

# Delirium

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Consultation-Liaison  
Psychiatry 2023

Integrating Care and Evidence Across the Lifespan



## CLP 2023

Disclosure: Beth Heaney, DNP

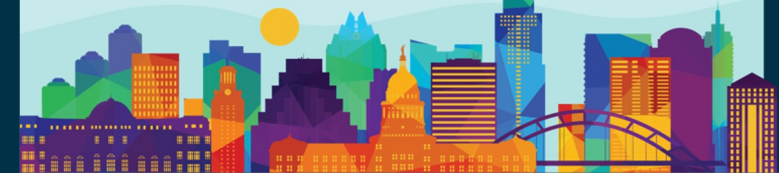
With respect to the following presentation, in the 24 months prior to this declaration there has been no financial relationship of any kind between the party listed above and any ACCME-defined ineligible company which could be considered a conflict of interest.



## CLP 2023

Disclosure: Hema Kher, MD

With respect to the following presentation, in the 24 months prior to this declaration there has been no financial relationship of any kind between the party listed above and any ACCME-defined ineligible company which could be considered a conflict of interest.



# Learning Objectives

- 1) Define delirium, and recognize the clinical features of delirium
- 2) Identify predisposing and precipitating factors of delirium
- 3) Describe the medical workup of delirium
- 4) Describe an approach for the prevention and management of delirium, including nonpharmacologic and pharmacologic interventions



# Consult Question:

It's your first day working on the psychiatry consult service at your hospital. You are paged by a concerned hospitalist with a new consult request.

“Mrs. Jones is an 85-year-old woman with Alzheimer’s dementia, admitted with a UTI. The patient will complete her antibiotic course today. Over the last few days, the patient has been somnolent during the day. Overnight, she was very agitated, pulled out her peripheral IV, and was placed in 4-point restraints. Family is distraught as this ‘isn’t like her at all!’ The primary team asks if the patient needs psychiatric hospitalization.”

What do you do next?



# Introducing: C-L How-To Guides!

The screenshot shows the ACLP website interface. At the top left is the ACLP logo and the text 'ACADEMY OF CONSULTATION-LIAISON PSYCHIATRY' and 'Advancing Integrated Psychiatric Care for the Medically Ill'. A search bar and a 'HELLO, HEMA' dropdown are on the top right. A navigation bar contains links for SIGS, About, News & Publications, Annual Meetings, Education, Training/Career, For Members, and Donate. The 'Training/Career' dropdown menu is open, with 'Resident Curriculum' and 'C-L How-To Guides' highlighted by red boxes. A red arrow points to the 'C-L How-To Guides' link. The main content area is titled 'C-L How To Guides' and includes a list of guide topics: [Doing a Consult](#), [Acute Agitation](#), [Alcohol Withdrawal](#), [Catatonia](#), [Clozapine](#), [Creating a Behavioral Plan](#), [Death and Dying](#), and [Delirium](#). The 'Delirium' link is also highlighted with a red box. A sidebar on the right contains a list of links including [Hackett Award Goes to Michael Sharpe, MA, MD, FACP](#), ['Intervening Earlier is Critical'](#), and a list of categories like [A&E](#), [Affiliate Organizations](#), [Announcements](#), [Annual Meeting](#), [Awards](#), [Clinical Practice](#), [Committees & Task Forces](#), [DEI](#), [Education & Recruitment](#), [Fellowship Program](#), and [President Updates](#).





# Introducing: CL How-To Guides!

## Academy of Consultation-Liaison Psychiatry How To Guide: Delirium

### How to Diagnose, Prevent, and Manage Delirium

#### Learning Objectives:

- 1) Understand the definition of delirium and recognize the signs and symptoms of the disorder.
- 2) Demonstrate an understanding of the pathophysiology of delirium.
- 3) Demonstrate knowledge of the most common etiologies of delirium and medical workup to evaluate for these etiologies.
- 4) Describe a treatment approach for the management of delirium, including nonpharmacologic and pharmacologic strategies.

#### Step 1: Familiarize oneself with the definition of delirium, including the signs and symptoms of delirium.

- Delirium is defined in the DSM-5 as an acute fluctuating disturbance of attention and awareness best explained by an underlying medical condition or combination of conditions.
- Signs and symptoms of delirium:
  - Diffuse cognitive deficits (attention, orientation, memory)
  - Temporal course (abrupt onset, fluctuations)
  - Psychosis (hallucinations, delusions)
  - Sleep-wake disturbance (fragmented sleep, reversal of normal cycle)
  - Psychomotor behavior (hyperactive, hypoactive, mixed)
  - Language impairment (word finding difficulties)
  - Altered affect (lability, irritability)
- Delirium has effects on affect, behavior, and cognition, or the “ABCs of delirium”:
  - Affect (anxiety or paranoia, irritability, apathy, mood shifts, personality changes)
  - Behavior (hallucinations, restlessness or agitation, sleep disturbances, psychomotor abnormalities)
  - Cognition (impaired memory, disorientation, disturbances in speech)

