MEDICAL INTELLIGENCE

CURRENT CONCEPTS

JANE F. DESFORGES, M.D., *Editor*

GERIATRICS

DELIRIUM IN THE ELDERLY PATIENT

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TRANSIENT global disorders of cognition and attention, usually referred to as delirium or acute confusional states, are one of the most common and important forms of psychopathology in later life.[1-6] Hodkinson has stated, "Acute mental confusion as a presenting symptom holds a central position in the medicine of old age. Its importance cannot be overemphasized, for acute confusion is a far more common herald of the onset of physical illness in an older person than are, for example, fever, pain or tachycardia."[7] The elderly, especially the very old, are uniquely prone to delirium as a consequence of almost any physical illness or of intoxication with even therapeutic doses of commonly used drugs. The factors that predispose the elderly to delirium[1-6] include aging processes in the brain, structural brain disease, a reduced capacity for homeostatic regulation and hence for resistance to stress, the impairment of vision and hearing, a high prevalence of chronic diseases, reduced resistance to acute diseases, and age-related changes in the pharmacokinetics and pharmacodynamics of drugs. Sleep loss, sensory deprivation, sensory overload, and psychosocial stress occasioned by bereavement or relocation to an unfamiliar environment are common precipitants of delirium.[4,8]

The clinical importance of delirium is enhanced by the fact that in later life it may be the main presenting feature of such conditions as myocardial infarction or pneumonia. Failure to recognize delirium and hence to diagnose and treat the underlying organic condition may have fatal consequences for the patient; this is most likely to happen in the case of a patient with dementia, whose delirium may be misinterpreted as merely an exacerbation of the dementia. Despite its frequent occurrence, delirium is often misdiagnosed and has been neglected by researchers.[4,8] An agitated delirious patient may be difficult to care for and is at risk for falls and fractures resulting from attempts to escape from an unfamiliar hospital environment or from hallucinated dangers. Medicolegal complications can follow such mishaps. Delirium in a hospitalized patient is likely to increase the length of stay and hence the cost.[2] These are sufficient reasons to diagnose delirium early and to prevent it whenever possible.

There are several explanations for the all too frequent failure to diagnose delirium. Its clinical picture is protean and may at times suggest a functional mental disorder such as depression, mania, or a paranoid psychosis. Delirium is often superimposed on dementia, another condition that features global cognitive impairment, and it may be misdiagnosed as dementia.[9] In one recent study,[10] about 40 percent of patients with dementia who were 55 years of age or older were delirious on admission to the hospital, whereas 25 percent of those who were delirious had dementia. The study of transient cognitive disorders has been plagued by a terminologic muddle that has impeded communication and education.[4,5,11] Some 30 synonyms for delirium have been found in the medical literature, including such terms as "acute confusion," "clouded state," "pseudosenility," "encephalopathy," "acute brain syndrome," and "acute brain failure."[5] The recently revised classification of mental disorders in the *Diagnostic and Statistical Manual of Mental Disorders,* third edition, revised (DSM-III-R),[12] provides both consistent terminology and explicit diagnostic criteria for organic mental syndromes — that is, for the psychopathologic manifestations of brain dysfunction. "Delirium" is the only designation for the disorders discussed here that is included in DSM-III-R; "acute confusional state" is its recognized synonym. Consistent application of the criteria presented in DSM-III-R in clinical practice would help diagnose delirium.[13] Failure to assess a patient's level of cognitive functioning on admission and to monitor his or her status periodically during hospitalization can also result in a missed diagnosis of delirium.

CLINICAL FEATURES

Delirium may be defined as a transient organic mental syndrome characterized by a global disorder of cognition and attention, a reduced level of consciousness, abnormally increased or reduced psychomotor activity, and a disturbed sleep–wake cycle.[3,4,11,12] Its onset is acute, often occurring at night, and its duration is relatively brief (less than one month). Typically, the severity of the symptoms fluctuates unpredictably during the daytime and peaks at night. The outcome for the majority of patients is full recovery, but in 20 to 30 percent, delirium is followed by death, probably because the syndrome often develops in the terminal stage of a disease such as cancer.[14]

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In an unknown proportion of patients, delirium is followed by dementia or some other organic mental syndrome.

