02 - 21.2 Delirium

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Fields J, Dumaop W, Langford TD, Rockenstein E, Masliah E. Role of neurotrophic factor alterations in the neurodegenerative process in HIV associated neurocognitive disorders. J Neuroimmune Pharmacol. 2014;9(2):102–116. Jack CR Jr, Lowe VJ, Senjem ML, Weigand SD, Kemp BJ. 11C PiB and structural MRI provide complementary information in imaging of Alzheimer's disease and amnestic mild cognitive impairment. Brain. 2008;131:665. Launer LJ. Epidemiologic insight into blood pressure and cognitive disorders. In: Yaffe K, ed. Chronic Medical Disease and Cognitive Aging: Toward a Healthy Body and Brain. New York: Oxford University Press; 2013:1. Mayeux R, Reitz C, Brickman AM, Haan MN, Manly JJ, Glymour MM, Weiss CC, Yaffe K, Middleton L, Hendrie HC, Warren LH, Hayden KM, Welsh-Bohmer KA, Breitner JCS, Morris JC. Operationalizing diagnostic criteria for Alzheimer's disease and other age-related cognitive impairment—Part 1. Alzheimer's Demen. 2011;7:15. Schneider JA, Arvanitakis Z, Bang W, Bennett DA. Mixed brain pathologies account for most dementia cases in communitydwelling older persons. Neurology. 2007;69:2197. Sonnen JA, Larson EB, Crane PK, Haneuse S, Li G. Pathological correlates of dementia in a longitudinal, population-based sample of aging. Ann Neurol. 2007;62:406. Sweet RA. Cognitive disorders: Introduction. In: Sadock BJ, Sadock VA, Ruiz P, eds. Kaplan & Sadock's Comprehensive Textbook of Psychiatry. 9th ed. Philadelphia Lippincott Williams & Wilkins; 2009:1152. Verdelho A, Madureira S, Moleiro C, Ferro JM, Santos CO, Erkinjuntti T, Pantoni L, Fazekas F, Visser M, Waldemar G, Wallin A, Hennerici M, Inzitari D. White matter changes and diabetes predict cognitive decline in the elderly: The LADIS study. Neurology. 2010;75(2):160. Weiner MF. Cognitive disorders as psychobiological processes. In: Weiner MF, Lipton AM. The American Psychiatric Publishing Textbook of Alzheimer Disease and Other Dementias. Arlington, VA: American Psychiatric Publishing; 2009:137. Zarit SH, Zarit JM. Disorders of aging: Delirium, dementia and other cognitive problems. In: Zarit SH, Zarit JM. Mental Disorders in Older Adults: Fundamentals of Assessment and Treatment. 2nd ed. New York: Guilford Press; 2007:40. 21.2 Delirium Delirium is characterized by an acute decline in both the level of consciousness and cognition with particular impairment in attention. A life threatening, yet potentially reversible disorder of the central nervous system (CNS), delirium often involves perceptual disturbances, abnormal psychomotor activity, and sleep cycle impairment. Delirium is often underrecognized by health care workers. Part of the problem is that the syndrome has a variety of other names (Table 21.2-1). Table 21.2-1 Delirium by Other Names

The hallmark symptom of delirium is an impairment of consciousness, usually occurring in association with global impairments of cognitive functions. Abnormalities of mood, perception, and behavior are common psychiatric symptoms. Tremor, asterixis, nystagmus, incoordination, and urinary incontinence are common neurological symptoms. Classically, delirium has a sudden onset (hours or days), a brief and fluctuating course, and rapid improvement when the causative factor is

identified and eliminated, but each of these characteristic features can vary in individual patients. Physicians must recognize delirium to identify and treat the underlying cause and to avert the development of delirium-related complications such as accidental injury because of the patient's clouded consciousness. EPIDEMIOLOGY Delirium is a common disorder, with most incidence and prevalence rates reported in elderly adults. In community studies, 1 percent of elderly persons age 55 years or older have delirium (13 percent in the age 85 years and older group in the community). Among elderly emergency department patients, 5 to 10 percent have been reported to have delirium. At the time of admission to medical wards, between 15 and 21 percent of older patients meet criteria for delirium-prevalent cases. Of patients free of delirium at time of hospital admission, 5 to 30 percent reported subsequent incidences of delirium during hospitalization. Delirium has been reported in 10 to 15 percent of general surgical patients, 30 percent of open heart surgery patients, and more than 50 percent of patients treated for hip fractures. Delirium occurs in 70 to 87 percent of those in intensive care units and in up to 83 percent of all patients at the end of life care. Sixty percent of patients in nursing homes or postacute care settings have delirium. An estimated 21 percent of patients with severe burns and 30 to 40 percent of patients with acquired immune deficiency syndrome (AIDS) have episodes of delirium while they are hospitalized. Delirium develops in 80 percent of terminally ill patients. The causes of postoperative delirium include the stress of surgery, postoperative pain, insomnia, pain medication, electrolyte imbalances, infection, fever, and blood loss. The incidence and prevalence rates for delirium across settings are shown in Table 21.2-2. Table 21.2-2 Delirium Incidence and Prevalence in Multiple Settings

