Prevention and Management of Delirium in Surgical and Critically Ill Patients

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Learning Objectives

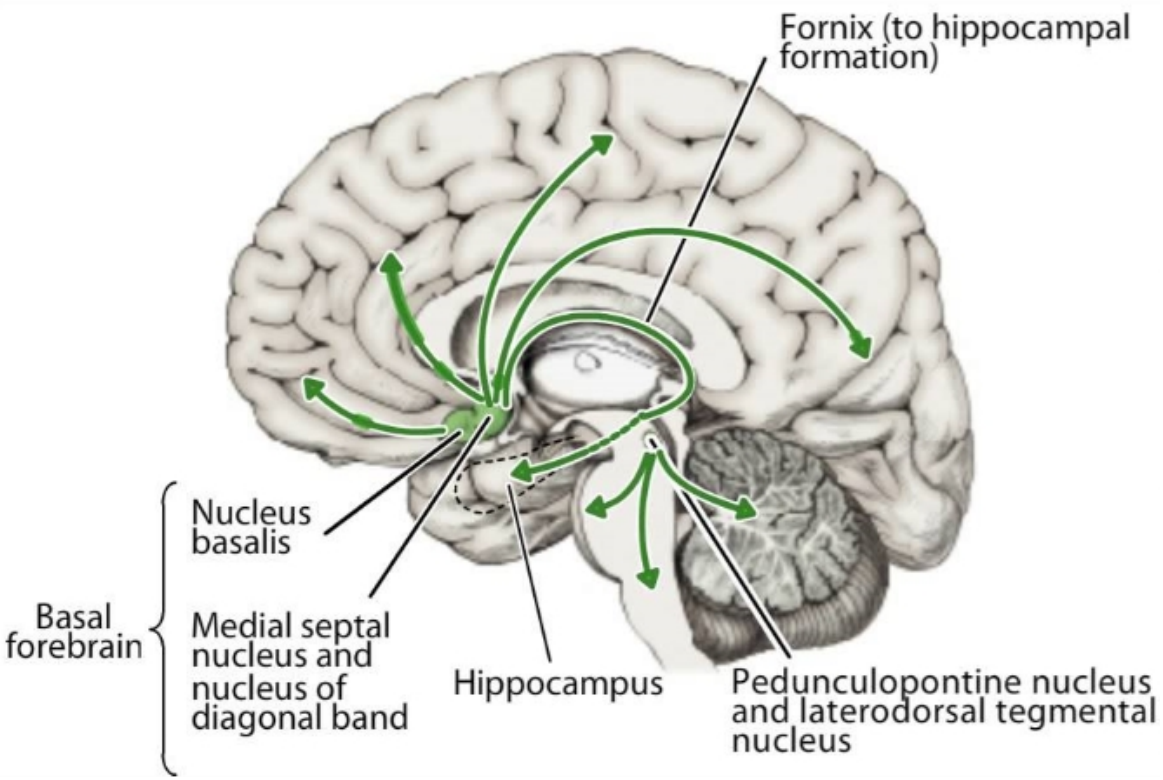
- Demonstrate a basic understanding of delirium
- Appreciate why post-surgical and critically ill patients are such a high-risk population for developing delirium
- Understand pharmacologic approaches to managing both hypoactive and hyperactive types of delirium

Overview

- Delirium
  - Overview of causes, prevalence, consequences, CAM-ICU, RASS
- Pharmacologic interventions in delirium
  - Brief review of the evidence for delirium prevention/management strategies
- ABCDEF Bundle
  - ICU liberation strategy – best evidence to date
- Clinical examples
  - Management of delirium in a patient with polysubstance abuse and respiratory failure

Background – What is Delirium?