In delirium the main aspects of cognition — thinking, perception, and memory — are all disordered in some degree, hence the term "global." Thinking is disorganized, incoherent, often dreamlike, and difficult to direct at will to solve problems and plan and guide action. The patient's ability to grasp his or her situation, distinguish imagery and dreams from facts, and relate new information to previously acquired knowledge is compromised. Transient, poorly systematized, and usually persecutory delusions occur in about half the patients with delirium.[4] Perceptual disturbances may include illusions and hallucinations, most often visual or both visual and auditory, which occur in about 40 percent of elderly patients with delirium.[4] When present, the hallucinations tend to be vivid and frightening; the patient accepts them as real perceptions and often attempts to escape from or fight the hallucinated people or animals. Accidents and attacks on others may result. Short-term memory is impaired, and both anterograde and retrograde amnesia are usually present and last for some time. As a result of the disturbances of cognition and attention, the patient is usually disoriented, at least in regard to time, at some point during the day. In more severe delirium, he or she is also disoriented in regard to places and persons and tends to mistake unfamiliar for familiar surroundings and people. Usually, partial or total amnesia about the whole experience occurs after the delirium resolves.

A global disorder of attention is also invariably present in delirium.[11,12] Alertness — i.e., the readiness to respond to stimuli — may be abnormally heightened or reduced. In either case, however, the patient's ability to mobilize, sustain, and direct attention selectively and at will is diminished; he or she is distractible. The severity of these disturbances of attention tends to fluctuate in the course of a day, rendering the patient more or less accessible to family members or care givers. A delirious patient typically has abnormalities of speech and movement (and thus of psychomotor activity). Three clinical variants of delirium may be distinguished[4,11]: the hypoalert–hypoactive type, the hyperalert–hyperactive type, and the mixed type. A hypoalert–hypoactive patient appears lethargic and drowsy, responds to questions slowly, initiates hardly any action, and is apt to be overlooked or misdiagnosed as depressed. It is important to keep in mind that delirium is by no means invariably associated with hyperactivity.[15] A hyperalert–hyperactive patient is restless and agitated, speaks as if under pressure and often loudly, and moves frequently. The agitation is usually associated with overactivity of the sympathetic nervous system. This variant is typically seen in patients withdrawing from alcohol or sedatives. The mixed type is characterized by unpredictable shifts from hypoactivity to hyperactivity, and vice versa. Patients with metabolic encephalopathy commonly have asterixis, whereas those with alcohol or sedative–hypnotic withdrawal syndrome have a coarse tremor.

Disturbance in the sleep–wake cycle is another essential feature of delirium, one reported by medical writers since Hippocrates.[11] Wakefulness is often reduced during the day, and the patient is drowsy and tends to nap, whereas at night sleep is, as a rule, shortened and fragmented. A typical elderly patient with delirium is awake, restless, agitated, and often hallucinating during the night and may oscillate between sleeping and waking and between dreaming and hallucinating.[4] Such nocturnal exacerbation of symptoms is characteristic of delirium and hence diagnostically important.

In addition to the essential diagnostic features already described, a delirious patient may express the gamut of emotions, ranging from apathy or depression to fear or rage. Such emotional lability gives the syndrome the protean clinical quality that creates diagnostic problems. Despite its manifold clinical features, however, delirium is relatively easy to diagnose. The sudden appearance of disturbances of cognition and attention that tend to fluctuate in severity during the day and be worst at night is virtually diagnostic. Bedside examination of the patient's cognitive functioning is crucial, since it helps to identify and quantify cognitive and attentional impairments.[16-18] In a doubtful case, an electroencephalogram may assist in the diagnosis, as it usually shows diffuse slowing of the background activity.[11,15] Delirium due to withdrawal from alcohol or sedative–hypnotic agents is an exception to this rule, in that the electroencephalogram shows excessive low-amplitude fast activity.[19]

