

*Confusion*, a mental and behavioral state of reduced comprehension, coherence, and capacity to reason, is one of the most common problems encountered in medicine, accounting for a large number of emergency department visits, hospital admissions, and inpatient consultations. *Delirium*, a term used to describe an acute confusional state, remains a major cause of morbidity and mortality, costing over \$150 billion dollars yearly in health care costs in the United States alone. Despite increased efforts targeting awareness of this condition, delirium often goes unrecognized in the face of evidence that it is usually the cognitive manifestation of serious underlying medical or neurologic illness.

#### CLINICAL FEATURES OF DELIRIUM

A multitude of terms are used to describe patients with delirium, including *encephalopathy*, *acute brain failure*, *acute confusional state*, and *postoperative* or *intensive care unit (ICU) psychosis*. Delirium has many clinical manifestations, but is defined as a relatively acute decline in cognition that fluctuates over hours or days. The hallmark of delirium is a deficit of attention, although all cognitive domains—including memory, executive function, visuospatial tasks, and language—are variably involved. Associated symptoms that may be present in some cases include altered sleep-wake cycles, perceptual disturbances such as hallucinations or delusions, affect changes, and autonomic findings that include heart rate and blood pressure instability.

Delirium is a clinical diagnosis that is made only at the bedside. Two subtypes have been described—hyperactive and hypoactive—based on differential psychomotor features. The cognitive syndrome associated with severe alcohol withdrawal (i.e., “delirium tremens”) remains the classic example of the hyperactive subtype, featuring prominent hallucinations, agitation, and hyperarousal, often accompanied by life-threatening autonomic instability. In striking contrast is the hypoactive subtype, exemplified by benzodiazepine intoxication, in which patients are withdrawn and quiet, with prominent apathy and psychomotor slowing.

This dichotomy between subtypes of delirium is a useful construct, but patients often fall somewhere along a spectrum between the hyperactive and hypoactive extremes, sometimes fluctuating from one to the other. Therefore, clinicians must recognize this broad range of presentations of delirium to identify all patients with this potentially reversible cognitive disturbance. Hyperactive patients are often easily recognized by their characteristic severe agitation, tremor, hallucinations, and autonomic instability. Patients who are quietly hypoactive are more often overlooked on the medical wards and in the ICU.

The reversibility of delirium is emphasized because many etiologies, such as systemic infection and medication effects, can be treated easily. The long-term cognitive effects of delirium remain largely unknown. Some episodes of delirium continue for weeks, months, or even years. The persistence of delirium in some patients and its high recurrence rate may be due to inadequate initial treatment of the underlying etiology. In other instances, delirium appears to cause permanent neuronal damage and cognitive decline. Even if an episode of delirium completely resolves, there may be lingering effects of the disorder; a patient’s recall of events after delirium varies widely, ranging from complete amnesia to repeated re-experiencing of the frightening period of confusion, similar to what is seen in patients with posttraumatic stress disorder.

#### RISK FACTORS

An effective primary prevention strategy for delirium begins with identification of patients at high risk for this disorder, including those preparing for elective surgery or being admitted to the hospital. Although no single validated scoring system has been widely accepted as a screen for asymptomatic patients, there are multiple well-established risk factors for delirium.

The two most consistently identified risks are older age and baseline cognitive dysfunction. Individuals who are over age 65 or exhibit low scores on standardized tests of cognition develop delirium upon hospitalization at a rate approaching 50%. Whether age and baseline cognitive dysfunction are truly independent risk factors is uncertain. Other predisposing factors include sensory deprivation, such as preexisting hearing and visual impairment, as well as indices for poor overall health, including baseline immobility, malnutrition, and underlying medical or neurologic illness.

In-hospital risks for delirium include the use of bladder catheterization, physical restraints, sleep and sensory deprivation, and the addition of three or more new medications. Avoiding such risks remains a key component of delirium prevention as well as treatment. Surgical and anesthetic risk factors for the development of postoperative delirium include specific procedures such as those involving cardiopulmonary bypass, inadequate or excessive treatment of pain in the immediate postoperative period, and perhaps specific agents such as inhalational anesthetics.

The relationship between delirium and dementia ([Chap. 448](#)) is complicated by significant overlap between the two conditions, and it is not always simple to distinguish between them. Dementia and preexisting cognitive dysfunction serve as major risk factors for delirium, and at least two-thirds of cases of delirium occur in patients with coexisting underlying dementia. A form of dementia with parkinsonism, termed *dementia with Lewy bodies*, is characterized by a fluctuating course, prominent visual hallucinations, parkinsonism, and an attentional deficit that clinically resembles hyperactive delirium; patients with this condition are particularly vulnerable to delirium. Delirium in the elderly often reflects an insult to the brain that is vulnerable due to an underlying neurodegenerative condition. Therefore, the development of delirium sometimes heralds the onset of a previously unrecognized brain disorder.

#### EPIDEMIOLOGY

Delirium is common, but its reported incidence has varied widely with the criteria used to define this disorder. Estimates of delirium in hospitalized patients range from 18 to 64%, with higher rates reported for elderly patients and patients undergoing hip surgery. Older patients in the ICU have especially high rates of delirium that approach 75%. The condition is not recognized in up to one-third of delirious inpatients, and the diagnosis is especially problematic in the ICU environment, where cognitive dysfunction is often difficult to appreciate in the setting of serious systemic illness and sedation. Delirium in the ICU should be viewed as an important manifestation of organ dysfunction not unlike liver, kidney, or heart failure. Outside the acute hospital setting, delirium occurs in nearly one-quarter of patients in nursing homes and in 50 to 80% of those at the end of life. These estimates emphasize the remarkably high frequency of this cognitive syndrome in older patients, a population expected to grow in the upcoming decades.

Until recently, an episode of delirium was viewed as a transient condition that carried a benign prognosis. It is now recognized as a disorder with a substantial morbidity rate and increased mortality rate and often represents the first manifestation of a serious underlying illness. Recent estimates of in-hospital mortality rates among delirious patients have ranged from 25 to 33%, a rate similar to that of patients with sepsis. Patients with an in-hospital episode of delirium have a fivefold higher mortality rate in the months after their illness compared with age-matched nondelirious hospitalized patients. Delirious hospitalized patients have a longer length of stay, are more likely to be discharged to a nursing home, and are more likely to experience subsequent episodes of delirium and cognitive decline; as a result, this condition has enormous economic implications.

#### PATHOGENESIS

The pathogenesis and anatomy of delirium are incompletely understood. The attentional deficit that serves as the neuropsychological hallmark of delirium has a diffuse localization within the brainstem, thalamus, prefrontal cortex, and parietal lobes. Rarely, focal lesions