- Rapid onset change in mental status
- Direct physiological consequence of
  - Medical conditions
  - Substance intoxication or withdrawal
  - Multiple etiologies
- Clinical features
  - Waxing and waning course
  - Inattention, Disorientation
  - Paranoia, hallucinations, agitation



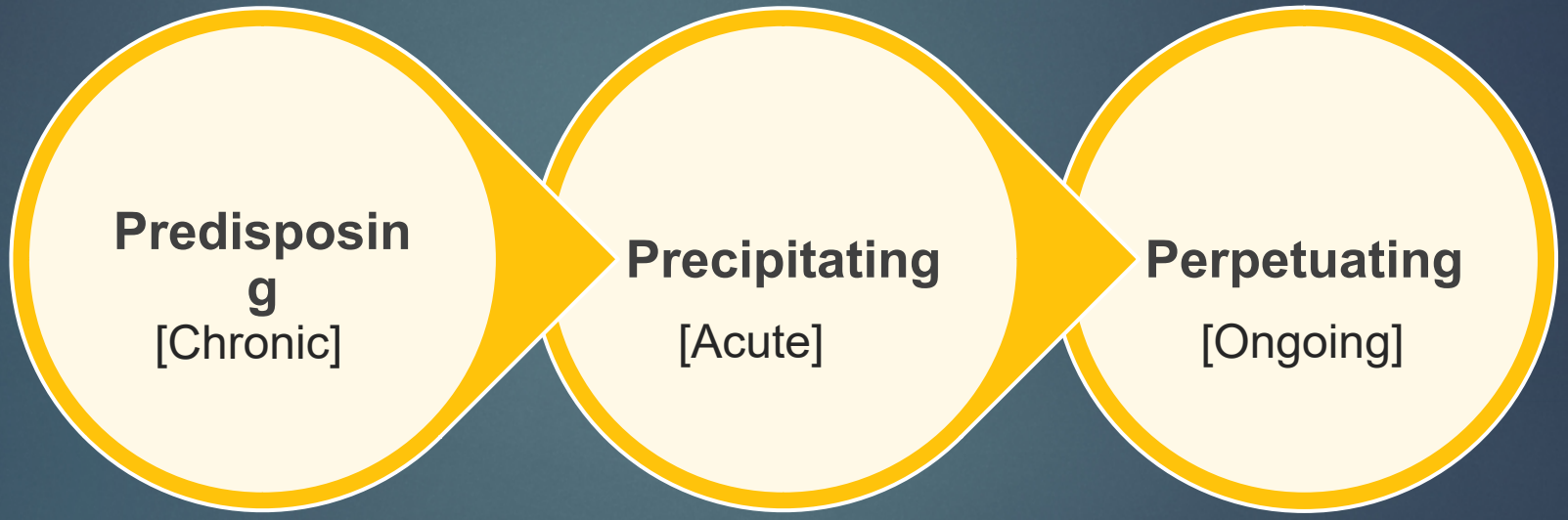
Cholinergic Projections

- Amygdala
- Hippocampus
- Cerebral Cortex
- Reticular Activating System

Acetylcholine: A Cholinergic Deficiency Hypothesis of Delirium

Background – What is Delirium?

- Not all delirium is created equally



- The more hits the brain takes, the more likely delirium is to develop

Delirium – Snowglobe metaphor

Predisposing

- Age >70
- Pre-existing dementia
- Severe medical Illness
- History of delirium
- Visual and hearing impairment
- Functional impairment
- Depression
- Polypharmacy
- Alcohol/ Benzodiazepine use

