** → CAM-ICU negative
   **> 2 Errors** →  

3. Altered Level of Consciousness
   - Current RASS level
   - RASS = zero

   **> 1 Error** → CAM-ICU positive
   **< 1 Error** → CAM-ICU negative

4. Disorganized Thinking:
   1. Will a stone float on water?
   2. Are there fish in the sea?
   3. Does one pound weigh more than two?
   4. Can you use a hammer to pound a nail?

   **Command:** “Hold up this many fingers” (Hold up 2 fingers)
   **Command:** “Now do the same thing with the other hand” (Do not demonstrate)
   **OR** “Add one more finger” (If patient unable to move both arms)

   **> 0 Errors** → CAM-ICU negative
   **< 0 Errors** → CAM-ICU positive

Pooled Test Characteristics:
- Sensitivity 80%
- Specificity 96%
- > 0.91

Figure: www.ICUdelirium.org
Intensive Care Delirium Screening Checklist (ICDSC)

1. Altered level of consciousness
2. Inattention
3. Disorientation
4. Hallucination, delusion, or psychosis
5. Psychomotor agitation or retardation
6. Inappropriate speech or mood
7. Sleep/wake cycle disturbances
8. Symptom fluctuation

Score 1 point per domain present

Delirium if > 4

Pooled Test Characteristics:
- Sensitivity 74%
- Specificity 82%
- > 0.80

Figure: www.ICUdelirium.org
Gusmao-Flores D. *Crit Care*. 2012;16:R115-R125
Screening: Implementation Strategies

• **Case-based scenarios**¹
  • Before-and-after case studies
  • Strategy increased usage of the ICDSC by 70% and accuracy of assessment by 54%

• **Spot-checking**²,³
  • Systematic comparison of users with expert raters
  • Identifies areas for fine tuning education

• **Get it into the water**
  • Incorporate delirium into hospital nursing orientation

Rounding Presentations: Emphasizing Mind and Body

• **Pain**
  • Pain controlled or uncontrolled on... (current analgesics)
  • Most recent pain score, source of pain (when known)

• **Agitation and Delirium**
  • Target RASS/SAS for the day
  • Current RASS/SAS
  • Delirium status
  • Current psychoactive medications

• **Physical Activity**
  • Prior level of activity
  • PT/OT consulted
  • Target activity level for the day
# ABCDEF+ ICU RN Presentation Outline

## Awake

<table>
<thead>
<tr>
<th>SWU</th>
<th>Yes - response:</th>
</tr>
</thead>
<tbody>
<tr>
<td>No - reason:</td>
<td></td>
</tr>
<tr>
<td>Target:</td>
<td></td>
</tr>
</tbody>
</table>

| RASS | Actual (acceptable range is Target RASS +/- 1): |

Did the patient sleep?

- Performed - response:
- Not performed - reason:

## Breathing

<table>
<thead>
<tr>
<th>SBT</th>
</tr>
</thead>
</table>

## Choice of Analgesia &/or Sedation

**Acceptable level of pain:**

- **NRS:**
- **Pain Score (pick 1 scale):**
- **Verbal descriptor:**
- **CPOT:**

**RASS:**

- **Target:**
- **Actual:**

Current **analgesia/sedative/NMBA doses/rates:**

- Are analgesic orders adequate?
- Are sedation orders adequate?

## Delirium

- **CAM-ICU score:**
- **SLP consult** Ordered? Occurring?
- **OT consult** Ordered? Occurring?

## Early Mobility

- **PT consult** Ordered? Occurring?

**Activity order:**

Yesterday's highest activity Mobility Score:

Today's mobility target:

## Family

Expectations/Goals/Concerns:

## Fluid Balance

- **CRRT therapy & fluid balance:**
- **I/O goal** from other team(s):

## Vascular Access

- Current **other continuous infusion doses/rates:**
- Number of **central lumens required:**
- Current **venous access** (include # lumens per CVC):
- Request for **line placement/removal:**

## Team Communications
## Anticipating Delirium: Risk Factors

### Baseline Vulnerability
- Underlying brain disease (dementia, stroke, Parkinson)
- Increased age
- Institutionalization
- Chronic disease (HIV, HTN, ETOH dependency, diabetes, etc.)
- Visual/hearing deficits

