Lumbar puncture (LP) must be obtained immediately after appropriate neuroimaging in all patients in whom CNS infection is suspected. Spinal fluid examination can also be useful in identifying inflammatory and neoplastic conditions. As a result, LP should be considered in any delirious patient with a negative workup. EEG does not have a routine role in the workup of delirium, but it remains invaluable if seizure-related etiologies are considered.

TREATMENT DELIRIUM

Management of delirium begins with treatment of the underlying inciting factor (e.g., patients with systemic infections should be given appropriate antibiotics, and underlying electrolyte disturbances judiciously corrected). These treatments often lead to prompt resolution of delirium. Blindly targeting the symptoms of delirium pharmacologically only serves to prolong the time patients remain in the confused state and may mask important diagnostic information.

Relatively simple methods of supportive care can be highly effective in treating patients with delirium. Reorientation by the nursing staff and family combined with visible clocks, calendars, and outside-facing windows can reduce confusion. Sensory isolation should be prevented by providing glasses and hearing aids to patients who need them. Sundowning can be addressed to a large extent through vigilance to appropriate sleep-wake cycles. During the day, a well-lit room should be accompanied by activities or exercises to prevent napping. At night, a quiet, dark environment with limited interruptions by staff can assure proper rest. These sleep-wake cycle interventions are especially important in the ICU setting as the usual constant 24-h activity commonly provokes delirium. Attempting to mimic the home environment as much as possible also has been shown to help treat and even prevent delirium. Visits from friends and family throughout the day minimize the anxiety associated with the constant flow of new faces of staff and physicians. Allowing hospitalized patients to have access to home bedding, clothing, and nightstand objects makes the hospital environment less foreign and therefore less confusing. Simple standard nursing practices such as maintaining proper nutrition and volume status as well as managing incontinence and skin breakdown also help alleviate discomfort and resulting confusion.

In some instances, patients pose a threat to their own safety or to the safety of staff members, and acute management is required. Bed alarms and personal sitters are more effective and much less disorienting than physical restraints. Chemical restraints should be avoided, but only when necessary, very-low-dose typical or atypical antipsychotic medications administered on an as-needed basis are effective. The recent association of antipsychotic use in the elderly with increased mortality rates underscores the importance of using these medications judiciously and only as a last resort. Benzodiazepines often worsen confusion through their sedative properties. Although many clinicians still use benzodiazepines to treat acute confusion, their use should be limited to cases in which delirium is caused by alcohol or benzodiazepine withdrawal.

PREVENTION

In light of the high morbidity associated with delirium and the tremendously increased health care costs that accompany it, development of an effective strategy to prevent delirium in hospitalized patients is extremely important. Successful identification of high-risk patients is the first step, followed by initiation of appropriate interventions. Simple standardized protocols used to manage risk factors for delirium, including sleep-wake cycle reversal, immobility, visual impairment, hearing impairment, sleep deprivation, and dehydration, have been shown to be effective. Recent trials in the ICU have focused both on identifying sedatives, such as dexmedetomidine, that are less likely to lead to delirium in critically ill patients and on developing protocols for daily awakenings in which infusions of sedative medications are interrupted and the patient is reorientated by the staff. All hospitals and health care systems should work toward decreasing the incidence of delirium.

35 Dementia

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Dementia, a syndrome with many causes, affects >5 million people in the United States and results in a total annual health care cost between $157 and $215 billion. Dementia is defined as an acquired deterioration in cognitive abilities that impairs the successful performance of activities of daily living. Episodic memory, the ability to recall events specific in time and place, is the cognitive function most commonly lost; 10% of persons age >70 years and 20–40% of individuals age >85 years have clinically identifiable memory loss. In addition to memory, dementia may erode other mental faculties, including language, visuospatial, praxis, calculation, judgment, and problem-solving abilities. Neuropsychiatric and social deficits also arise in many dementia syndromes, manifesting as depression, apathy, anxiety, hallucinations, delusions, agitation, insomnia, sleep disturbances, compulsions, or disinhibition. The clinical course may be slowly progressive, as in Alzheimer's disease (AD); static, as in anoxic encephalopathy; or may fluctuate from day to day or minute to minute, as in dementia with Lewy bodies. Most patients with AD, the most prevalent form of dementia, begin with episodic memory impairment, although in other dementias, such as frontotemporal dementia, memory loss is not typically a presenting feature. **Focal cerebral disorders are discussed in Chap. 36 and illustrated in a video library in Chap. 37e; the pathogenesis of AD and related disorders is discussed in Chap. 448.**

FUNCTIONAL ANATOMY OF THE DEMENTIAS

Dementia syndromes result from the disruption of specific large-scale neuronal networks; the location and severity of synaptic and neuronal loss combine to produce the clinical features **(Chap. 36)**. Behavior, mood, and attention are modulated by ascending noradrenergic, serotonergic, and dopaminergic pathways, whereas cholinergic signaling is critical for attention and memory functions. The dementias differ in the relative neurotransmitter deficit profiles; accordingly, accurate diagnosis guides effective pharmacologic therapy.

AD begins in the entorhinal region of the medial temporal lobe, spreads to the hippocampus, and then moves to lateral and posterior temporal and parietal neocortex, eventually causing a more widespread degeneration. *Vascular dementia* is associated with focal damage in a variable patchwork of cortical and subcortical regions or white matter tracts that disconnect nodes within distributed networks. In keeping with its anatomy, AD typically presents with episodic memory loss accompanied later by aphasia or navigational problems. In contrast, dementias that begin in frontal or subcortical regions, such as *frontotemporal dementia* (FTD) or *Huntington's disease* (HD), are less likely to begin with memory problems and more likely to present with difficulties with judgment, mood, executive control, movement, and behavior.

Lesions of frontal-striatal[1] pathways produce specific and predictable effects on behavior. The dorsolateral prefrontal cortex has connections with a central band of the caudate nucleus. Lesions of either the caudate or dorsolateral prefrontal cortex, or their connecting white matter pathways, may result in executive dysfunction, manifesting as poor organization and planning, decreased cognitive flexibility, and impaired working memory. The lateral orbital frontal cortex connects with the ventromedial caudate, and lesions of this system cause impulsiveness, distractibility, and disinhibition. The anterior cingulate cortex and adjacent medial prefrontal cortex project to the nucleus accumbens, and interruption of this system produces apathy, poverty of speech, emotional blunting, or even akinetic mutism. All corticostriatal systems also include topographically organized projections through the globus pallidus and thalamus, and damage to these nodes

[1]The striatum comprises the caudate/putamen.