#### Step 2: Demonstrate an understanding of the basic pathophysiology of delirium.

- Delirium is characterized by a widespread disturbance of neural networks.
- Neurochemically, the principle disturbances that are linked to delirium involve reduced cholinergic function and excess of dopaminergic activity.
- Delirium syndrome reflects complex interactions among direct brain insults, aberrant stress responses, and neuroinflammatory mechanisms.
  - Direct brain insults include those caused by hypoxia, hypoglycemia, hyponatremia, stroke, trauma, and drug effects
  - Abnormal or exaggerated stress response from peripheral disturbances such as a

## Academy of Consultation-Liaison Psychiatry How To Guide: Delirium

- Neuroinflammatory mechanisms such as elevated cortisol levels or elevated levels of proinflammatory cytokines

#### Step 3: Investigate potential causes of delirium.

- Delirium has a wide variety of etiologies which may occur alone or in combination.
- No clear cause has been found in approximately 10% of cases.
- Once delirium is identified, a thorough search for underlying causes must be conducted.

Table 1: Selected etiologies of delirium and examples

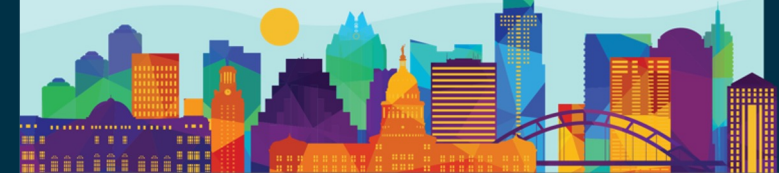
<b>Drug intoxication or withdrawal</b>	Alcohol Sedative-hypnotics Psychostimulants Hallucinogens
<b>Metabolic and endocrine disturbances</b>	Hypoxia Hypoglycemia or hyperglycemia Hypocalcemia or hypercalcemia Hepatic failure Thyroid storm Uremia Anemia
<b>Trauma</b>	Traumatic brain injury Subdural hematoma
<b>Infection</b>	Meningitis Neurosyphilis HIV Bacteremia Fungal infections (systemic or CNS)
<b>Cerebrovascular</b>	Stroke Subarachnoid hemorrhage Seizures
<b>Autoimmune</b>	CNS vasculitis Systemic lupus erythematosus
<b>Cardiac</b>	Heart failure Endocarditis
<b>Other</b>	Prescription medication effects Post-operative state Disseminated intravascular coagulation Hyperthermia or hypothermia

#### Step 4: Ensure that management plans incorporate strategies for the prevention of delirium.

- Prevention interventions involve the recognition and reduction of modifiable risk factors along with management of the conditions that predispose the patient to develop delirium.
- The National Institute for Health and Care Excellence (NICE) clinical guidelines identified 10 core recommendations for delirium prevention.
- The recommendations include addressing the following:

Ann Schwartz M.D., Residency Education Subcommittee  
Vers. 10/09/2020





# What is delirium?

- From the Latin phrases “de” (away from) and “lira” (furrow/track) → Delirium means “to be off track”
- Medical condition with neuropsychiatric presentation
- Prevalence:
  - 20-80% of patients in the ICU (depending on study design)
  - 33-50% of elderly inpatients
  - 82% of ventilated patients
  - 4-39% of inpatient psych consults
- Hypoactive, hyperactive, and mixed level of activity subtypes:
  - Hypoactive most common but least likely to be recognized
- Worse outcomes: associated with increased healthcare costs, prolonged hospitalization, accelerated cognitive decline, and increased rates of institutionalization after discharge





