

## Critical Care PRN and Society of Critical Care Medicine Focus Session—Sedation and Delirium in the ICU: Update on the Status of the 2011 SCCM Guidelines

Activity No. 0217-0000-11-079-L01-P

### Monday, October 17

3:45 p.m.–5:45 p.m.

Convention Center: Spirit of Pittsburgh Ballroom A

*Moderator: Jeremy D. Flynn, Pharm.D., BCPS*

Assistant Professor, Department of Pharmacy Practice and Science, University of Kentucky, Lexington, Kentucky

### Agenda

- 3:45 p.m. Pharmacologic Options for Analgesia and Sedation in the Critically Ill  
*Joseph F. Dasta, M.S., FCCP*  
Professor Emeritus, The Ohio State University College of Pharmacy, Adjunct Professor, The University of Texas College of Pharmacy, Austin, Texas
- 4:15 p.m. Interruption and Mobilization  
*John Kress, M.D.*  
Associate Professor of Medicine, University of Chicago  
Department of Medicine, Section of Pulmonary and Critical Care  
Director, MICU, Chicago, Illinois
- 4:45 p.m. Recognizing, Preventing, and Treating Delirium in the Critically Ill  
*John W. Devlin, Pharm.D., FCCP, BCPS*  
Associate Professor of Pharmacy, Northeastern University,  
Boston, Massachusetts
- 5:15 p.m. Practical Application of the Guidelines to Daily Practice  
*Gilles L. Fraser, Pharm.D., FCCM*  
Professor of Medicine, Tufts University School of Medicine;  
Clinical Specialist, Critical Care, Maine Medical Center,  
Portland, Maine

### Faculty Conflict of Interest Disclosures

Joseph F. Dasta: consultant/member of advisory board for Cadence Pharmaceuticals, Hospira, Pacira Pharmaceuticals, Otsuka America Pharmaceuticals, Edge Therapeutics; speaker's bureau for Cadence Pharmaceuticals.

John W. Devlin: speaker's bureau for Hospira Pharma; received grant funding/research support from Hospira Pharma.

Gilles L. Fraser: no conflicts to disclose.

John Kress: information not provided to ACCP.

## Learning Objectives

1. Summarize the pharmacologic options for analgesia and sedation in ICU patient populations.
2. Review and implement the guideline recommendations, specifically those that represent significant changes in practice.
3. Discuss the current literature that supports the recommendations.
4. Discuss the barriers and challenges to daily sedation interruption in a heterogeneous group of ICU patients (medical, surgical, neuro, etc.) .
5. Review the literature and benefit of early mobilization in ICU patients and its association with clinical outcomes .
6. Determine the potential influence of sedation pharmacotherapy on mobilization, neuromuscular weakness, and clinical outcomes.
7. Describe the association between sedation interruption, mobilization, and functional outcomes of ICU patients.
8. Describe the clinical significance of delirium in patients in the ICU.
9. Describe how to incorporate the use of delirium screening tools into daily practice.
10. Identify reversible risk factors for delirium in critically-ill patients and then develop practice strategies to minimize the exposure of patients to these risk.
11. Develop an evidence-based treatment plan for delirium in a critically-ill patient.
12. Discuss the potential difficulties with incorporating the major changes suggested in the guidelines to daily practice.
13. Review potential strategies to successfully implement daily interruption of sedation and early mobilization into daily practice.
14. Develop a comprehensive sedation plan to minimize adverse events, avoid delirium and hasten separation from mechanical ventilation.

## Self-Assessment Questions

Self-assessment questions are available online at [www.accp.com/am](http://www.accp.com/am)

## Pharmacologic options for analgesia and sedation in the critically ill

*Joseph F. Dasta, M.Sc., FCCM, FCCP*  
Professor Emeritus  
The Ohio State University  
Adjunct Professor  
University of Texas

## Disclosures

- Consultant
  - Cadence, Hospira, Pacira
- Member, speakers bureau
  - Cadence
  - France Foundation (funded by Hospira)

## Update on the SCCM Guideline *Pain, Agitation, Delirium (PAD)*

- First official meeting January 2006
- 20 expert panel members -3 Pharmacists
  - pain, sedation, delirium, outcomes teams
- Database >19,000 articles
- GRADE system used
  - Quality of the evidence
  - Strength of the recommendations
- Each team developed relevant questions

