ACUTE DELIRIUM

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1. Core Definition

Acute delirium represents a severe and sudden disturbance in mental function characterized by a decline in awareness and an inability to focus or sustain attention. Fundamentally, it is a disorder of brain operation, manifesting as an unexpected and typically short-time-span cognitive fluctuation. The defining characteristic is the acute onset and fluctuating course, distinguishing it from more chronic conditions such as dementia. Delirium is not considered a disease itself, but rather a syndrome--a constellation of symptoms arising from underlying physiological disturbances affecting the brain's ability to process information and regulate consciousness. The severity of this disruption can vary dramatically, oscillating between states of considerable agitation and hyperactivity to profound lethargy, sometimes mimicking a coma-like state. This syndrome signals a medical emergency, indicating that the patient's physical health has deteriorated to the point where cerebral functioning is compromised.

The core pathology revolves around a global disturbance in cognition, rather than a localized deficit. Patients experiencing **acute delirium** often demonstrate profound disorientation regarding time, place, and person, coupled with disturbances in the sleep-wake cycle. The acute nature means the symptoms develop over hours or days, marking a sharp change from the individual's baseline mental status. This rapid onset is crucial for diagnosis, particularly when differentiating it from the slow, insidious decline associated with degenerative neurocognitive disorders. The underlying cause is almost always systemic, triggered by physical illness, infection, metabolic imbalance, substance withdrawal, or drug toxicity. As the source content implies, severe physiological stress, such as a high fever accompanying an infection, directly impairs normal neuronal communication, leading to the clinical manifestations of delirium.

It is critical to recognize that while delirium is often reversible, especially if the underlying cause is rapidly identified and treated, its presence carries a significant prognostic weight. The diagnostic criteria emphasize the disturbance in attention and the fluctuating nature of the symptoms over the course of the day. A patient may appear relatively lucid in the morning but descend into profound confusion and agitation by nightfall. Healthcare professionals must use standardized screening tools, such as the Confusion Assessment Method (CAM), to objectively identify these fluctuating states, as diagnosing delirium based solely on casual observation can be challenging, particularly in busy hospital settings where symptoms may be misattributed to psychiatric illness or simply old age.

2. Classification and Subtypes

Acute delirium is broadly categorized into three distinct subtypes based on the dominant psychomotor presentation, which significantly influences both the clinical recognition and the management approach. These classifications--hyperactive, hypoactive, and mixed--reflect different patterns of neurotransmitter dysregulation and cerebral activity. Recognizing the subtype is vital because **hypoactive delirium** is often missed, despite carrying equally poor outcomes compared to the more dramatic presentations.

The **hyperactive subtype** is the most readily recognized form and aligns with the common stereotype of "delirium." Patients in this state exhibit excessive arousal, vigilance, restlessness, agitation, and aggression. They may pull out medical lines, attempt to escape, or experience vivid hallucinations and delusions, often paranoid in nature. This subtype is commonly associated with drug withdrawal (such as alcohol withdrawal, or delirium tremens) or drug intoxication. While highly distressing for both the patient and caregivers, the overt nature of hyperactive delirium ensures timely clinical attention, though management often requires urgent control of agitation to prevent self-harm or injury to others.

Conversely, the **hypoactive subtype** presents a significant diagnostic challenge. Patients are lethargic, withdrawn, apathetic, and demonstrate severe psychomotor retardation, appearing sleepy or stuporous. They may exhibit minimal spontaneous movement, decreased verbal response, and profound inattention, often leading clinicians to mistakenly interpret their state as depression, fatigue, or simply the expected behavior of a frail, elderly patient. Because these patients are quiet and do not pose behavioral problems, their critical cerebral dysfunction can be overlooked, leading to delays in identifying and treating the underlying medical illness, which is directly correlated with higher rates of complications, prolonged hospitalization, and increased mortality.

The third category, **mixed delirium**, involves fluctuation between hyperactive and hypoactive states within a 24-hour period. A patient might be agitated and paranoid during the night, leading to severe sleep disruption, and then become severely lethargic and unresponsive during the day. This oscillating pattern underscores the unstable nature of cerebral metabolism and function in the delirious state. The management strategy for mixed delirium must dynamically adapt to the changing psychomotor presentation, requiring careful monitoring and adjustment of non-pharmacological and, if necessary, pharmacological interventions.