# Confused about confusion?

## confusion

organic brain syndrome

*acute organic syndrome*

*reversible toxic psychosis*

cerebral insufficiency

acute dementia

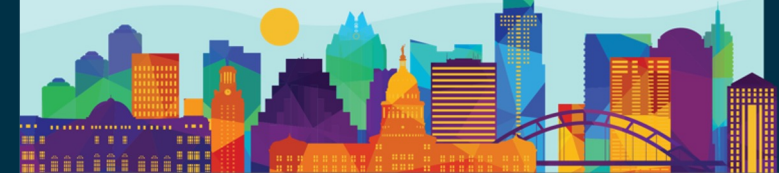
ICU psychosis

*acute brain failure*

toxic metabolic encephalopathy

acute confusional state

## encephalopathy



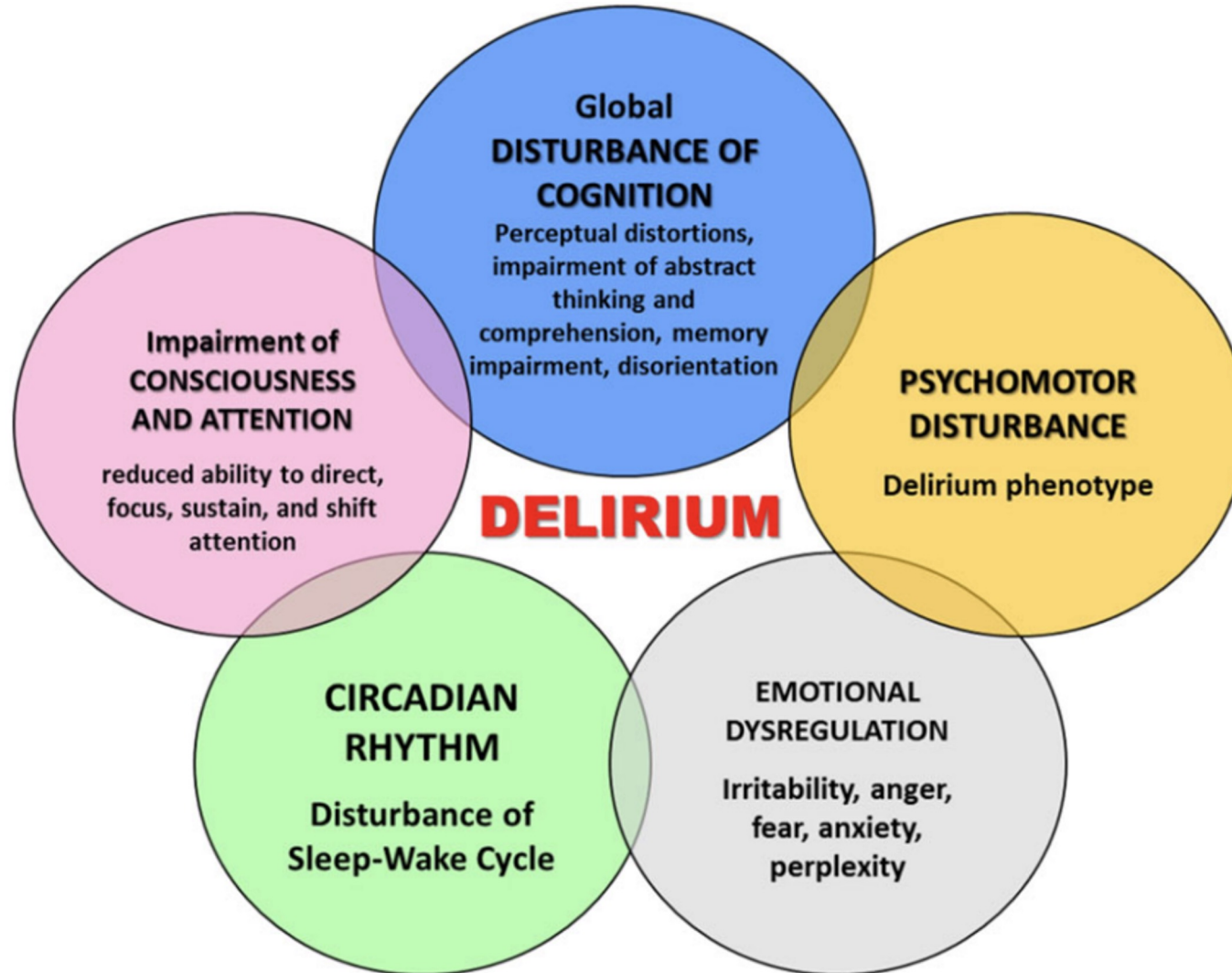
# Core Domains

Delirium defined by impairment in:

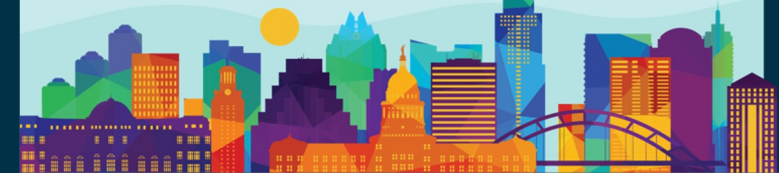
- ❖ Attention
- ❖ Global Cognition
- ❖ Activity level



# The Broad Impact of Delirium



- ★ Acute onset
- ★ May have fluctuating course



# Case: Assessment

What to do: MSE (CAM, MMSE/MoCA, attention tasks), talk with people familiar with patient (nursing staff, family, team)

What do you find?