## Update of the SCCM Guideline *Pain, Agitation, Delirium (PAD)*

- Each question
  - Evidence (high, moderate, low/very low)
  - Strength of recommendation
    - Strong, i.e., We recommend....
    - Weak, i.e., We suggest....
    - No recommendation (expert opinion not permitted)
- No industry funding or involvement
- Conflict of interest statement reported by all members

## Update of the SCCM Guideline *Pain, Agitation, Delirium (PAD)*

- Published in full Critical Care Medicine
- Executive summary AJHP
  - ASHP is a sponsoring organization
- Due to rigorous process there should be
  - No surprises
- Task force members embargoed until guideline appears in public forum (in press)

## ICU Analgesic Pharmacopeia

- IV opioids
- IV NSAIDS
- IV acetaminophen
- Elastomeric pumps with local anesthetics delivered to the wound site
- IV ketamine
- Epidural, neuraxial administration
- Potential future drugs
  - IV diclofenac
  - Depo-bupivacaine injected at wound site
  - Sublingual sufentanil delivery device
  - Morphine 6-glucuronide

### Clinical and Economics of Inappropriate Acute Pain Management

- Continued pain can result in increased complications, delirium, and longer LOS
- Oversedation prolongs ventilator time & LOS
- Difficult to implement early mobilization efforts when ICU patients experience pain
- Multimodal approach is often successful
- Analgesic ADEs are expensive
- Most analgesics have a low acquisition cost
- No cost-effectiveness studies exist

### Pain in the ICU

- >50% of ICU patients experience pain
  - Procedural and non-procedural pain
- Too many patients relate the terrors of experiencing pain acutely, which can lead to chronic pain
- We just aren't doing a very good job
- Pain should be assessed repeatedly
- Validated pain assessment tools should be used – examples include BPS, CPOT

### Treating Agitation

- Trend towards titrating to a lighter degree of sedation
- Increasing use of early mobilization
- Trend to minimizing wide-spread use of benzodiazepines
- Increased appreciation of pharmacoeconomic implications of Inadequate or excessive sedation
  - Effects on LOS and time on the ventilator
  - Increase in health care costs

### Life in the real world

- Greater than 40% patients are more deeply sedated than desired
- Drug-induced coma present during 32% of patient evaluations
  - Yet only 2.6% rated as “oversedated”
- How could this be?
- Not in my ICU

*Crit Care Med 2007;35:393 Anesthesiology 2007;106:687*

### ICU Sedation Pharmacopeia

- Benzodiazepines – GABA agonists
  - Long history of use acutely and long-term
  - Differ by pharmacokinetic properties
  - Recent appreciation of deliriogenic effects
  - Respiratory and cardiovascular depression
- Propofol – GABA agonist
  - Long history of use in OR and ICU
  - Respiratory and cardiovascular depression
  - Recent appreciation of PRIS

### ICU Sedation Pharmacopeia

- Fospropofol (Aqueous solution)
  - Prodrug converted to propofol in blood
  - One pilot study in ICU patients
    - Sedation target achieved
    - Triglyceride concentrations fell by 6 mg/dL with fospropofol; increase by 31 mg/dL with propofol
- Ketamine
  - Resurgence of interest
  - Use in non-dissociative dosages
  - Opioid sparing and sedative sparing

*Anesth Analg 2011;113:550*

### Dexmedetomidine

- Alpha-2-adrenergic agonist
  - Sedating, anxiolytic, and opioid-sparing properties
  - Permits patient awareness and responsiveness upon stimulation (“cooperative” sedation)
- Clinical perspective
  - No loading dose needed
  - Does not cause respiratory depression
  - May play a role in ventilator weaning
  - Sympatholytic (hypotension and bradycardia)
  - Don’t adjust dosage any sooner than q 20-30 min
  - Increasing experience in alcohol withdrawal