3. Etiology and Risk Factors

Delirium is etiologically complex, rarely resulting from a single cause but rather from the interaction of predisposing factors (vulnerabilities inherent to the patient) and precipitating factors (acute physiological stressors). The brain, like any organ, has a reserve capacity; when systemic insults

overwhelm this reserve, delirium ensues. Crucially, the elderly, especially those with pre-existing cognitive impairment such as mild cognitive impairment or dementia, possess a diminished reserve and are thus profoundly susceptible to developing delirium even in response to minor stressors.

The array of **precipitating factors** is vast and includes virtually any acute medical condition. Common triggers include severe infections (e.g., pneumonia, urinary tract infections, sepsis), metabolic derangements (e.g., hypoglycemia, severe dehydration, electrolyte imbalances like hyponatremia or hypercalcemia), organ failure (hepatic or renal failure leading to toxin accumulation), and hypoxia. Furthermore, surgical procedures, particularly major orthopedic or cardiac surgery, are significant precipitants due to anesthesia, pain, post-operative stress, and blood loss. Drug-related causes are also paramount, including intoxication, withdrawal (especially from alcohol or benzodiazepines), or the initiation of medications with strong anticholinergic properties, which disrupt critical neurotransmitter systems necessary for consciousness.

Predisposing risk factors include advanced age (over 65), pre-existing cognitive deficits (dementia), multiple comorbidities (polypharmacy, chronic heart failure, stroke history), sensory impairment (severe visual or hearing loss), and functional dependence prior to hospitalization. These factors raise the baseline vulnerability of the central nervous system. For example, a young, healthy individual might tolerate a high fever without delirium, whereas an 80-year-old with early-stage dementia and poor hearing aids might become acutely delirious following a minor change in environment or a low-grade urinary tract infection. The confluence of several predisposing factors lowers the threshold at which a precipitating factor can induce an acute brain failure episode.

4. Clinical Presentation and Diagnostic Criteria

Diagnosis of acute delirium relies on recognizing the specific pattern of symptoms outlined in authoritative diagnostic manuals, such as the Diagnostic and Statistical Manual of Mental Disorders, 5th Edition (DSM-5). The DSM-5 criteria define delirium as a disturbance in attention (reduced ability to direct, focus, sustain, and shift attention) and awareness (reduced orientation to the environment). The key diagnostic differentiator is the acute onset, developing over a short period (hours to days), and the tendency for symptoms to fluctuate in severity throughout the day.

In addition to disturbances in attention and awareness, a patient must present with an additional disturbance in cognition, such as memory deficit, disorientation, language disturbance, or perceptual disturbances (hallucinations or illusions). These symptoms must not be better explained by another pre-existing, established, or evolving neurocognitive disorder, although chronic disorders like dementia do not preclude a diagnosis of superimposed delirium. Furthermore, there must be evidence from the history, physical examination, or laboratory findings that the disturbance is a direct physiological consequence of another medical condition, substance intoxication or withdrawal, or exposure to a toxin.

The clinical manifestations extend beyond mere confusion. Patients frequently experience severe disruption of the sleep-wake cycle, often manifesting as nocturnal worsening of symptoms (known as sundowning) and insomnia during the night, coupled with excessive daytime sleepiness. Emotional lability is common, with rapid shifts between fear, irritability, euphoria, and depression. Psychomotor changes, whether hyperactive or hypoactive, are often the most visible features. Because the clinical presentation is highly variable and depends heavily on the underlying cause and the patient's baseline function, systematic screening tools like the Confusion Assessment Method (CAM) are essential in the clinical setting to ensure that subtle, hypoactive cases are not missed.

5. Pathophysiology

While the exact pathophysiology of acute delirium is not fully elucidated, current models focus on widespread neuroinflammation, disrupted neurotransmission, and global cerebral metabolic stress. The central hypothesis involves a deficiency in cholinergic activity combined with excess dopaminergic activity, leading to a state of imbalance that impairs the reticular activating system (RAS) and the prefrontal cortex--structures essential for maintaining attention and consciousness.