The Differential Diagnosis

It is important to distinguish delirium from dementia, functional psychosis, and a psychogenic dissociative disorder (Table 1). The patient's history is crucial in differentiating delirium from dementia, the only other organic mental syndrome characterized by global cognitive impairment. The two syndromes merge, and it is unclear when the diagnosis of delirium should be replaced by that of dementia. Some authors contend that delirium lasting for several weeks or months should be classified as dementia.[20] In contrast with dementia, delirium is usually acute in onset, it lasts for days or a few weeks rather than months or years, and its course fluctuates, in the sense that the severity of symptoms varies irregularly in the daytime and tends to be greatest during the night.

Functional psychosis, whether depressive, manic, paranoid, or schizophrenic, may at times resemble delirium, especially in an elderly patient with some degree of chronic cognitive impairment.[4] The term "pseudodelirium" has been proposed to designate a delirium-like transient functional psychosis when

Table 1. Clinical Features of Delirium, Dementia, and Acute Functional Psychosis.

Characteristic	Delirium	Dementia	Acute Functional Psychosis
Onset	Sudden	Insidious	Sudden
Course over 24 hr	Fluctuating, with nocturnal exacerbation	Stable	Stable
Consciousness	Reduced	Clear	Clear
Attention	Globally disordered	Normal, except in severe cases	May be disordered
Cognition	Globally disordered	Globally impaired	May be selectively impaired
Hallucinations	Usually visual or visual and auditory	Often absent	Predominantly auditory
Delusions	Fleeting, poorly systematized	Often absent	Sustained, systematized
Orientation	Usually impaired, at least for a time	Often impaired	May be impaired
Psychomotor activity	Increased, reduced, or shifting unpredictably	Often normal	Varies from psychomotor retardation to severe hyperactivity, depending on the type of psychosis
Speech	Often incoherent, slow or rapid	Patient has difficulty finding words, perseveration	Normal, slow or rapid
Involuntary movements	Often asterixis or coarse tremor	Often absent	Usually absent
Physical illness or drug toxicity	One or both are present	Often absent, especially in senile dementia of the Alzheimer's type	Usually absent

there is no demonstrable evidence of an organic cause.[4] A patient with pseudodelirium is likely to have inconsistent results on cognitive testing, may have a past history of psychiatric illness, tends to have markedly depressive or manic behavior and systematized rather than fleeting delusions, and does not have the characteristic fluctuation and nocturnal worsening of symptoms. In patients with functional psychosis, the electroencephalogram is usually normal. A psychogenic dissociative disorder, such as psychogenic amnesia or fugue, is characterized by the sudden inability to recall important aspects of personal history, including a loss of the sense of personal identity.[12] The electroencephalogram is normal in patients with such disorders.

Organic Causes

Delirium is a nonspecific psychopathologic manifestation of a widespread reduction in cerebral metabolism and a derangement of neurotransmission,[1-6,11,15] which may be brought about by a wide range of organic factors. Four major groups of such causal factors can be distinguished[8]: primary intracranial disease, systemic diseases secondarily affecting the brain, exogenous toxic agents, and withdrawal from substances of abuse, primarily alcohol and sedative–hypnotic agents. In the elderly, the cause of delirium is often more complex, in that several factors acting concurrently can precipitate it. Probably the most common single cause of delirium in later life is intoxication due to medications, particularly anticholinergic drugs.[4] The central cholinergic system is affected by aging and even more by degenerative cerebral disease; these factors render the elderly particularly sensitive to the effects of widely prescribed anticholinergic medications.[21,22] Moreover, relative cholinergic deficiency — notably that seen in toxic–metabolic encephalopathy[23] — appears to be a major pathogenetic mechanism in delirium, if not the only one. A general reduction in cerebral oxidative metabolism from any cause has been proposed to account for the cognitive and attentional impairment seen in delirium and for the slowing of the electroencephalographic background activity commonly associated with delirium.[15] Such reduced metabolism results in decreased synthesis of the cerebral neurotransmitters, especially acetylcholine and epinephrine.[23] Thus, an elderly person, notably one with Alzheimer's disease, is uniquely prone to the development of delirium in response to any factor that further reduces the availability of acetylcholine, a neurotransmitter that is essential for normal learning, memory, information processing, and attention.