Ann Pharmacother 2009;43:2064

### SEDCOM:

#### Dexmedetomidine vs Midazolam

- Double-blind, randomized, multicenter trial comparing long-term (> 24 hr) dexmedetomidine (dex, n = 244) with midazolam (mz, n = 122)
- Sedatives (dex 0.2-1.4 ug/kg/hr or mz 0.02-0.1 mg/kg/hr) titrated to light sedation (RASS -2 to +1), administered up to 30 days
- All patients underwent daily arousal assessments and drug titration Q 4 hours

Outcome	Midazolam (n = 122)	Dexmedetomidine (n = 244)	P-Value
Time in target sedation range, %	75.1	77.3	0.18
Duration of sedation, days	4.1	3.5	0.01
Time to extubation, days	5.6	3.7	0.01
ICU LOS, days	7.6	5.9	0.24
Delirium prevalence	93 (77%)	132 (54%)	0.001
Delirium-free days	1.7	2.5	0.002

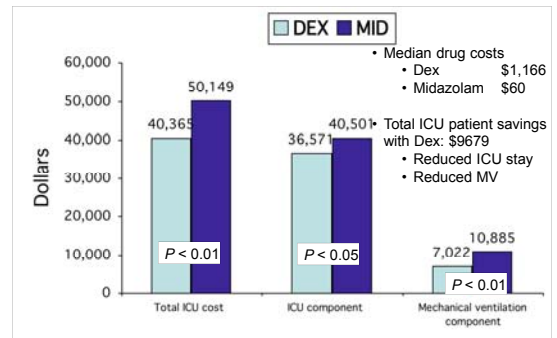
JAMA. 2009;301(5):489

### SEDCOM Trial: Safety Outcomes

Outcome	Midazolam (n = 122)	Dexmedetomidine (n = 244)	P-Value
Bradycardia	23 (18.9%)	103 (42.2%)	0.001
Bradycardia needing treatment	1 (0.8%)	12 (4.9%)	0.07
Tachycardia	54 (44.3%)	62 (25.4%)	0.001
Hypertension requiring intervention	36 (29.5%)	46 (18.9%)	0.02
Hyperglycemia	52 (42.6%)	138 (56.6%)	0.02
Infections	24 (19.7%)	25 (10.2%)	0.02

JAMA. 2009;301(5):489

### SEDCOM Cost of Care



Crit Care Med. 2010;38:497-503.

### Effects of Early Mobilization in Mechanically-ventilated ICU patients

- Shift in care from deep to light sedation
- Early mobilization of patients may improve functional outcomes and delirium
- 104 ICU patients ventilated <72 hours
- Randomized trial
  - Daily sedation interruption with early exercise and mobilization (PT and OT)
  - Daily sedation interruption and standard care

Lancet 2009;373:1874.

### Results

Variable	Control	Intervention	P-value
Days ICU delirium	4 (2-7)	2 (0-6)	0.03
% time with delirium	57 (33-69)	33 (0-58)	0.02
Days of ventilation	6.1 (4-9)	3.4 (2-7)	0.02
Days of ICU stay	7.9 (6-13)	5.9 (4-13)	0.08

Lancet 2009;373:1874.

## Analgo-sedation

- Provide analgesics First, then supplement with sedative-hypnotic, if needed
- Also known as analgesia-first (A-1) sedation
- Acknowledges that pain is a cause of agitation
- Nine trials in Europe, one trial in Thailand
- Continuous infusion of remifentanyl or fentanyl vs. sedative-hypnotic based regimen and prn opioids
- 30–74% required benzodiazepine/propofol rescue
- Encouraging results of shorter ICU time with analgo-sedation regimen but the final word isn't in yet

*Anesthesiology*, 2004;101:640  
*Br J Anaesth*, 2007;98:76  
*Intensive Care Med*, 2009;35:291  
*Lancet*, 2010;375(9713):475

## Summary

- Renewed focus on pain, then agitation
- Better understanding of benefits and risks of the pharmacopeia of available agents
- Protocolized care is preferred
- Evaluate total cost of care
- Promising new analgesics that may reduce the incidence of opioid-associated ADEs
- No new sedatives in the horizon

## Rationale and Bedside Application of the “proposed” SCCM Guidelines for the Management of Pain, Agitation, Delirium

Gil Fraser, Pharm.D., FCCM  
Clinical Pharmacist in Critical Care Medicine  
Maine Medical Center