Systemic inflammatory responses play a key role. When the body fights infection or undergoes major trauma (e.g., surgery), pro-inflammatory cytokines (such as IL-1, IL-6, and TNF-alpha) are released into the circulation. These mediators can cross the compromised blood-brain barrier, or signal to the brain via vagal afferents, activating microglial cells within the central nervous system. This cascade results in neuroinflammation, which directly interferes with neuronal function, particularly affecting the synthesis and release of acetylcholine, a neurotransmitter critical for cognitive processes. The reduction in cholinergic tone is thought to be central to the attentional deficits characteristic of delirium.

Furthermore, conditions like hypoxia, metabolic acidosis, and severe malnutrition impair the delivery of oxygen and nutrients to the brain, stressing neuronal energy production. Neurons are highly sensitive to these metabolic insults. In states of organ failure, circulating toxins (e.g., ammonia in hepatic encephalopathy or urea in uremia) directly interfere with synaptic transmission and neuronal integrity. The cumulative effect of neuroinflammation, cholinergic deficits, and metabolic stress leads to a transient, reversible failure of complex neural networks responsible for executive function, orientation, and attention, culminating in the clinical syndrome of acute delirium.

6. Significance and Impact (Clinical Outcomes)

The presence of acute delirium carries profound significance, marking a serious threat to patient health and long-term functional status. Delirium is strongly associated with adverse clinical outcomes across all age groups, but particularly in the geriatric population. It is not merely an

irritating symptom; it is an independent risk factor for increased morbidity and mortality.

Patients who experience delirium often face significantly prolonged hospital stays. The complications stemming from the delirious state--such as falls, aspiration pneumonia, development of pressure ulcers due to immobility, and accidental removal of necessary medical devices--contribute substantially to increased resource utilization and healthcare costs. Furthermore, the inability of the patient to cooperate with rehabilitation or follow complex medical instructions during their acute confusion compromises the recovery process from the precipitating illness or surgery.

Perhaps the most concerning long-term impact is the link between delirium and permanent cognitive decline. Accumulating evidence suggests that delirium may accelerate or precipitate dementia. Even in patients without pre-existing cognitive impairment, episodes of acute delirium are associated with new or worsened cognitive deficits that persist long after the delirium resolves. For those already suffering from dementia, delirium often leads to a rapid, irreversible step-down in functional and cognitive baseline, preventing them from returning to their pre-illness living environment and necessitating placement in long-term care facilities. Therefore, preventing, promptly recognizing, and effectively managing delirium is paramount for maximizing patient independence and long-term quality of life.

7. Management and Treatment

The cornerstone of treating acute delirium is the immediate identification and elimination of the underlying cause(s). Delirium management must be holistic, focusing intensely on non-pharmacological interventions while judiciously using medications only when necessary to control dangerous agitation or severe distress.

Non-pharmacological strategies constitute the first line of defense and focus on creating a supportive, therapeutic environment. This includes orientation protocols (frequent verbal reassurance, providing clocks and calendars), ensuring adequate hydration and nutrition, optimizing the sleep-wake cycle (reducing noise at night, maximizing light exposure during the day), and correcting sensory deficits (ensuring patients use their glasses and hearing aids). Mobility protocols, encouraging early ambulation and reducing restraint use, are also crucial for preventing deconditioning and further confusion. Dedicated delirium prevention programs, such as the Hospital Elder Life Program (HELP), have proven effective in reducing the incidence and duration of delirium in hospitalized patients.

Pharmacological intervention is reserved for severe symptoms. Antipsychotic medications, particularly low doses of atypical antipsychotics like haloperidol or risperidone, may be used to manage severe agitation, aggression, or distressing hallucinations that place the patient or staff at risk. However, these drugs carry risks, particularly in the elderly (e.g., increased risk of stroke, QTc prolongation), and should be used cautiously, prioritizing the lowest effective dose for the shortest

possible duration. Benzodiazepines are generally avoided, as they can worsen delirium, unless the delirium is specifically caused by alcohol or sedative-hypnotic withdrawal, where they are life-saving. The goal of medication is symptom control, not sedation, and the overriding focus must always remain on resolving the underlying medical trigger, such as treating the infection or correcting the metabolic imbalance.

Further Reading

American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders, 5th Edition (DSM-5).
Wikipedia: Delirium
UpToDate: Delirium: Clinical features, assessment, and diagnosis
Wikipedia: Blood-brain barrier