

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 urinary tract infection

- 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

Drug intoxication or withdrawal	Alcohol Sedative-hypnotics Psychostimulants Hallucinogens
Metabolic and endocrine disturbances	Hypoxia Hypoglycemia or hyperglycemia Hypocalcemia or hypercalcemia Hepatic failure Thyroid storm Uremia Anemia
Trauma	Traumatic brain injury Subdural hematoma
Infection	Meningitis Neurosyphilis HIV Bacteremia Fungal infections (systemic or CNS)
Cerebrovascular	Stroke Subarachnoid hemorrhage Seizures
Autoimmune	CNS vasculitis Systemic lupus erythematosus
Cardiac	Heart failure Endocarditis
Other	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:

- Cognitive impairment or disorientation (provide appropriate lighting, clock, calendar)
- Hypoxia (optimize oxygen saturation)
- Immobility (encourage mobilization)
- Multiple medications (review medications and minimize if possible)
- Infection (look for and treat infection, avoid unnecessary catheters)
- Sleep disturbance (avoid disruptions during sleeping hours)
- Dehydration or constipation (adequate fluid intake)
- Pain (assess for pain and treat appropriately)
- Poor nutrition (provide appropriate nutrition, ensure dentures fit properly)
- Sensory impairment (ensure hearing aids and visual aids are available if needed)

Step 5: Complete the medical workup of delirium.

- Rule out potentially life-threatening causes of delirium – the “WHIMPS” mnemonic can assist in recalling these conditions.
 - W – Wernicke’s disease
 - H – Hypoxia, hypoglycemia, hypertensive encephalopathy, hyperthermia, hypothermia
 - I – Intracerebral hemorrhage
 - M – Meningitis or encephalitis
 - P – Poisoning (exogenous or iatrogenic)
 - S – Status epilepticus
- Basic studies including metabolic panel, liver function tests, complete blood count, drug screen, urinalysis, thyroid-stimulating hormone (TSH), vitamin B12, and folate.
- In at-risk patients, consider HIV serology, rapid plasma reagin (RPR) serology, ammonia level, thiamine, blood culture, cardiac enzymes, cerebral spinal fluid analysis, cortisol, and serum drug levels.
- Consider neuroimaging (e.g., magnetic resonance imaging) and electroencephalogram (EEG) in certain patients.

Step 6: Develop a treatment plan, including nonpharmacologic and pharmacologic strategies, for the management of delirium.

- General Strategies:
 - In order to treat delirium, it must be recognized.
 - Screen at-risk patients with validated instruments (e.g., Confusion Assessment Method [CAM]).
 - Once recognized, treat the underlying condition(s) contributing to the delirium and minimize additional risk factors that may contribute to delirium.
- Nonpharmacologic Strategies:
 - Nonpharmacologic strategies include environmental and behavioral modification.
 - Provide supportive care including hydration, nutrition, and mobilization.

- Provide frequent reorientation, reassurance, and redirection.
- Minimize physical restraints and utilize the least restrictive monitoring possible (e.g., sitters or patient safety monitors).
- Include cues to make the environment more familiar (e.g., include pictures and favorite objects from home).
- Maintain patient's sleep-wake cycle and avoid overnight sleep interruptions.
- Maintain staff continuity and minimize transfers within the hospital.
- Pharmacologic Strategies:
 - Pharmacologic strategies are used for the prevention of delirium in the medically ill as well as treatment in delirium.
 - Pharmacologic strategies are typically reserved for patients experiencing agitation, distressing symptoms such as hallucinations, or in danger or harming themselves or others.
 - No pharmacologic intervention is approved by the Federal Drug Administration (FDA) for the prevention or treatment of delirium.
 - The number of medications used should be minimized and reviewed frequently.
 - Antipsychotics have historically been used in the prevention and treatment of delirium.
 - Haloperidol, high-potency first generation antipsychotic, is the most studied and widely used.
 - Haloperidol is typically initiated in doses of 0.5-1mg and titrated as needed based on response.
 - Low-potency antipsychotics including chlorpromazine are typically avoided due to the risk of hypotension and anticholinergic side effects.
 - Second generation antipsychotics (e.g., risperidone, olanzapine, aripiprazole) have also been reported to be effective.
 - Patients with delirium are often at risk for QTc prolongation and the development of torsades de pointe. Therefore, caution must be used in patients at risk for arrhythmias and careful monitoring of the QTc interval is necessary when using antipsychotics.
 - Other agents have been used with varying levels of success (e.g., melatonin, dexmedetomidine).
 - Melatonin and melatonin agonists have been studied as medically ill patients have been shown to experience altered sleep patterns, abnormal levels of melatonin, and loss of circadian rhythms.
 - Dexmedetomidine (selective alpha-2 agonist) has been utilized and studies suggest that its use can help reduce ICU stay in critically ill patients.
 - Benzodiazepines are typically avoided except in the cases when the delirium is related to withdrawal from alcohol or sedative-hypnotic agents.

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