Risk for delirium could be conceptualized into two categories, predisposing and precipitating factors (Tables 21.2-3 and 21.2-4). Current approaches to delirium focus primarily on the precipitation factors and do little to address the predisposing factors. Managing predisposing factors for delirium becomes essential in decreasing future episodes of delirium and the morbidity and mortality associated with it. Table 21.2-4 Precipitating Factors for Delirium

Table 21.2-3 Predisposing Factors for Delirium

Advanced age is a major risk factor for the development of delirium. Approximately 30 to 40 percent of hospitalized patients older than age 65 years have an episode of delirium, and another 10 to 15 percent of elderly persons exhibit delirium on admission to the hospital. Of nursing home residents older than age 75 years, 60 percent have repeated episodes of delirium. Male gender is also an independent risk factor for delirium. Delirium is a poor prognostic sign. Rates of institutionalization are increased threefold for patients 65 years and older who exhibit delirium while in the hospital. The 3-month mortality rate of patients who have an episode of delirium is estimated to be 23 to 33 percent. The 1-year mortality rate for patients who have an episode of delirium may be as high as 50 percent. Elderly patients who experience delirium while hospitalized have a 21 to 75 percent mortality rate during that hospitalization. After discharge, up to 15 percent of these persons die within a 1-month period, and 25 percent die within 6 months. ETIOLOGY The major causes of delirium are CNS disease (e.g., epilepsy), systemic disease (e.g., cardiac failure), and either intoxication or withdrawal from pharmacological or toxic

agents (Table 21.2-5). When evaluating patients with delirium, clinicians should assume that any drug that a patient has taken may be etiologically relevant to the delirium. Table 21.2-5 Common Causes of Delirium

DIAGNOSIS AND CLINICAL FEATURES The DSM-5 diagnostic criteria for delirium are listed in Table 21.2-6. The syndrome of delirium is almost always caused by one or more systemic or cerebral derangements that affect brain function. Table 21.2-6 DSM-5 Diagnostic Criteria for Delirium

A 70-year old woman, Mrs. K, was brought to the emergency department by the police. The police had responded to complaints from neighbors that Mrs. K was wandering the neighborhood and was not taking care of herself. When the police found Mrs. K in her apartment, she was dirty, foul smelling, and wearing nothing but a bra. Her apartment was also filthy with garbage and rotting food everywhere. When interviewed, Mrs. K would not look at the interviewer and was confused and unresponsive to most of the questions asked. She knew her name and address but not the date. She was unable to describe the events that led to her admission. The next day, the supervising psychiatrist attempted to interview Mrs. K. Her facial expression was still unresponsive, and she still did not know the month or the name of the hospital she was in. She explained that the neighbors called the police because she