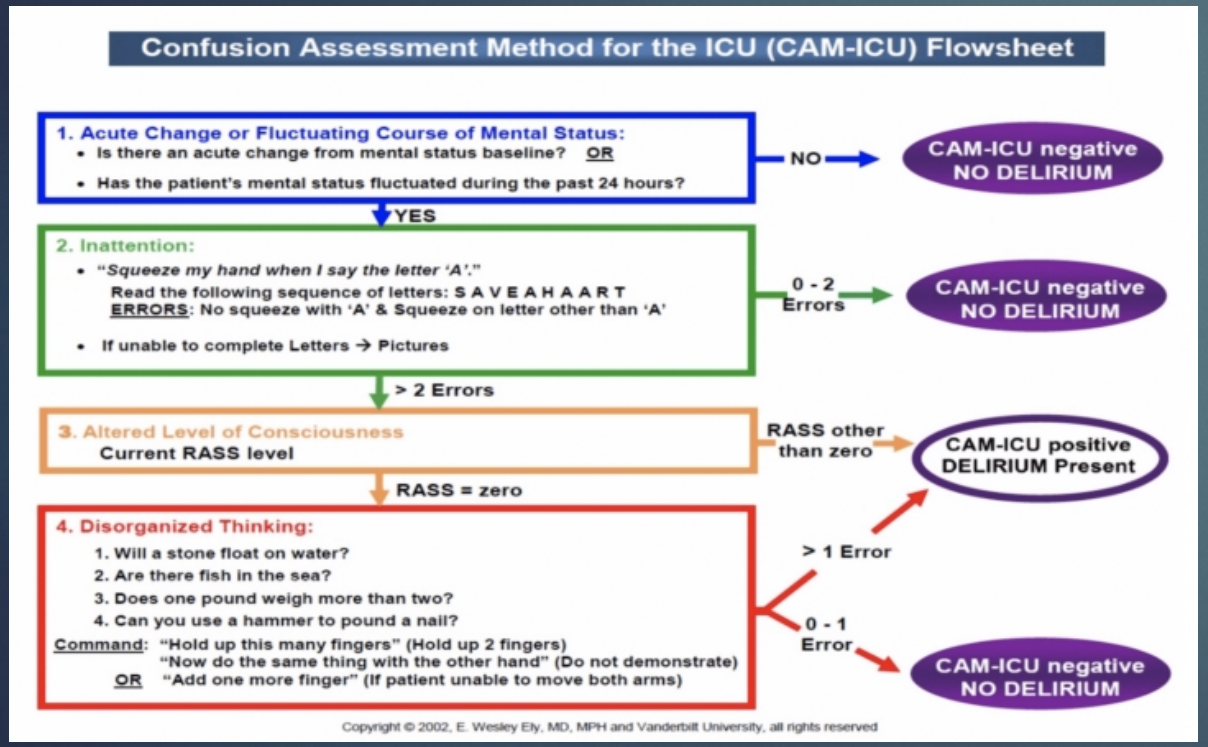
Precipitating

- Use of physical restraint
- Indwelling catheter
- Adding multiple meds
  - Sedative/hypnotic
- Abnormal Na, K, glucose
- Malnutrition/dehydration
- Surgery/Anesthesia
- Trauma or urgent admission
- Infection
- Hypoxia
- Pain

Inouye, SK, Westendorp, RG, Saczynski, JS. Delirium in elderly people. Lancet. 2014. 8;383(9920):911-922.

Delirium – How do we measure it?

CAM-ICU (Confusion Assessment Method – ICU)



RASS (Richmond Agitation Sedation Scale)

Richmond Agitation-Sedation Scale (RASS)

Score	Term	Description	
+4	Combative	Overtly combative, violent, immediate danger to staff	
+3	Very agitated	Pulls or removes tube(s) or catheter(s), aggressive	
+2	Agitated	Frequent nonpurposeful movement, fights ventilator	
+1	Restless	Anxious but movements not aggressively vigorous	
0	Alert and calm		
-1	Drowsy	Not fully alert but has sustained awakening (eye opening/eye contact) to *voice* (≥10 seconds)	Verbal Stimulation
-2	Light sedation	Briefly awakens to *voice* with eye contact (<10 seconds)	Verbal Stimulation
-3	Moderate sedation	Movement or eye opening to *voice* (but no eye contact)	Verbal Stimulation
-4	Deep sedation	No response to voice but movement or eye opening to *physical* stimulation	Physical Stimulation
-5	Unarousable	No response to *voice* or *physical* stimulation	Physical Stimulation

Significance

Why does it matter?

