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Confusion, Delirium, and Dementia: Organic Brain Syndromes and the Elderly Patient

1. A 42-year-old man had an uneventful cholecystectomy in the hospital. He was given meperidine, 75 mg, intramuscularly for postoperative pain. Several hours following the injection, he became confused and assaultive and accused the nursing staff of poisoning him. He was also observed to converse loudly with an invisible figure in the room. There was no past or family history of psychiatric disorder concerning this patient.

2. A 70-year-old man was brought to the emergency room in a coma. The patient lived alone in an apartment. He had been hospitalized two weeks ago for congestive heart failure, for which a digitalis preparation was prescribed. He had been discharged one week ago, with one month's supply of Digoxin tablets, one to be taken every day. A nearly empty bottle of Digoxin was found at his bedside when he was discovered comatose by his neighbor.

3. A 17-year-old woman was admitted to the hospital in acute renal failure. At the time of admission, she seemed to be quite drowsy. When the resident physician attempted to take her history, she was confused and disoriented. She kept referring to the doctor as "waiter," and seemed to think she was in a restaurant.

4. A 78-year-old man was admitted to a nursing home. The admission became necessary when the patient's son, with whom he had been living for the past five years since the death of his wife, was transferred to another

state. At the time of admission, the son told the nursing home staff that he had noticed his father to be forgetful in the past two years, but that he had no behavioral problems whatsoever. He had been able to do work in the garden and to go to the grocery store, and he seemed to be, in general, content. He had agreed to go to the nursing home rather than attempt to move with the son's family to an unfamiliar state. On the third day of admission, however, the patient became confused and agitated, and his behavior became grossly inappropriate. For example, he urinated and defecated in his room, and tried to grab and kiss a nurse. Diazepam, 5 mg, was given intramuscularly, and the psychiatric consultant was called.

5. A 67-year-old widow was brought to the physician by her daughter. The patient had been living in a housing project for the elderly since the death of her husband seven years ago. Her daughter, who visited her every week, had noticed over the past four weeks that her mother was becoming apathetic, forgetful, and withdrawn. For example, she was unable to tell her daughter what she had done during the previous day. She also seemed to be inattentive, often not responding to her daughter's questions. The daughter arranged for a psychiatric consultation for her mother.

See also the vignettes in Chapters 13 and 14.

In the previous chapters on anxiety, affect, and psychosis, we examined the final common pathway syndromes presumptively associated with the limbic system, hypothalamus, and other areas of the brain stem. In this chapter, we will discuss the organic brain syndromes of delirium and dementia, which are final common pathway syndromes associated with global brain dysfunction or general cerebrocortical dysfunction or both.

DEFINITIONS AND PHENOMENOLOGY

Organic Brain Syndrome (Organic Mental Syndrome)

Organic brain syndrome refers to a constellation of behavioral and psychological symptoms and signs that reflect reversible or irreversible brain dysfunction, particularly in the areas of orientation, attention, concentration, memory, logical thinking, abstraction, judgment, and affect. In fact, Engel and Romano (1959) defined organic brain syndrome as a syndrome of cerebral insufficiency.

Delirium

Delirium is an organic brain syndrome in which clouding of consciousness (or reduction in awareness of the environment) is a prominent

feature. The patient is disoriented (see Chapter 13), with memory deficits (particularly recent memory), and major difficulties with attention and concentration are seen. Perceptual disturbances are also common, such as illusions, hallucinations, and misinterpretations of stimuli. Speech may be at times incoherent, and disturbances of sleep–wakefulness cycle are common, such as insomnia or daytime drowsiness. There may be agitation or psychomotor retardation (see vignettes 1 and 3). Delirium usually develops over a relatively short period (hours to days), and one of its outstanding features is that level of consciousness tends to fluctuate markedly during the course of a day; periods of lucidity often alternate with confusion and disorientation.

Dementia

Dementia is an organic brain syndrome in which there is an acquired loss of intellectual abilities to the extent that it interferes with social or occupational functioning. Also prominent are memory loss and impairment of abstract thinking and judgment. Personality changes and changes in behavioral patterns are also common. Neurological signs of brain dysfunction may be present, such as aphasia (language dysfunction), apraxia (inability to carry out motor activities despite intact comprehension and motor apparatus), and agnosia (inability to recognize objects in the presence of intact sensory apparatus). Dementia generally has an insidious onset, but the mode of onset depends largely on the underlying disease. For example, the onset of dementia secondary to a head trauma may be rapid. In pure dementia, there is no clouding of consciousness. However, delirium and dementia often do coexist.