- inattention
- disorientation
- disorganized speech
- hallucinations (visual, tactile)
- affective changes (mood lability, dysphoria)
- paranoia
- psychomotor activation (restless, fidgeting, trying to get out of bed, floccillation)
- waxing/waning mental status



# Differential Diagnosis of Delirium

## Primary Psychiatric Disorders:

- Primary mood disorders (e.g. major depressive disorder, bipolar disorder)
- Primary psychotic disorders (e.g. schizophrenia, schizoaffective disorder)
- Catatonia
- Trauma and anxiety disorders
- Personality disorders
- Substance intoxication

## Medical and Neurologic disorders:

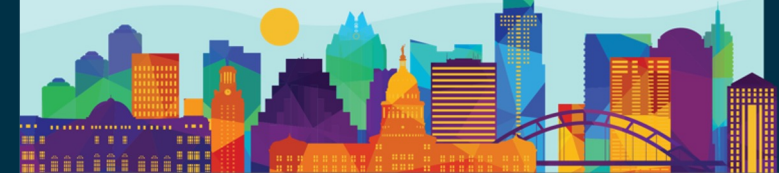
- Dementia or mild cognitive impairment
- Sleep disorders (e.g. OSA, narcolepsy)
- Focal neurologic disorders: seizure, stroke syndrome, nonconvulsive status epilepticus