Delirium worsens patient outcomes

- ↑ Length of Stay (LOS)
- ↑ Mortality
- ↑ Institutionalization
- ↑ Cognitive decline
- ↑ Depression, anxiety

Evolutionary History of Pharmacotherapy for ICU Delirium

- Cholinesterase Inhibitors
- Antipsychotics
- Melatonin and Ramelteon
- Choice of sedative
- Interruption of sedation
- No sedation
- A-F Bundle

Effect of rivastigmine as an adjunct to usual care with haloperidol on duration of delirium and mortality in critically ill patients: a multicentre, double-blind, placebo-controlled randomised trial

Maarten M J van Eijk, Kit C B Roes, Marina L H Honing, Michael A Kuiper, Attila Karakus, Mathieu van der Jagt, Peter E Spronk, Willem A van Gool, Roos C van der Mast, Jozef Kesecioglu, Arjen J C Slooter

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Efficacy and safety of quetiapine in critically ill patients with delirium: A prospective, multicenter, randomized, double-blind, placebo-controlled pilot study*

John W. Devlin, PharmD; Russel J. Roberts, PharmD; Jeffrey J. Fong, PharmD; Yoanna Skrobik, MD; Richard R. Riker, MD; Nicholas S. Hill, MD; Tracey Robbins, RN; Erik Garpestad, MD

Psychosomatics 2013:xx:xxx

Original Research Reports

Prophylaxis with Antipsychotic Medication Reduces the Risk of Post-Operative Delirium in Elderly Patients: A Meta-Analysis

Polina Teslyar, M.D., Veronika M. Stock, M.D., Christopher M. Wilk, M.D., Ulas Camsari, M.D., Mark J. Ehrenreich, M.D., Seth Himelhoch, M.D., M.P.H.

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The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Haloperidol and Ziprasidone for Treatment of Delirium in Critical Illness

T.D. Girard, M.C. Exline, S.S. Carson, C.L. Hough, P. Rock, M.N. Gong, I.S. Douglas, A. Malhotra, R.L. Owens, D.J. Feinstein, B. Khan, M.A. Pisani, R.C. Hyzy, G.A. Schmidt, W.D. Schweickert, R.D. Hite, D.L. Bowton, A.L. Masica, J.L. Thompson, R. Chandrasekhar, B.T. Pun, C. Strength, L.M. Boehm, J.C. Jackson, P.P. Pandharipande, N.E. Brummel, C.G. Hughes, M.B. Patel, J.L. Stollings, G.R. Bernard, R.S. Dittus, and E.W. Ely, for the MIND-USA Investigators*

JAMA Internal Medicine | Original Investigation

Efficacy of Oral Risperidone, Haloperidol, or Placebo for Symptoms of Delirium Among Patients in Palliative Care
A Randomized Clinical Trial

Meera R. Agar, PhD; Peter G. Lawlor, MB; Stephen Quinn, PhD; Brian Draper, MD; Gideon A. Caplan, MBBS; Debra Rowett, BPharm; Christine Sanderson, MPH; Janet Hardy, MD; Brian Le, MBBS; Simon Eckermann, PhD; Nicola McCaffrey, PhD; Linda Devilee, MBus; Belinda Fazekas, BN; Mark Hill, PhD; David C Currow, PhD

PADIS Guidelines - 2018

- *This evidence suggests that the use of the typical antipsychotic, haloperidol, an atypical antipsychotic, or a statin was not associated with a shorter duration of delirium, mechanical ventilation or ICU LOS, or decreased mortality*
  - Discourages the “routine” use of antipsychotic agents in the treatment of delirium, the shortterm use of haloperidol or an atypical antipsychotic in patients may be warranted, despite a lack of evidence, for those who experience significant distress secondary to the symptoms of a delirium, such as:
    - hallucination and/or delusion-associated fearfulness
    - agitation that may be physically harmful to themselves or others
  - However, all antipsychotic agents should be discontinued immediately following the resolution of the patient’s distressful symptoms.