Organic brain syndromes include, in addition to delirium and dementia, amnestic syndrome (loss of memory is the prominent feature), organic hallucinosis (hallucinations are the prominent feature), and organic personality change (prominent personality change in the absence of dementia).

EPIDEMIOLOGY OF ORGANIC BRAIN SYNDROMES

Organic brain syndromes are perhaps the most common psychiatric conditions with which a general physician deals in his or her daily practice. In the general hospital, metabolic and electrolyte changes that may

accompany acute and chronic illness, surgery, and administration of drugs all predispose and contribute to delirium.

Approximately 5–15% of patients on medical or surgical inpatient units are thought to manifest evidence of delirium (Lipowski, 1980; Titchener *et al.*, 1956). The incidence of delirium in surgical intensive care units has been reported to be 18–30% and in coronary care units, 2–20% (Lipowski, 1980). Approximately 30% of the 20- to 70-year-old population is expected to experience an episode of delirium within their lifetimes (Lipowski, 1967).

Dementia is prevalent among the elderly. Approximately 4–5% of the Northern European population aged 65 years and older were reported to have severe dementia and 11–12% to have mild to moderate dementia (Katzman, 1976; Terry, 1976a). In one study, 17% of an elderly community population was reported to have evidence of dementia (Fisch *et al.*, 1968).

In the general hospital, many elderly patients with mild dementia may develop superimposed delirium due to metabolic changes associated with disease.

PATHOPHYSIOLOGY OF ORGANIC BRAIN SYNDROMES

By definition, organic brain syndrome denotes (potentially) demonstrable brain dysfunction.

In the case of delirium, the dysfunction is predominantly caused by a metabolic derangement of the neurons due to a change in the extracellular environment, i.e., presence of toxic substances such as drugs, hypoxia, abnormal metabolites, or electrolyte imbalance. Since these chemical or electrolyte abnormalities usually affect the whole brain, the resulting symptoms include global changes such as clouding of consciousness. The EEG often shows a general slowing as compared to premorbid tracings. In severe delirium, delta waves may be prominent (see Chapter 11).

Dementia is generally considered to result from widespread destruction of neurons, particularly in the cerebral cortex. Thus, cortical atrophy, widening of the sulci, and enlarged ventricles are common findings on computerized axial tomographic (CAT or CT) scans. The specific lesions depend on the underlying disease (see below), e.g., ischemic lesions in multiinfarct dementia, neurofibrillary tangles, senile plaques, and granulovacuolar bodies in Alzheimer's disease, and mass in brain tumor.

The term *subcortical dementia* has been used to denote dementia associated with lesions of the subcortical structures, such as the basal ganglia, with relative sparing of the cortical neurons. In subcortical dementia, verbal and perceptuomotor abilities may be largely preserved, while there is impairment of memory, abstraction, personality change, and a marked slowing of thought processes. Parkinson's disease, Huntington's chorea, Wilson's disease, and progressive supranuclear palsy are examples of diseases that may cause cortical or subcortical dementia (Albert *et al.*, 1974).

PREVALENCE OF DEMENTIA IN THE ELDERLY

Dementia is primarily a disorder of the elderly and, in the past, was considered to be normal in an elderly person. While dementia is the major psychiatric problem in the elderly, it is now known that severe memory loss and confusion are pathological, even in the aged population. About 10% of persons over the age of 65 are estimated to have clinically significant intellectual impairment, based on data from the United Kingdom (Beck *et al.*, 1982). About half of the intellectually impaired population have dementia. In the United States, approximately 1 million people may be afflicted with severe dementia and another 3 million with mild to moderate dementia (Schneck *et al.*, 1982). Dementia is likely to become an increasingly greater problem in the future, since the number of persons over 65 years of age is estimated to increase by 1600 a day or about 600,000 per year in the United States (Beck *et al.*, 1982).

In conclusion, dementia, or intellectual impairment severe enough to interfere with social and occupational function, is a common but abnormal condition in the elderly, affecting 10–20% of that population.

ALZHEIMER'S DISEASE AND MULTIINFARCT DEMENTIA

In the past, dementia in the elderly was considered to be caused by cerebral arteriosclerosis. Alzheimer's disease (see below) was considered to be a dementing disease of the presenium (below the age of 65). It was shown in the 1960s, however, that there were approximately the same amounts of arteriosclerosis in the brains of both demented and nondemented elderly persons (Corsellis and Evans, 1965). In a study of

the brains of 50 demented and 28 nondemented elderly patients, 50% of the dementia brains showed the histological features of Alzheimer's disease without evidence of ischemic lesions. Twelve percent of the dementia brains showed primarily infarct lesions, and another 5% were also associated with cerebrovascular changes. Some 8–18% of the dementia brains were associated with both Alzheimer's changes and infarcts. Ten percent could not be classified, and 5% were secondary to other causes. Histologically and clinically, there is no difference between Alzheimer's disease occurring before or after the age of 65.