### Precipitants
- Medications
- Infection
- Dehydration
- Immobility/restraints
- Malnutrition
- Tubes/catheters
- Electrolyte imbalance
- Sleep deprivation
Limits of Evidence: Delirium Prevention

- Perform early mobilization of adult ICU patients whenever feasible to reduce the incidence and duration of delirium (+1B)

- No recommendation for
  - Using pharmacologic delirium prevention protocol
  - Using combined nonpharmacologic and pharmacologic delirium prevention protocol
    as no compelling data demonstrate that these reduce the incidence or duration of delirium (0,C)

- We do not suggest that either haloperidol or atypical antipsychotics be administered to prevent delirium in adult ICU patients (-2C)

- We provide no recommendation for the use of dexmedetomidine to prevent delirium in adult ICU patients, as there is no compelling evidence regarding its effectiveness in these patients (O,C)

Interventions for Delirium

• Early mobility and rehabilitation
• Sleep enhancement (via nonpharm and hygiene)
• Reducing unnecessary and deliriogenic medications
• Structured reorientation
• Adequate oxygenation

Interventions on Delirium

• Pain management
• Constipation relief
• Nutrition and fluid repletion
• Sensory assistive devices (vision and hearing)
• Cognitive stimulation/rehabilitation

Wake Up, Breathe, and Exercise

• Dual center, RCT of 104 sedated, MV patients
• Both (B) SATs + SBTs for ALL patients
• Intervention patients
  • If unresponsive, passive range of motion
  • If following commands, PT/OT coordinated with DIS
• Daily PT/OT until return to independence or hospital discharge

<table>
<thead>
<tr>
<th>Days from intubation to milestone</th>
<th>Intervention (n=49)</th>
<th>Control (n=54)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Out of bed</td>
<td>1.7</td>
<td>6.6</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Standing</td>
<td>3.2</td>
<td>6.0</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Marching in place</td>
<td>3.3</td>
<td>6.2</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Transferring to chair</td>
<td>3.1</td>
<td>6.2</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Ambulating</td>
<td>3.8</td>
<td>7.3</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Early Exercise

- Patient’s functional performance improved
  - Independent functional status at hospital discharge: intervention 59% vs. control 35%
- Shorter duration of MV
- Substantial reduction in duration of delirium
  - 2 vs. 4 days

Delirium and Sleep in the ICU

- **Sleep and delirium**
  - Sleep disruption is a manifestation of delirium
  - Sleep deprivation yields delirium

- **Sleep deprivation and fragmentation commonly occur**

- **Etiologies:**
  - Loss of night-day cues, constant environmental stimuli
  - Pain, sedatives, MV, stress

- **ICU sleep hygiene programs**
  - Decrease both incidence and duration of delirium in patients

- **Nighttime sedation sleep promotion**

ICU Environment, Sleep, and Delirium

• Daytime Interventions
  • Blinds raised
  • Less than 50% of the day napping
  • Avoid caffeine after 3 PM

• Nighttime Interventions
  • Before 10 PM
    • Room lights dimmed
    • Room curtain closed
    • Warm bath
  • Unnecessary alarms prevented
  • Room temperature optimized
  • Pain appropriately controlled
  • Television off

Result: No difference in perceived sleep quality, but...
• Reductions in delirium/coma incidence (49% vs. 69%)
• Improved daily noise rating

Reorienting ICU Patients

• Before-after observations in 214 ICU patients

• Interventions:
  • Night environment, music therapy, visual cues (clock)
  • Reorientation with 5 W’s and 1 H
    • Who? Who are you? Who is the nurse/physician?
    • What? What happened?
    • Where? Where are you/we?
    • Why? Why did it happen?
    • How? How did it happen? And what is the illness progression?

• Result: Delirium incidence reduction
  • Pre 35% vs. post 22%

Bundle Implementation Success: key findings from a meta-analysis

• 21 studies, all including process measures and 9 with clinical outcomes data
Bundle Implementation Success: key findings from a meta-analysis

• A variety of programs improved process measures
  • e.g., 92% Delirium screening adherence

• Using **more** implementation strategies (6 or more) and integrating **PAD** guidelines or **ABCDE** bundle:
  • Statistically lower mortality and shorter ICU LOS
  • Delirium “incidence” static; delirium duration may be better metric

• Strategies targeting **organizational changes** in addition to provider behavior also associated with reduced mortality

Trogrlić Z. **Critical Care** 2015; 19:157
Helpful Approach to Delirium Management