Professor  
Tufts University School of Medicine  
Boston

## Conflicts of Interest

### Your Job for Today

- Understand new data that redefine risks and benefits of drug management options
- Identify barriers to the bedside incorporation of the major changes of the revised PAD guidelines
- Evaluate various strategies for bedside implementation of best practice
- Develop a comprehensive plan to provide patient comfort in the ICU

### My Job for Today

- Indirectly discuss details of the upcoming SCCM guidelines (currently proprietary)
  - Data supporting these guidelines IS a matter of public record

### Step 1...Incorporate Valid and Reliable Assessment Tools (and know their limitations!)

- Pain
  - Patient self report = NRS
    - Otherwise, BPS and CPOT
      - In patients with motor function
  - Hemodynamic changes are not specific
- Agitation and Sedation
  - RASS, SAS, etc
    - Not useful for deep sedation or with therapeutic paralysis
  - Intentionally deep sedation or with pharmacologic paralysis
  - Auditory evoked potential, bispectral index, patient state index, state entropy
    - Only if clinical evaluation is unavailable or when EMG artifact is limited
- Delirium
  - CAM-ICU, ICDSC, etc
    - Scoring may be dependent on status of sedation

### Assessing ICU Pain and Discomfort

- Why is this so difficult for caregivers?
  - What is routine to us is hardly routine to the patient
    - Mere presence of an ETT, repositioning, catheters in every orifice, machines, noise, sleep deprivation, inability to communicate, loss of autonomy, drug-induced stupor, confusion, delirium, fear, loss of health, constipation, being tethered and tied down, etc, etc
  - Underappreciation for how poorly we assess pain
    - 82% remember pain and discomfort as traumatic. Schelling CCM 2003
  - Underuse of validated behavioral pain scales
    - CPOT (Critical Care Pain Observation Tool) and BPS (Behavioral Pain Score)
      - Based on facial expression, body movement, and compliance with the vent
  - Underuse of analgesia including pre-emptive use with painful procedures Puntillo. Am J Crit Care 2001

Clinical practice pearl: Patient self-report remains the gold standard and if not possible—and motor function is intact--- behavioral pain scales should be utilized. Hemodynamic derangement is not an adequate indicator of pain, but can be used to prompt further evaluation.

### Monitoring Agitation and Sedation

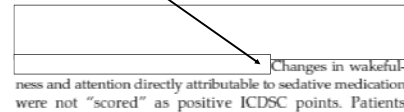
- Several validated scales available
  - RASS, SAS, etc
  - Associated with improved outcomes by identifying aberrant behaviors early
    - 60% reduction in severe agitation Charques. CCM 2006
  - Only for patients who are able to respond...once coma or paralyzed, these scales do not provide useful information
    - Computerized processed EEG may be helpful for these patients as long as EMG artifact is appreciated.
      - Auditory evoked potential, bispectral index, patient state index, state entropy

## Why Systematically Assess Delirium?

- Any data suggesting that this reduces delirium prevalence?
  - No!
- Any data suggesting that this reduces its severity?
  - No!
- So why bother?
  - Prompts timely identification of clinically relevant reversible causes ...infections, etc
  - Prompts scrutiny of drug therapy

## Validated Delirium Screening Tools

- CAM-ICU
  - Twice daily evaluations involving patient-nurse interactions
- ICDS-C
  - Twice daily evaluations based on nursing observations
- Both based on DSM IV criteria, but sedation influence is less with ICDS-C



**Assessment of Delirium Relative to Daily Sedative Interruption**

JF Poston MD, MW Sjoding MD, AS Pohlman RN MSN, BK Gehlbach MD, JB Hall MD, JP Krass MD  
Section of Pulmonary and Critical Care Medicine  
University of Chicago

55 blinded delirium assessments in 21 MICU patients

**CAM results are highly influenced by degree of sedation at the time of delirium assessment**

Before sedative interruption: Delirium-Coma free: 1, **Delirious: 40**, Coma: 14  
 After sedative interruption: Delirium-Coma free: 23, **Delirious: 27**, Coma: 5

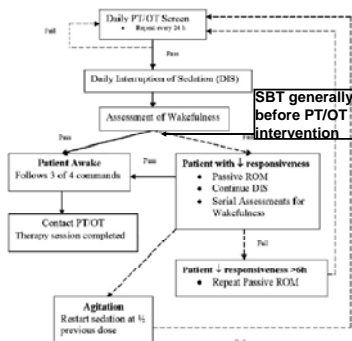
Are all deliria the same?