Now, the DSM-III-R classifies dementia in the elderly into (1) primary degenerative dementia (Alzheimer's disease), senile or presenile onset, and (2) multiinfarct dementia. Alzheimer's disease and multiinfarct dementia together comprise approximately 75% of all dementias in the elderly.

Alzheimer's Disease

Primary degenerative dementia, or Alzheimer's disease, is the most common dementing disease of the elderly. The prevalence rate is approximately 6% (0.38–18.2%) (Schneck *et al.*, 1982). Although some report a higher prevalence rate for women than for men, there is controversy concerning the sex ratio for Alzheimer's disease.

Pathology. Grossly, the Alzheimer brain tends to weigh less than the normal brain and often shows generalized cortical atrophy, which may be particularly prominent in the parietal, temporal, and frontal lobes. Ventricular dilatation, even if slight, is always found (Tomlinson *et al.*, 1968, 1970). Significant correlations between the ventricular size measured on the CT scan and the degree of cognitive impairment in early mild to moderate cases of Alzheimer's disease have been reported (DeLeon *et al.*, 1980; Merskey *et al.*, 1980).

While cortical atrophy may seem to indicate diffuse neuronal loss, aging itself causes a loss of cortical neurons, and there seems to be little difference in the neuronal density between the brains of normal aged persons and those of Alzheimer's disease patients (Terry *et al.*, 1977). There seem to be specific areas of the brain in which marked neuronal loss occurs in Alzheimer's disease: the hippocampus, the medial temporal lobe, and the subiculum (Schneck *et al.*, 1982).

The major microscopic abnormalities in Alzheimer's disease are *neurofibrillary tangles, senile plaques,* and *granulovacuolar bodies.*

The neurofibrillary tangles are visualized by reduced silver stain to extend from the cell body into the dendrites, progressively occluding

cytoplasmic space previously devoted to protein synthesis and transport (Beck *et al.*, 1982). They are particularly abundant in the cerebral cortex, especially in the hippocampus (see Figure 4 [Chapter 4]). Electron microscopy reveals that the neurofibrillary tangles consist of paired helical filaments, twisted linear structures with a half-period of 800 Å and a maximum width of 240 Å (Terry, 1976b; Terry *et al.*, 1964; Wisniewski and Soifer, 1979).

Neurofibrillary tangles are also seen in more than 50% of the brains of normal nonpsychotic, nondemented persons between the ages of 50 and 59 years, in more than 80% of patients aged 60–69, and in 100% of patients over 70 years of age according to one study (Matsuyama and Nakamura, 1978). They have also been found in a variety of brain diseases, including adult Down's syndrome and postencephalitic Parkinson's disease.

It is interesting that neurofibrillary tangles are not found naturally in any other species than man. Injection of aluminum into the brains of animals, however, causes neurofibrillary tangles that are similar but not identical in structure to the neurofibrillary tangles found in man.

Senile plaques consist of multiple, small necrotic foci with amyloid-rich centers surrounded by radial palisades of degenerating axons and dendrites. They are found mostly in the cerebral cortex, particularly in the temporal areas, although they may also be found in the white matter, basal ganglia, brain stem, and cerebellum. The degree of intellectual deterioration in Alzheimer's disease seems to correlate with the number of senile plaques per unit area of the brain (Schneck *et al.*, 1982). Senile plaques also occur in normal aging brains. In kuru and Creutzfeldt–Jakob disease, both of which are dementing slow-virus diseases, senile plaques are characteristically present in the patients' brains.

Recent evidence indicates that the major component of amyloid substances in the Alzheimer brain is a macromolecule fragment called *amyloid β protein* (AβP). AβP is a 40 amino acid fragment of the macromolecule called *amyloid β protein precursor* (APP), which is a membrane-spanning glycoprotein expressed in many mammalian tissues and is encoded by a gene found on chromosome 21 in humans (Selkoe, 1990). AβP deposition may be an early and important pathogenic event in Alzheimer's disease.

The granulovacuolar body or degeneration is characterized by foamy inclusions at soma–dendrite junctions. These inclusions are present in large numbers in the hippocampus of Alzheimer patients. Granulovacuolar bodies are also found in normal elderly brains, but patients with Alzheimer's disease seem to have 2–100 times greater incidence of granulovacuolar degeneration than age-matched controls.