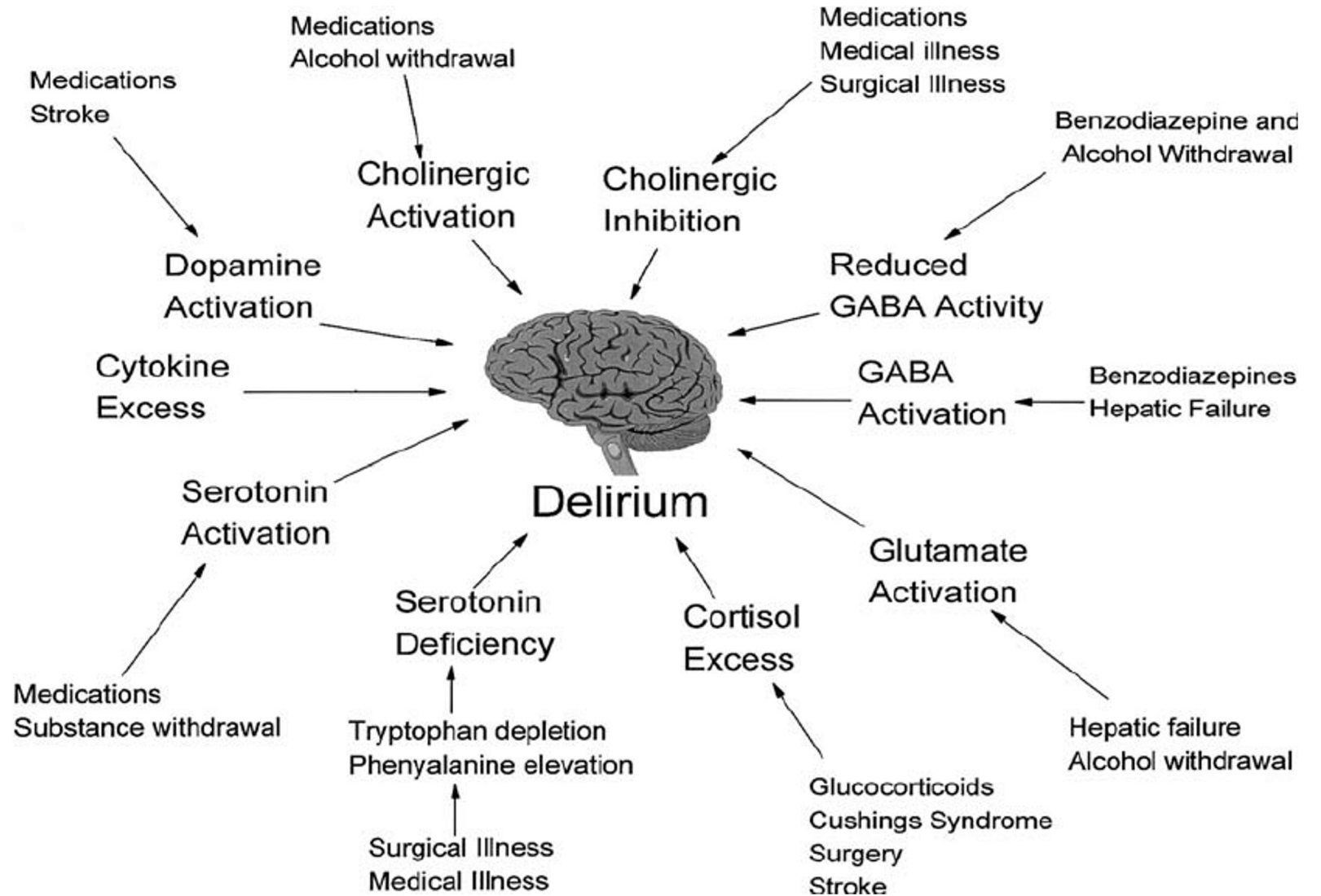


# Pathophysiology of Delirium

- Poorly understood, multiple proposed theories, likely heterogenous pathophysiology
- A widespread disturbance of neural networks
- Historically attributed to **reduced cholinergic function** and **excess of dopaminergic activity**
- Complex interactions among direct brain insults, aberrant stress responses, and neuroinflammatory mechanisms:
  - **Direct brain insults** include those caused by hypoxia, hypoglycemia, hyponatremia, stroke, trauma, and drug effects
  - **Abnormal or exaggerated stress response** from peripheral disturbances such as a UTI
  - **Neuroinflammatory mechanisms** such as elevated cortisol levels or elevated levels of proinflammatory cytokines