Is ICU delirium similar to geriatric medical delirium?  
 Is drug induced delirium similar to delirium from a metabolic or infectious cause?

## Practical Points About Assessing PAD

- Optimal time for assessment = when patient is awakened to the point of responding to commands
  - Allows self-report for pain
  - Facilitates patient readiness for extubation and helps to avoid iatrogenic coma
  - Identifies sedative medications as a potential source for delirium
  - Facilitates early mobility efforts

## Early Mobility; A Matter of Coordination



Pohlman, CCM 2010

## More Practical Aspects of Early Mobilization

- Coordination of efforts
  - Frequent communication between RN, RT, PT/OT re: SAT, SBT, and EM efforts
- Timing may be critical
  - NO SENSE to do this when patients are busy with exams, imaging, and travel
    - If standardized, done in the late morning or afternoon?
- Short acting drugs (fentanyl, propofol, dexmedetomidine) facilitate effort Tanios J Crit Care 2009
- May require expansion of ICU PT/OT resources



## Typical Sedation Titration Goal = "Light" Sedation

- But what is light sedation?
- No consensus on this definition
- Overarching goal is to consistently focus on patient safety and comfort
  - If sedation is required, titrate to responsiveness and awareness
- Wakefulness = ability to respond to commands: open eyes, maintain eye contact, squeeze hand, stick out tongue, wiggle toes

## Providing Pharmacologically Based Interventions: Importance of Protocolization

- Helps bring "best practice" to the bedside
- Limits practice variation
- Reduces delays in management
  - Encourages regular assessment of pain, agitation, delirium
  - Facilitates pharmacologic interventions: drug choice, dosing, titration

## Surveys of ICU Sedation Practices

Mehta Crit Care Clin 2009

Author	Assessment Tools	16-88%	20-80%	1-78%
Chomarov & Therasolep, 1997 <sup>1</sup>	16% (all Ramsay)	33%	NR	NR
Murdoch & Cohen, 2000 <sup>2</sup>	67% (20% Ramsay)	NR	NR	NR
Soltman et al., 2001 <sup>3</sup>	43% (74% Ramsay)	NR	NR	NR
Samuelson et al., 2003 <sup>4</sup>	14% (Ramsay, Addenbrooke, neuro-ethic, sedo)	27%	1%	NR
Rhoney & Murray, 2003 <sup>5</sup>	78% (43% GCS, 42% Ramsay)	33%	NR	NR
Gustbrand et al., 2004 <sup>6</sup>	3.7% (14% MAA5, 3% Ramsay)	41%	13%	NR
Martin et al., 2005 <sup>7</sup>	31% (8% Ramsay)	21%	NR	NR
Ambridge et al., 2005 <sup>8</sup>	NR	NR	NR	NR
Kanoo et al., 2005 <sup>9</sup>	14% (all Ramsay)	30%	NR	NR
Tamos et al., 2005 <sup>10</sup>	NR	64%	40%	NR
Mehta et al., 2006 <sup>11</sup>	49% (87% Ramsay, 10% SAS, 9% GCS, 8% MAA5)	29%	40%	NR
Egerod et al., 2006 <sup>12</sup>	44% (mostly Ramsay)	23%	31%	NR
Martin et al., 2006 <sup>13</sup>	46% (mostly Ramsay)	52%	34%	NR
Martin et al., 2007 <sup>14</sup>	33% (mostly Ramsay)	38%	14%	NR
Ahmed et al., 2007 <sup>15</sup>	28% (48% Ramsay, 16% RASS, 15% SAS)	36%	0%	NR
Payen et al., 2007 <sup>16</sup>	88% (86% Ramsay)	80%	78%	NR
Reichner et al., 2008 <sup>17</sup>	75% (GCS 56%, SAS 25%, 8% RASS)	54% sedation	62%	NR
O'Connor & Bucknall, 2009 <sup>18</sup>	8%	43%	43%	NR
Patel et al., 2009 <sup>19</sup>	80% (88% Ramsay, 26% RASS)	71%	71%	NR