was “sick” and that she did indeed feel sick and weak, with pains in her shoulder. She also reported not eating for 3 days. She denied ever being in a psychiatric hospital or hearing voices but acknowledged seeing a psychiatrist at one point because she had trouble sleeping. She said the doctor had prescribed medication, but she could not remember the name. The core features of delirium include altered consciousness, such as decreased level of consciousness; altered attention, which can include diminished ability to focus, sustain, or shift attention; impairment in other realms of cognitive function, which can manifest as disorientation (especially to time and space) and decreased memory; relatively rapid onset (usually hours to days); brief duration (usually days to weeks); and often marked, unpredictable fluctuations in severity and other clinical manifestations during the course of the day, sometimes worse at night (sundowning), which may range from periods of lucidity to severe cognitive impairment and disorganization. Associated clinical features are often present and may be prominent. They can include disorganization of thought processes (ranging from mild tangentiality to frank incoherence), perceptual disturbances such as illusions and hallucinations, psychomotor hyperactivity and hypoactivity, disruption of the sleep–wake cycle (often manifested as fragmented sleep at night, with or without daytime drowsiness), mood alterations (from subtle irritability to obvious dysphoria, anxiety, or even euphoria), and other manifestations of altered neurological function (e.g., autonomic hyperactivity or instability, myoclonic jerking, and dysarthria). The EEG usually shows diffuse slowing of background activity, although patients with delirium caused by alcohol or sedative– hypnotic withdrawal have low-voltage fast activity. The major neurotransmitter hypothesized to be involved in delirium is acetylcholine, and the major neuroanatomical area is the reticular formation. The reticular formation of the brainstem is the principal area regulating attention and arousal; the major pathway implicated in delirium is the dorsal tegmental pathway, which projects from the mesencephalic reticular formation to the tectum and thalamus. Several studies have reported that a variety of delirium-inducing factors result in decreased acetylcholine activity in the brain. One of the most common causes of delirium is toxicity from too many prescribed medications with anticholinergic activity. Researchers have suggested other pathophysiological mechanisms for delirium. In particular, the delirium associated with alcohol withdrawal has been associated with hyperactivity of the locus ceruleus and its noradrenergic neurons. Other neurotransmitters that have been implicated are serotonin and glutamate. PHYSICAL AND LABORATORY EXAMINATIONS Delirium is usually diagnosed at the bedside and is characterized by the sudden onset of

symptoms. A bedside mental status examination—such as the Mini-Mental State Examination, the mental status examination, or neurological signs—can be used to document the cognitive impairment and to provide a baseline from which to measure

the patient's clinical course. The physical examination often reveals clues to the cause of the delirium (Table 21.2-7). The presence of a known physical illness or a history of head trauma or alcohol or other substance dependence increases the likelihood of the diagnosis. Table 21.2-7 Physical Examination of the Delirious Patient

The laboratory workup of a patient with delirium should include standard tests and additional studies indicated by the clinical situation (Table 21.2-8). In delirium, the EEG characteristically shows a generalized slowing of activity and may be useful in differentiating delirium from depression or psychosis. The EEG of a delirious patient

sometimes shows focal areas of hyperactivity. In rare cases, it may be difficult to differentiate delirium related to epilepsy from delirium related to other causes. Table 21.2-8 Laboratory Workup of the Patient with Delirium DIFFERENTIAL DIAGNOSIS Delirium versus Dementia A number of clinical features help distinguish delirium from dementia (Table 21.2-9). The major differential points between dementia and delirium are the time to development of the condition and the fluctuation in level of attention in delirium compared with relatively consistent attention in dementia. The time to development of symptoms is usually short in delirium, and except for vascular dementia caused by stroke, it is usually gradual and insidious in dementia. Although both conditions include cognitive impairment, the changes in dementia are more stable over time and, for example, usually do not fluctuate over the course of a day. A patient with dementia is usually alert; a patient with delirium has episodes of decreased consciousness. Occasionally, delirium occurs in a patient with dementia, a condition known as beclouded dementia. A dual diagnosis of delirium can be made when there is a definite history of preexisting dementia. Table 21.2-9 Frequency of Clinical Features of Delirium Contrasted with Dementia

Delirium versus Schizophrenia or Depression Delirium must also be differentiated from schizophrenia and depressive disorder. Some patients with psychotic disorders, usually schizophrenia or manic episodes, can have periods of extremely disorganized behavior difficult to distinguish from delirium. In general, however, the hallucinations and delusions of patients with schizophrenia are more constant and better organized than those of patients with delirium. Patients with schizophrenia usually experience no change in their level of consciousness or in their orientation. Patients with hypoactive symptoms of delirium may appear somewhat similar to severely depressed patients, but they can be distinguished on the basis of an EEG. Other psychiatric diagnoses to consider in the differential diagnosis of delirium are brief psychotic disorder, schizophreniform disorder, and dissociative disorders. Patients with factitious disorders may attempt to simulate the symptoms of delirium but usually reveal the factitious nature of their symptoms by inconsistencies on their mental status examinations, and an EEG can easily separate the two diagnoses. COURSE AND PROGNOSIS Although the onset of delirium is usually sudden, prodromal symptoms (e.g., restlessness and fearfulness) can occur in the days preceding the onset of florid symptoms. The symptoms of delirium usually persist as long as the causally relevant factors are present, although delirium generally lasts less than 1 week. After identification and removal of the causative factors, the symptoms of delirium usually recede over a 3- to 7-day