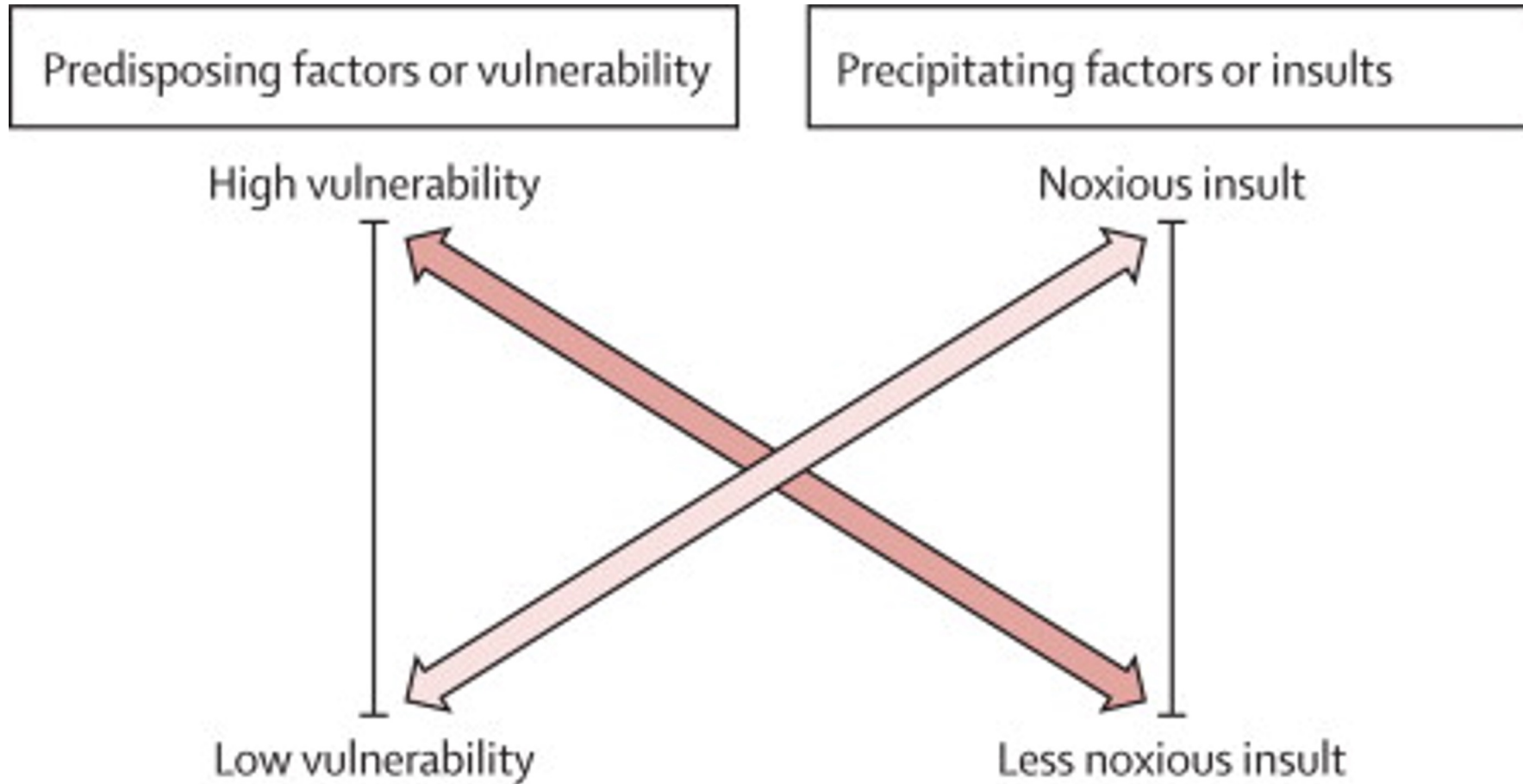


# Many Paths to Delirium





# Predisposing and Precipitating Factors



Inouye, Westendorp, & Saczynski, 2014



# Risk Factors of Delirium

Predisposing Factors	Precipitating Factors
<p>                     Dementia or cognitive impairment                      History of delirium                      Sensory (i.e. visual/hearing) impairment                      Advanced age                      Functional impairments                      Depression                      Prior CVA                      Alcohol misuse                      Multiple comorbidities/severe illness                 </p>	<p>                     Medication effects                      Ventilation/Deep sedation                      Surgery                      Drug intoxication or withdrawal                      Infection                      Metabolic disturbances (glucose, ammonia, BUN, thyroid, calcium, etc)                      Autoimmune/inflammatory conditions                      Trauma                      Stroke                      Seizure                      Pain                      Restraints                 </p>

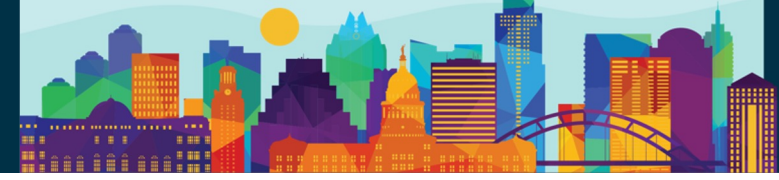


**Table 4. High-Risk Drugs in Delirium and Potential Substitutes.\***

Drug	Mechanism of Adverse Effect	Substitutes or Alternative Strategies	Comments
Benzodiazepines	CNS sedation and withdrawal	Nonpharmacologic sleep protocol <sup>36</sup>	Associated with delirium in hospitalized patients; if patient is already taking, maintain or lower dose, but do not discontinue abruptly
Opioid analgesics (especially meperidine)	Anticholinergic toxicity, CNS sedation, and fecal impaction	Local and regional analgesic measures; non-psychoactive pain medications (e.g., acetaminophen and NSAIDs) around the clock; reserve opioids for breakthrough and severe pain	Consider risks versus benefits, since uncontrolled pain can also cause delirium; patients with renal insufficiency are at elevated risk for adverse effects; naloxone can be used for severe overdoses
Nonbenzodiazepine sedative hypnotics (e.g., zolpidem)	CNS sedation and withdrawal	Nonpharmacologic sleep protocol <sup>36</sup>	Like other sedatives, these agents can cause delirium
Antihistamines, especially first-generation sedating agents (e.g., doxylamine and diphenhydramine)	Anticholinergic toxicity	Nonpharmacologic sleep protocol, <sup>36</sup> pseudoephedrine for upper respiratory congestion, and nonsedating antihistamines for allergies	Patients should be asked about the use of over-the-counter medications; many patients do not realize that drugs with names ending in “PM” contain diphenhydramine or other sedating antihistamines
Alcohol	CNS sedation and withdrawal	If patient has a history of heavy intake, monitor closely and use benzodiazepines for withdrawal symptoms	The history taking must include questions about alcohol intake
Anticholinergics (e.g., oxybutynin and benztropine)	Anticholinergic toxicity	Lower the dose or use behavioral approaches for urinary incontinence (e.g., scheduled toileting)	Delirium is unusual at low doses
Anticonvulsants (e.g., primidone, phenobarbital, and phenytoin)	CNS sedation	Use an alternative agent or consider stopping if patient is at low risk for seizures and has no recent history of them	Delirium can occur despite therapeutic drug concentrations
Tricyclic antidepressants, especially tertiary amines (e.g., amitriptyline, imipramine, and doxepin)	Anticholinergic toxicity	Serotonin-reuptake inhibitors, serotonin–norepinephrine reuptake inhibitors, and secondary amine tricyclics (e.g., nortriptyline and desipramine)	Newer agents (e.g., duloxetine) are as effective as tertiary amines for adjuvant treatment of chronic pain
Histamine H <sub>2</sub> -receptor blockers	Anticholinergic toxicity	Lower the dose or substitute antacids or proton-pump inhibitors	Anticholinergic toxic effects occur primarily with high-dose intravenous infusions
Antiparkinsonian agents (e.g., levodopa and amantadine)	Dopaminergic toxicity	Lower the dose or adjust dosing schedule	Dopaminergic toxic effects occur primarily in advanced disease and at high doses
Antipsychotics, especially low-potency typical antipsychotics (e.g., chlorpromazine and thioridazine)	Anticholinergic toxicity as well as CNS sedation	Discontinue entirely or, if necessary, use low doses of high-potency agents	Carefully consider risks vs. benefits of use in delirium
Barbiturates	CNS sedation and severe withdrawal syndrome	Gradual discontinuation or benzodiazepine substitution	In most cases, barbiturates should not be prescribed; avoid inadvertent or abrupt discontinuation

\* In older adults, the risks and benefits of all medications should be considered carefully. Adverse effects should be monitored whenever any medication is started or the dose is adjusted. CNS denotes central nervous system, and NSAIDs nonsteroidal antiinflammatory drugs.