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Research

Original Investigation

Preventive Effects of Ramelteon on Delirium
A Randomized Placebo-Controlled Trial

Kotaro Hatta, MD, PhD; Yasuhiro Kishi, MD, PhD; Ken Wada, MD, PhD; Takashi Takeuchi, MD, PhD; Toshinari Odawara, MD, PhD; Chie Usui, MD, PhD; Hiroyuki Nakamura, MD, PhD; for the DELIRIA-J Group

Mol Neurobiol
DOI 10.1007/s12035-015-9350-8

CrossMark

Exogenous Melatonin for Delirium Prevention: a Meta-analysis of Randomized Controlled Trials

Sheng Chen[1] · LiGen Shi[1] · Feng Liang[1] · Liang Xu[1] · Doycheva Desislava[2] · Qun Wu[1] · Jianmin Zhang[1]

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MIDEX

PRODEX

CLINICAL INVESTIGATION

Comparative study of propofol versus midazolam in the sedation of critically ill patients

Results of a prospective, randomized, multicenter trial

Chamorro, Carlos MD; de Latorre, Francisco J. MD; Montero, Antonio MD; Sanchez-Izquierdo, Jose A. MD; Jareno, Antonio MD; Moreno, Jose A. MD; Gonzalez, Ester MD; Barrios, Manuel MD; Carpintero, Jose L. MD; Martin-Santos, Fernando MD; Otero, Beatriz MD; Ginestal, Ricardo MD **Author Information**

Critical Care Medicine: June 1996 - Volume 24 - Issue 6 - p 932-939

CARING FOR THE CRITICALLY ILL PATIENT

Dexmedetomidine vs Midazolam or Propofol for Sedation During Prolonged Mechanical Ventilation

Two Randomized Controlled Trials

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Efficacy and safety of a paired sedation and ventilator weaning protocol for mechanically ventilated patients in intensive care (Awakening and Breathing Controlled trial): a randomised controlled trial

Timothy D Girard, John P Kress, Barry D Fuchs, Jason W W Thomason, William D Schweickert, Brenda T Pun, Darren B Taichman, Jan G Dunn, Anne S Pohlman, Paul A Kinniry, James C Jackson, Angelo E Canonico, Richard W Light, Ayumi K Shintani, Jennifer L Thompson, Sharon M Gordon, Jesse B Hall, Robert S Dittus, Gordon R Bernard, E Wesley Ely

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ORIGINAL ARTICLE

Nonsedation or Light Sedation in Critically Ill, Mechanically Ventilated Patients

Hanne T. Olsen, M.D., Helene K. Nedergaard, M.D., Ph.D., Thomas Strøm, M.D., Ph.D., Jakob Oxlund, M.D., Karl-Andre Wian, M.D., Lars M. Ytrebø, M.D., Ph.D., Bjørn A. Kroken, M.D., Michelle Chew, M.D., Ph.D., Serkan Korkmaz, Jørgen T. Lauridsen, M.Sc., and Palle Toft, M.D., D.M.Sc.

A protocol of no sedation for critically ill patients receiving mechanical ventilation: a randomised trial