Adherence to protocols ~50%

Tamos, J Crit Care 2009

## Why Are Protocols Not Used?

- Potential barriers
  - Nursing acceptance, potential for medical device removal, airway compromise, and patient discomfort. Roberts. J Crit Care 2010, Tanios Crit Care Med 2005: A793
  - Lack of a physician order along with difficulties in managing patient issues in real time Tanios, J Crit Care 2009
  - *ICU patients and protocols are too complex*

## Facilitating Rapid Knowledge Transfer to the Bedside

- Options
  - Use clinical practice guideline as a model
  - Develop protocols for managing pain/agitation/delirium
  - Develop preprinted or electronic "order sets" based on institution specific protocols
  - Offer real time clinical decision support
- Create "bundles" for implementing essential components of practice guidelines
  - Consider daily rounding pharmacist or quality checklist with these elements Marshall, Crit Care Med 2008, Dubose J Trauma 2008

Hint: ADAPT then ADOPT previously developed tools

## ICU Care Bundles

- Many examples: VAP, sepsis, central line placement, etc
- Elements should
  - Be easy to implement and measure
  - Have proven benefit
  - Be supported by sound scientific and clinical reasoning
  - Be relevant across a wide range of patient populations and health-care systems
- Bundle metrics can be used for caregiver feedback and as part of a rapid-cycle change process improvement effort

### Pain, Agitation, Delirium (PAD) Bundle

Major Components = *Identify, Manage, Monitor* with Metrics

Make your own "bundle" with elements and metrics

1. Systematically assess and document PAD
  - At least 4x/shift for pain and agitation and 1x/shift for delirium
2. Ensure that measures to prevent and treat PAD are a part of routine ICU care
  - Adhere to institution-specific protocols
  - Provision of analgesia prior to painful procedures
  - Provide management < 0.5 h of discomfort or agitation
  - Achieve sedation goal without coma or dangerous agitation
  - Document strategies to prevent delirium each day
3. Monitor the effectiveness of these strategies
  - % time spent in drug induced coma (SAS 1-2)
  - % patients reporting moderate to severe pain
  - % SBT failed due to excessive sedation or agitation
  - ICU ventilator time (or ventilator-free time)
  - % patients developing delirium during the ICU stay

### Translation Into Practice

*Assumes that*

- 1) primary causes for pain, agitation, and delirium are addressed
- 2) non-pharm management options are in place including adjustment of vent settings
- 3) patient behaviors are troublesome and/or pose a risk

**Step 1** → Assess and treat pain

- Routinely assess pain in all ICU patients using self-report if possible (NRS)
- For patients with intact motor function, but unable to self-report, assess pain with BPS or CPOT
- Preemptively treat procedural pain
- Opiates may be preferred especially if an analgesia-first approach is used.

### Translation Into Practice

*Assumes that*

- 1) primary causes for pain, agitation, and delirium are addressed
- 2) non-pharm management options are in place including adjustment of vent settings
- 3) patient behaviors are troublesome and/or pose a risk

**Step 2** → Assess delirium and the need for sedation

- Assessment for delirium and agitation/sedation should be routine for all ICU patients
  - Use CAM-ICU or ICDSC assessment tools for delirium
  - Use RASS or SAS assessment tools for sedation
  - Use protocols and checklists to facilitate sedation management

### Translation Into Practice

*Assumes that*

- 1) primary causes for pain, agitation, and delirium are addressed
- 2) non-pharm management options are in place including adjustment of vent settings
- 3) patient behaviors are troublesome and/or pose a risk

**Step 3** → Treat delirium and manage sedation

- Early mobilization
- Employ analgesia-first sedation in intubated patients
- Avoid benzodiazepines when delirium is not related to alcohol or benzodiazepine withdrawal
- Target lightest level of sedation possible or use daily sedation interruption

To improve is to change; to be perfect is to change often. **Winston Churchill**



For questions/comments/copy of slides  
email: fraseg@mmc.org