# Case: Potential Causes

On chart review, you notice Mrs. Jones has received:

- Complete course of ceftriaxone for UTI
- 3 doses of lorazepam 1 mg IV for “agitation”
- 25 mg diphenhydramine for sleep

What are you thinking as potential causes of delirium?

What work up would you want?



# Medical Workup of Delirium

## Labs:

- Metabolic panel, LFTs, CBC, tox screen, urinalysis, TSH, B12, folate
- At-risk patients: HIV, rapid plasma reagent (RPR), ammonia, thiamine, BUN, blood cultures, cardiac enzymes, cortisol, serum drug levels

## Imaging:

- Head imaging: MRI is more sensitive than CT
- Imaging of potential sources of infection/inflammation

**EEG:** generalized slowing is the hallmark of delirium

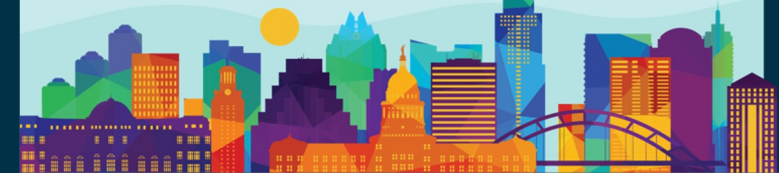
**LP** (in some cases): evaluate for infection, encephalitis, or malignancy

**EKG:** evaluate for arrhythmia, monitor QTc if pharmacologic management is provided



# An ounce of prevention...

- Prevention: identifying and reducing **modifiable** risk factors, managing underlying conditions
- General guidelines:
  - Avoid lines and tethers
  - Maintain sleep/wake cycle
  - Minimize restraints
  - Avoid deliriogenic meds (AGS Beers criteria, anticholinergic, etc)



# NICE 10 Core Recommendations for Preventing Delirium

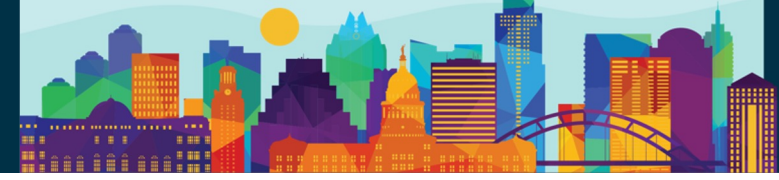
<b>Risk Factor</b>	<b>Intervention</b>
Cognitive impairment	Frequent orientation
Hypoxia	Optimize O2 Saturation
Immobility	Mobilize, out of bed
Polypharmacy	Review and simplify medications
Infection	Treat infections, remove catheters
Sleep disturbance	Optimize sleep/wake cycle (am light, avoid disruptions overnight)
Dehydration/constipation	Adequate fluid intake
Pain	Assess and treat pain (around the clock medications)
Poor nutrition	Make sure dentures fit, provide supplements
Sensory impairment	Hearing and visual aids



# Managing Delirium's Neuropsychiatric Disturbances

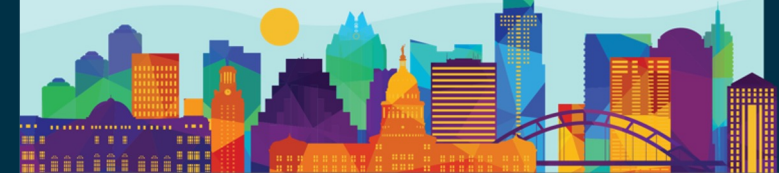
- Non-pharmacologic management is 1st line
- **No FDA approved treatments for delirium**
- Indications/targets for medications: severe patient distress, risk of harm to self/others, sleep-wake disturbance
- Use minimal number/dose of meds necessary, review frequently
- Start low, go slow





# Pharmacologic Management, cont.

- **1<sup>st</sup> generation antipsychotics:** Haloperidol used most often
  - Improved delirium outcomes in some studies
  - May be associated with decreased mortality
  - Available in multiple forms (IM, IV, PO tabs, liquid)
  - Usual starting dose 0.5mg to 1mg, titrate to effect as tolerated
- **2<sup>nd</sup> generation antipsychotics:** Quetiapine, risperidone, olanzapine, aripiprazole
  - Quetiapine associated with improved outcomes
  - Consider method of administration (PO, IV, IM, ODT) and clinical picture
- Potential adverse effects: QTc prolongation, sedation, EPS
- Black box warning: increased mortality risk in dementia related psychosis
- Generally avoid antipsychotics in patients with known Parkinson's or DLB