Thomas Strøm, Torben Martinussen, Palle Toft

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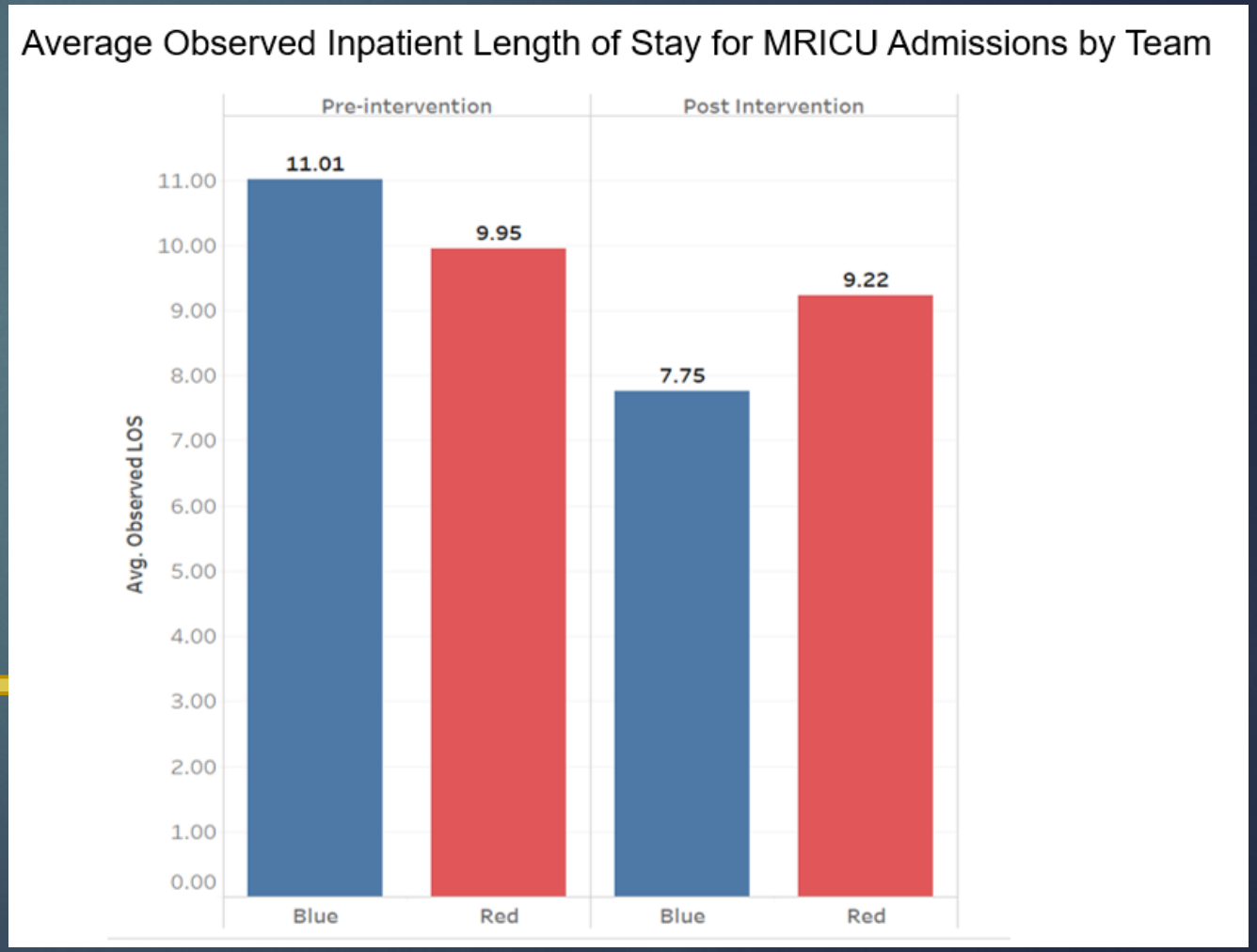


Clinical Example – Polysubstance abuse and Respiratory Failure

- HPI: 45 yo M with DM, COPD, CKD and alcohol dependence who was admitted to the STICU after getting into a MVA now with open tib fib fx, intubated in the field
- Substance Hx:
  - EtOH: Drinks 2 pints of vodka daily
    - Hx prior DTs, seizures, ICU stays for alcohol withdrawal
  - Drug use: Pt has a documented history of opportunistic use of cocaine, amphetamines, benzodiazepines and other street drugs
    - Pt has been unable to sustain sobriety despite multiple inpatient and outpatient treatment programs
  - Tobacco: 1 PPD, 30 pack year smoker