• Stop

• THINK

• Lastly medicate
Helpful Approach to Delirium Management

• Stop

• THINK

• Lastly medicate
Reducing Unnecessary Medications

• STOP: especially consider *sedatives*

• Is your patient on the minimal amount necessary?
  – Review medications
  – Doses adjusted for elderly, renal failure, liver failure

• Do you have a plan to reduce drug exposure?
  • Spontaneous awakening trial
  • Nurse empowerment to titrate drug to a team-determined target level of arousal
Delirium Risk Factor: Drug Exposure

- Measuring the probability of being delirious the next day

<table>
<thead>
<tr>
<th>Medication</th>
<th>Transitioning to Delirium Only Odds Ratio (95% CI)</th>
<th>$P$ Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lorazepam</td>
<td>1.2 (1.1–1.4)</td>
<td>0.003</td>
</tr>
<tr>
<td>Midazolam</td>
<td>1.7 (0.9–3.2)</td>
<td>0.09</td>
</tr>
<tr>
<td>Fentanyl</td>
<td>1.2 (1.0–1.5)</td>
<td>0.09</td>
</tr>
<tr>
<td>Morphine</td>
<td>1.1 (0.9–1.2)</td>
<td>0.24</td>
</tr>
<tr>
<td>Propofol</td>
<td>1.2 (0.9–1.7)</td>
<td>0.18</td>
</tr>
</tbody>
</table>

- Result: Drugs have the potential for contributing to delirium
  - Lorazepam particularly susceptible

Helpful Approach to Delirium Management

- Stop
- THINK
- Lastly medicate
What to THINK if positive for delirium

- **T**oxic Situations
  - Congestive heart failure, shock, dehydration
  - Deliriogenic medications (tight titration)
  - New organ failure (liver, kidney, etc.)
- **H**ypoxemia
- **I**nfection/sepsis (nosocomial), **I**mmobilization
- **N**onpharmacological interventions
- **K**+ or electrolyte problems
Helpful Approach to Delirium Management

• Stop

• THINK

• Lastly medicate
PAD Treatment of Delirium
Recommendations

• There are no published data that treatment with haloperidol reduces the duration of delirium in adult ICU patients (no evidence).

• Atypical antipsychotics may reduce the duration of delirium in adult ICU patients (C).

Antipsychotics and Delirium

• Unknown efficacy for delirium prevention and management
  • Studies are ongoing

• Indication: delirium with agitation and risk for self-harm
  • Unresponsive to nonpharmacologic strategies
  • Not proven to aid in delirium prevention/management
  • Ensure agitation not from untreated pain or withdrawal

• Do no harm
  • Measure QTc interval regularly
    • Avoid when baseline prolongation of QTc or history of torsades
    • Caution with concomitant meds known to prolong the QTc interval
  • Discontinue antipsychotics within 48 hours of delirium resolution

Dexmedetomidine and Delirium

Multicenter, double-blind RCTs studying dexmedetomidine with delirium as an endpoint.

MENDS: dexmedetomidine vs. lorazepam\(^1\)
  - Dex: more combined delirium and coma-free days

DEXCOM: dexmedetomidine vs. morphine\(^2\)
  - Dex: shorter duration of delirium

SEDCOM: dexmedetomidine vs. midazolam\(^3\)
  - Dex: shorter duration of delirium

\(^1\)Pandharipande PP *JAMA*. 2007;298(22):2644-2653.
\(^3\)Riker RR *JAMA*. 2009;301(5):489-499.
Dexmedetomidine and Delirium

• In MV patients at risk for developing delirium, dexmedetomidine administered for sedation may be associated with a lower prevalence of delirium compared to benzodiazepine infusions (B).

• We suggest that sedation strategies using nonbenzodiazepine sedatives (either propofol or dexmedetomidine) may be preferred over sedation with benzodiazepines to improve clinical outcomes in MV patients (+2B).

Reducing ICU Delirium

- Treat pain first!
- Promote consciousness!
- Prevent delirium
- Wean MV
- Increase mobility

- Increase patient participation
- Promote patient recovery
- Reduce complications
- Improve patient outcomes*


(Photo by Chris Hartlove for The New York Times)
Additional Slides
The DSM-5 criteria, level of arousal and delirium diagnosis: inclusiveness is safer

European Delirium Association* and American Delirium Society