# Pharmacologic Management, cont.

- **Dexmedetomidine:** selective alpha 2 agonist
  - efficacious for preventing and managing delirium
  - generally limited to ICU setting
- **Melatonin/Ramelteon:** conflicting evidence
- **Benzodiazepines:** avoid unless EtOH/sedative-hypnotic withdrawal
- **Valproic acid:** limited data suggests improvement in agitation in critically ill patients
- **Mirtazapine:** lack of data
- **Stimulants:** lack of data



# Case Wrap up

Find pt to have hypoactive delirium, not depression

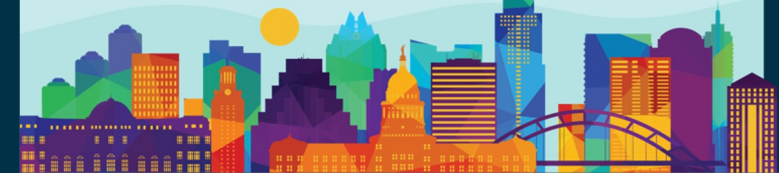
Not appropriate for inpt psych

Recommend avoiding potential deliriogens

Talk with nursing staff about behavioral interventions

Talk with primary team about recommendations

Talk with family about what to expect/timeline



# Delirium Take Home Points

- ★ Key delirium features: acute onset, inattention, waxing/waning mental status
- ★ Associated with poor outcomes → prevention is key
- ★ Treat the underlying condition, but delirium may not resolve immediately
- ★ Use psychiatric meds for symptoms distressing to patient or if they pose risk to patient/staff



# For additional light reading...

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Neurocognitive Disorders  
- Delirium





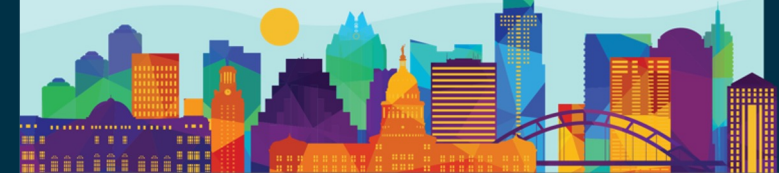
# Other Presentations on Delirium this Week...

## **Thursday, Nov. 9, 11:30AM-1:00 PM CST:**

- An Equal Opportunity Offender: Delirium Throughout the Lifespan. A Review as the Various Presentation, Diagnostic Approaches, and Impact of Delirium at the Various Stages of Life in the Medical Setting

## **Friday, Nov. 10: 9:15-10:45AM CST:**

- Reliability and Validity of the Spanish Adaptation of the Stanford Proxy Test for Delirium (S-PTDsv) in Two Clinical Communities
- Mapping Functional Brain Activity and Connectivity in Delirium with Diffuse Optical Tomography



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- Wilson, J.E., Mart, M.F., Cunningham, C. et al. Delirium. *Nat Rev Dis Primers* 6, 90 (2020). <https://doi.org/10.1038/s41572-020-00223-4>



# Delirium Case

*Mrs. Anita Help is an 85 year old woman with schizophrenia, alcohol use disorder in sustained remission, hypertension, and osteoarthritis who was admitted to the hospital for an elective hip replacement. She is post-op day #2. In the last 24 hours, she's demonstrated changes in behavior, including sleep disturbances, hallucinations, and agitation.*

*You are asked by the orthopedic surgery team to evaluate the patient and provide recommendations on medication management. The team asks if the patient needs to be transferred to inpatient psychiatry for treatment of schizophrenia. The floor nursing staff express frustration about the patient's frequent agitation and combativeness, stating the patient is not appropriate for the orthopedic floor.*



*On initial evaluation, the patient is in 2-point wrist restraints which she is trying to remove with her teeth. She frequently calls out for her son who she seems to think is in the room (but is not currently present). She is too preoccupied with the restraints to participate in the cognitive exam. On review of her medications, she has been continued on her home dose of aripiprazole. She was extubated shortly after surgery and has been receiving frequent doses of IV morphine for pain control. Labs and head imaging are unremarkable.*



# Case Discussion Questions

1. How would you explain the differential diagnosis to the primary team?
2. What are some of this patient's predisposing and precipitating risk factors for delirium?
3. What are the different teams involved in this patient's care, and what can each team's role be in managing this patient's symptoms of delirium?