period, although some symptoms may take up to 2 weeks to resolve completely. The older the patient and the longer the patient has been delirious, the longer the delirium takes to resolve. Recall of what transpired during a delirium, once it is over, is characteristically spotty; a patient may refer to the episode as a bad dream or a nightmare only vaguely remembered. As stated in the discussion on epidemiology, the occurrence of delirium is associated with a high mortality rate in the ensuing year, primarily because of the serious nature of the associated medical conditions that lead to delirium. Whether delirium progresses to dementia has not been demonstrated in carefully controlled studies, although many clinicians believe that they have seen such a

progression. A clinical observation that has been validated by some studies, however, is that periods of delirium are sometimes followed by depression or posttraumatic stress disorder. TREATMENT In treating delirium, the primary goal is to treat the underlying cause. When the underlying condition is anticholinergic toxicity, the use of physostigmine salicylate (Antilirium), 1 to 2 mg intravenously or intramuscularly, with repeated doses in 15 to 30 minutes may be indicated. The other important goal of treatment is to provide physical, sensory, and environmental support. Physical support is necessary so that delirious patients do not get into situations in which they may have accidents. Patients with delirium should be neither sensory deprived nor overly stimulated by the environment. They are usually helped by having a friend or relative in the room or by the presence of a regular sitter. Familiar pictures and decorations; the presence of a clock or a calendar; and regular orientations to person, place, and time help make patients with delirium comfortable. Delirium can sometimes occur in older patients wearing eye patches after cataract surgery (“black-patch delirium”). Such patients can be helped by placing pinholes in the patches to let in some stimuli or by occasionally removing one patch at a time during recovery. Pharmacotherapy The two major symptoms of delirium that may require pharmacological treatment are psychosis and insomnia. A commonly used drug for psychosis is haloperidol (Haldol), a butyrophenone antipsychotic drug. Depending on a patient’s age, weight, and physical condition, the initial dose may range from 2 to 6 mg intramuscularly, repeated in an hour if the patient remains agitated. As soon as the patient is calm, oral medication in liquid concentrate or tablet form should begin. Two daily oral doses should suffice, with two-thirds of the dose being given at bedtime. To achieve the same therapeutic effect, the oral dose should be approximately 1.5 times the parenteral dose. The effective total daily dose of haloperidol may range from 5 to 40 mg for most patients with delirium. Haloperidol has been associated with prolongation of QT interval. Clinicians should evaluate baseline and periodic electrocardiograms as well as monitor cardiac status of the patient. Droperidol (Inapsine) is a butyrophenone available as an alternative intravenous (IV) formulation, although careful monitoring of the electrocardiogram may be prudent with this treatment. The U.S. Food and Drug Administration (FDA) has issued a Black Box Warning because cases of QT prolongation and torsades de pointes have been reported in patients receiving droperidol. Because of its potential for serious proarrhythmic effects and death, it should be used only in patients who do not respond well to other treatments. Phenothiazines should be avoided in delirious patients because these drugs are associated with significant anticholinergic activity. Use of second-generation antipsychotics, such as risperidone (Risperdal), clozapine, olanzapine (Zyprexa), quetiapine (Seroquel), ziprasidone (Geodon), and aripiprazole

(Abilify), may be considered for delirium management, but clinical trial experience with these agents for delirium is limited. Ziprasidone appears to have an activating effect and may not be appropriate in delirium management. Olanzapine is available for intramuscular (IM) use and as a

rapidly disintegrating oral preparation. These routes of administration may be preferable for some patients with delirium who are poorly compliant with medications or who are too sedated to safely swallow medications. Insomnia is best treated with benzodiazepines with short or intermediate half-lives (e.g., lorazepam [Ativan] 1 to 2 mg at bedtime). Benzodiazepines with long half-lives and barbiturates should be avoided unless they are being used as part of the treatment for the underlying disorder (e.g., alcohol withdrawal). Clinicians should be aware that there is no conclusive evidence to support the use of benzodiazepines in non–alcoholrelated delirium. There have been case reports of improvement in or remission of delirious states caused by intractable medical illnesses with electroconvulsive therapy (ECT); however, routine consideration of ECT for delirium is not advised. If delirium is caused by severe pain or dyspnea, a physician should not hesitate to prescribe opioids for both their analgesic and sedative effects (Table 21.2-10). Table 21.2-10 Pharmacological Treatment Current trials are ongoing to see if dexmedetomidine (Precedex) is a more effective medication than haloperidol in the treatment of agitation and delirium in patients receiving mechanical ventilation in an intensive care unit. Treatment in Special Populations Parkinson’s Disease. In Parkinson’s disease, the antiparkinsonian agents are frequently implicated in causing delirium. If a coexistent dementia is present, delirium is twice as likely to develop in patients with Parkinson’s disease with dementia receiving antiparkinsonian agents than in those without dementia. Decreasing the dosage of the antiparkinsonian agent has to be weighed against a worsening of motor symptoms. If the antiparkinsonian agents cannot be further reduced, or if the delirium persists after attenuation of the antiparkinsonian agents, clozapine is recommended. If a patient is