Not only anticholinergic agents but practically every other drug as well can induce delirium in an elderly person, often even if the medication is taken at therapeutic doses. Diuretics, digoxin, cimetidine, antihypertensive and antiarrhythmic drugs, benzodiazepines, nonsteroidal antiinflammatory agents, and many other drugs commonly prescribed for the elderly can cause delirium.[1-3,5] Given the fact that the rates at which drugs are prescribed for elderly patients are high, polypharmacy is common, and misuse of drugs by the patients is frequent, it is not surprising that iatrogenic, drug-induced delirium often occurs.[24]

The diseases and disorders that most often cause delirium in later life include infections, cancer, congestive heart failure, myocardial infarction, uremia, diabetes, hypoglycemia, malnutrition, dehydration and sodium depletion, hypokalemia, stroke, and epilepsy.[1-6,11] Alcoholism is common and often unrecognized among hospitalized elderly patients. Withdrawal from alcohol or from sedative–hypnotic agents should always be considered as a possible causal factor in delirium.[25] General surgery in later life is followed by delirium in 10 to 15 percent of patients.[26] The frequency of delirium in patients with femoral neck

fractures approaches 50 percent.[27] Postoperative delirium associated with femoral neck fractures has been found to correlate with a history of depression and with the use of anticholinergic drugs and to have resulted in hospital stays almost four times as long as for patients without these factors.[27]

Treatment

The adequate treatment of delirium presupposes that the syndrome has been diagnosed and that its underlying cause or causes have been identified. It is essential to establish, by means of the history, clinical features, and mental-status examination, whether the patient has delirium, dementia, or both. Etiologic diagnosis calls for a physical examination, including a neurologic examination, and routine laboratory tests. All drugs taken by the patient are suspect and should be discontinued or reduced in dosage. If doubt about the diagnosis persists, special tests, such as electroencephalography, CT scanning, and magnetic resonance imaging, may be called for to rule out such causes as an apparent stroke.[28] Infarction in the distribution of the middle cerebral artery in the nondominant hemisphere, as well as of the posterior cerebral artery, may cause delirium.[29,30]

Treatment should be related to both the cause and the symptoms of delirium.[1-6,8,11] The underlying cause of the cerebral dysfunction needs to be removed, whenever possible, or treated. Adequate fluid and electrolyte balance, nutrition, and vitamin supply should be ensured. The provision of reassuring, supportive nursing care that assists the patient in reestablishing orientation is crucial. A proper sensory environment, one that avoids both extremes of sensory input, is helpful. A quiet and well-lighted room, a clearly visible clock and calendar, and a few familiar objects may help calm and orient the patient. Attention should be paid to the patient's concerns and fears, which may be expressed in the contents of delusions and hallucinations. Delirium is for most patients a highly stressful experience, which calls for sensitive care. Family members should be reassured that delirium is a transient disorder; they may worry that the patient has suddenly become demented. If the patient is agitated and restless, sedation is called for and may be lifesaving. No ideal sedative exists for patients with delirium, so the choice reflects personal preference. Haloperidol has been most often recommended in the literature because of its relatively limited anticholinergic effects and sedating potential and because it usually does not cause severe orthostatic hypotension.[1,11,31] It can cause extrapyramidal symptoms, however. A low dose (such as 0.5 mg given orally or intramuscularly twice a day) may suffice, but in cases of severe agitation, higher doses may be required. Benzodiazepines are the drugs of choice for the treatment of delirium due to withdrawal from alcohol and sedative–hypnotic agents.