Clinical Example – Polysubstance abuse and Respiratory Failure

- Now HD 3, s/p operative repair, remains on the ventilator on pressure support mode with PEEP of 5
- CAM-ICU assessments have consistently been positive
- RASS scores have ranged from -3 to +3 over the past 24 hours, and efforts to wean sedation have been complicated by agitation
  - Midazolam 4mg/hr
  - Fentanyl 175 mcg/hr + boluses
  - Dexmedetomidine 1.2 mcg/kg/hr
- Pt is on CIWA scale for alcohol withdrawal and has been receiving an average of 16mg lorazepam per day
  - He has also been getting PRN lorazepam 1st line for agitation

Clinical Example – Polysubstance abuse and Respiratory Failure

- Exam:
  - VS: T 37.1, HR 88, RR 16, BP 131/85
  - Mental Status:
    - On Sedation: RASS -3, intermittent spontaneous movement but no purposeful eye contact or other behavior
    - Off sedation: RASS +2, frequent nonpurposeful movement and fights against the ventilator and restraints. Unable to follow commands and not verbally redirectable
  - Workup for other causes of delirium have been unremarkable
    - Head CT normal, EEG notable for generalized slowing without evidence of seizures, LP unremarkable, no other evidence of infection, organ failure, etc.

Clinical Example – Polysubstance abuse and Respiratory Failure

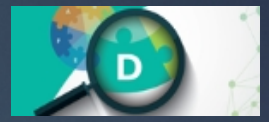
- Question:
  - How do you approach management of this patient's delirium?

- Start by identifying contributors to delirium:
  - Major trauma, emergency surgery
  - Polypharmacy – Midazolam, Lorazepam, Fentanyl, (Dexmedetomidine)
  - Alcohol dependence and alcohol withdrawal, on CIWA despite CAM-ICU+
  - Respiratory failure requiring invasive instrumentation (ETT, NGT)
  - Physical restraints, immobilization and deconditioning
  - Sleep/wake cycle disruption

Clinical Example – Polysubstance abuse and Respiratory Failure

- Contributors to delirium become **Targets** for intervention
  - Polypharmacy:
    - Wean sedation from most -> least deliriogenic. Consider analagosedation
    - Utilize PRN antipsychotics to target agitation
  - Substance withdrawal:
    - D/C CIWA protocol, avoid benzodiazepine intoxication
  - Respiratory failure:
    - Continue SAT/SBT daily, using PRN antipsychotics for breakthrough agitation
  - Physical restraints – Wrist restraints, ETT, NGT, foley catheter
  - Immobility
    - PT as soon as feasible to add on
  - Sleep/wake cycle disruption
    - Standing melatonin, quiet/restful environment at night, lights on during day

CHOICE OF ANALGESIA/SEDATION



DELIRIUM: ASSESS PREVENT/MANAGE

ASSESS, PREVENT & MANAGE PAIN

BOTH SAT & SBT

EARLY MOBILITY AND EXERCISE

FAMILY ENGAGEMENT AND EMPOWERMENT

Takeaway Conclusions

- Managing delirium in surgical patients
  - Identify contributors to delirium and reframe them as targets for intervention
  - Contribute to a culture of change which utilizes the A-F Bundle
  - Minimize deliriogenic exposures, particularly when considering:
    - Sedation
    - Management of substance withdrawal (avoid benzodiazepine intoxication)
  - Judicious use of antipsychotics for elevated RASS scores
    - Be sure to have a discontinuation plan in place
  - Consider melatonin to optimize sleep/wake cycle
  - Early mobilization with PT
  - Educate families about delirium and nonpharmacologic interventions they can help with
    - Frequent reorientation, mobilization, verbal redirection

Questions?

- Melissa.Bui@VCUHealth.org