not able to tolerate clozapine or the required blood monitoring, alternative antipsychotic agents should be considered. Quetiapine has not been as rigorously studied as clozapine and may have parkinsonian side effects, but it is used in clinical practice to treat psychosis in Parkinson’s disease. Terminally Ill Patients. When delirium occurs in the context of a terminal illness, issues about advanced directives and the existence of a health care proxy become more significant. This scenario emphasizes the importance of early development of advance directives for health care decision making while a person has the capacity to communicate the wishes regarding the extent of aggressive diagnostic tests at life’s end. The focus may change from an aggressive search for the etiology of the delirium to one of palliation, comfort, and assistance with dying. REFERENCES Caraceni A, Grassi L. Delirium: Acute Confusional States in Palliative Medicine. 2nd ed. New York: Oxford University Press; 2111. Franco JG, Trzepacz PT, Meagher DJ, Kean J, Lee Y, Kim J-L, Kishi Y, Furlanetto LM, Negreiros D, Huang M-C, Chen C-H, Leonard M, de Pablo J. Three core domains of delirium validated using exploratory and confirmatory factor analyses. Psychosomatics. 2113;54:227. Hosie A, Davidson PM, Agar M, Sanderson CR, Philips J. Delirium prevalence, incidence, and implications for screening in specialist palliative care inpatient settings: A systematic review. Palliative Med. 2113;27:486. Juliebö V, Björo K, Krogseth M, Skovlund E, Ranhoff AH, Wyller TB. Risk factors for preoperative and postoperative delirium in elderly patients with hip fracture. J Am Geriatr Soc. 2109;57:1354. Kiely DK, Marcantonio ER, Inouye SK, Shaffer ML, Bergmann MA, Yang FM, Fearing MA, Jones RN. Persistent delirium predicts greater mortality. J Am Geriatr Soc. 2109;57:55. Maldonado JR, Wysong A, van der Starre PJA, Block T, Miller C, Reitz BA. Dexmedetomidine and the reduction of postoperative delirium after cardiac surgery. Psychosomatics. 2109;50:216. Morandi A, McCurley J, Vasilevskis EE. Tools to detect delirium superimposed on dementia: A systematic review: Erratum. J Am Ger Soc. 2113;61:174. O’Mahony R, Murthy L, Akunne A, Young J. Synopsis of the National Institute for Health and Clinical Excellence guideline for prevention of delirium. Ann Intern Med. 2111;154(11):746. Pisani MA, Kong SYJ, Kasl

SV, Murphy TE, Araujo KLB, Van Ness PH. Days of delirium are associated with 1-year mortality in an older intensive care unit population. Am J Respir Crit Care. 2109;180:1092. Popeo DM. Delirium in older adults. MT Sinai J Med. 2111;78(4):571. Singh Joy SD. Delirium directly related to cognitive impairment. Am J Nurs. 2111;111:65. Solai LKK. Delirium. In: Sadock BJ, Sadock VA, Ruiz P, eds. Kaplan & Sadock’s Comprehensive Textbook of Psychiatry. 9th ed. Philadelphia: Lippincott Williams & Wilkins; 2109:1153. Thomas E, Smith JE, Forrester DA, Heider G, Jadotte YT, Holly C. The effectiveness of non-pharmacological multicomponent interventions for the prevention of delirium in non-intensive care unit older adult hospitalized patients: a systematic review. The JBI Database of Systematic Reviews and Implementation Reports. 2014;12(4):180–232. Witlox J, Eurelings LSM, de Jonghe JFM, Kalisvaart KJ, Eikelenboom P, van Gool WA. Delirium in elderly patients and the risk of postdischarge mortality, institutionalization, and dementia. JAMA. 2110;304(4):443.

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