Whenever possible, one should aim at preventing the occurrence of delirium and thus reduce the related risks and avoid prolonged hospital stays.[32] Drug intake by elderly patients needs to be closely monitored, and unnecessary polypharmacy, notably the concurrent use of more than one drug with anticholinergic effects, should be avoided. It is important to identify patients at high risk for delirium. The very old, patients with dementia, those with depression, and those with impaired vision and hearing are especially prone to the syndrome and need to be carefully monitored during hospitalization. Familiarity with delirium on the part of the medical and nursing staff is a precondition for the early detection of delirium. Its prodromal symptoms, such as insomnia, nightmares, fleeting hallucinations, and anxiety, need to be watched for. Because delirium often begins at night, observations by the night staff can provide an early warning that its onset is imminent or has actually occurred, and a diagnostic assessment should follow without delay.

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CASE RECORDS
OF THE
MASSACHUSETTS GENERAL HOSPITAL

Weekly Clinicopathological Exercises

CASE 9-1989

PRESENTATION OF CASE

A 32-year-old man was admitted to the hospital because of the acquired immunodeficiency syndrome (AIDS), dyspnea, substernal pain, and an apparent cavitary lesion in the right lung.

The patient was a practicing homosexual with a history of documented AIDS 15 months earlier. During the succeeding months he had several bouts of *Pneumocystis carinii* pneumonia, with the most recent episode occurring four months before entry. X-ray films of the chest (Fig. 1) that were obtained on that occasion showed diffuse linear and ground-glass opacities in both lungs; no hilar lymphadenopathy, pleural effusion, or cardiomegaly was seen. Because of intolerance to pentamidine and to trimethoprim–sulfamethoxazole the patient's two most recent episodes were treated with aerosolized pentamidine, with improvement. Two-and-a-half months before admission another x-ray film of the chest disclosed progression of the diffuse disease.

Three weeks before admission the patient experienced the onset of fever, dyspnea, and diarrhea after a vacation in the Dominican Republic. Medical evaluation showed evidence of campylobacter enteritis, and he was treated with erythromycin, with improvement. Microscopical examination of a specimen of sputum revealed no evidence of *P. carinii*. Two weeks later he began to have pleuritic right-sided chest pain and increasing exertional dyspnea, without radiation of pain or change in a chronic nonproductive cough. Another x-ray film of the chest revealed low lung volumes with a bilateral diffuse interstitial pattern that consisted of multiple linear opacities and small nodules, 2 to 5 mm; a focal area of abnormality in the right upper lobe appeared to be a cavity; the overall appearance had worsened since the last previous examination. During succeeding days the pleuritic pain diminished, and the dyspnea became more severe. The patient was admitted to the hospital.

The patient was a musician. There was a history of gonococcal proctitis, herpes zoster, oral candidiasis, cytomegalovirus infection, and granulocytopenia while he was taking azidothymidine (zidovudine), which was discontinued eight months before entry. He had noticed oral "sores" intermittently in recent months. He smoked one pack of cigarettes daily for 15 years and discontinued smoking one year before entry. He had recently experienced an occasional rise of the

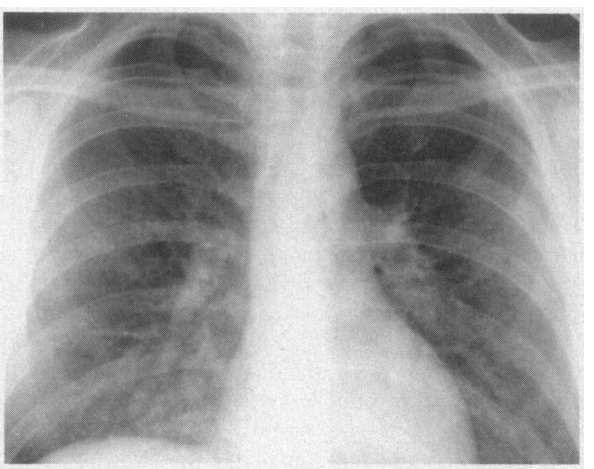

Figure 1. Radiograph of the Chest Obtained Four Months before Admission, Showing Mild Diffuse Linear and Ground-Glass Opacities in the Lungs.