Neurotransmitters in Alzheimer's Disease. Alterations in a number of neurotransmitter levels have been reported in Alzheimer patients. Of particular importance is a reduction in the cholinergic activity in the brain.

Decreased activities of the enzyme choline acetyltransferase (ChAT), the biosynthetic enzyme for acetylcholine, have been reported in autopsied Alzheimer cerebral cortices (Rossor, 1982). ChAT is confined to the cholinergic neurons and is stable after death; thus, this enzyme is a good indicator of the integrity of cholinergic neurons. Acetylcholinesterase activity has also been shown to be decreased in Alzheimer's disease. Biopsy studies of the temporal lobe have directly confirmed ChAT deficit and reduced acetylcholine synthesis in Alzheimer patients (Bowen *et al.*, 1979; Sims *et al.*, 1980; Spillane *et al.*, 1977).

Cholinergic neurons are very widespread in the CNS, including the cerebral cortex, basal ganglia, thalamus, cerebellum, and spinal cord. In Alzheimer's disease, the most marked reductions in the cholinergic activity seem to occur in the temporal cortex, the hippocampus, and the amygdala. The degree of this reduction, which may reach 95% of control values, has been positively correlated with the density of senile plaques and neurofibrillary tangles and the degree of dementia (Beck *et al.*, 1982).

The *cholinergic hypothesis* of Alzheimer's disease and geriatric memory dysfunction (Bartus *et al.*, 1982) postulates that a cholinergic dysfunction underlies the memory loss. Support for this hypothesis comes from several findings: Anticholinergic drugs such as atropine can produce transient memory dysfunction (as well as psychosis), which can be reversed with choline or physostigmine (acetylcholinesterase inhibitor). The administration of physostigmine, or the acetylcholine agonist arecholine, to normal humans and experimental animals can transiently improve some aspects of memory. The administration of choline, or its dietary precursor lecithin, may also transiently improve memory in experimental situations (Bartus *et al.*, 1982; Beck *et al.*, 1982). None of these choline enhancers has yet been demonstrated to be consistently beneficial for the memory impairment in Alzheimer's patients.

Decreased amounts of dopamine, norepinephrine, and somatostatin have been found in the brains of Alzheimer's disease patients (Beck *et al.*, 1982). A reduction of 15–85% in the number of noradrenergic cell bodies in the locus ceruleus has also been reported in Alzheimer's disease.

Etiological Considerations. The etiology of Alzheimer's disease is yet unknown, but at least in a subset of the disease, genetic factors seems to play a predominant role. Other etiological theories include genetic, viral, autoimmune, and toxic theories.

Evidence for *genetic* contribution to Alzheimer's disease comes from two observations: (1) all Down's syndrome (trisomy 21) patients who survive to adulthood eventually develop Alzheimer's disease (and Alzheimer's brain pathology) (Heston, 1979; Sinex and Merril, 1982); and (2) Alzheimer's disease seems to run in families (Sinex and Myers, 1982). In fact, a familial form of Alzheimer's disease (FAD) has been identified, which is an autosomal dominant trait due to a genetic defect in chromosome 21 (Neve, 1990; St. George-Hyslop *et al.*, 1987). Although both are located on chromosome 21, the gene implicated in the familial Alzheimer's seems to be distinct from the gene coding for amyloid protein precursor (APP), which may be responsible for early deposits of amyloid substance in sporadic Alzheimer's disease (Selkoe, 1989). The mechanism by which these deposits occur in Alzheimer's disease is not yet known.

A *viral* etiology for Alzheimer's disease may be suspected from the findings that (1) many viral encephalitides cause late-onset dementia (e.g., subacute sclerosing panencephalitis, which is presumed to be a sequela of measles virus infection, and dementia associated with postencephalitic Parkinson's disease) and (2) Creutzfeldt–Jakob disease and kuru, both of which are caused by slow viruses, have clinical and histological features similar to those of Alzheimer's disease. When the brains of chimpanzees were injected with tissues from the diseased brains of two patients with familial Alzheimer's disease, a chronic, progressive neurological illness ensued in these animals, perhaps demonstrating the transmission of Alzheimer's disease (Crapper and De Boni, 1979).

Autoimmune mechanisms have been postulated for Alzheimer's disease on the basis of antibrain antibodies (Tkach and Hokama, 1970) in Alzheimer patients and in aging rats. Also, the immunological abnormalities associated with Down's syndrome (reduced T-cell function) may also be implicated in Alzheimer's disease. There is, however, no conclusive evidence concerning an immunological etiology of Alzheimer's disease.

An intriguing etiological hypothesis for Alzheimer's disease is that *aluminum* may serve as a toxic agent in the lesions. Aluminum levels of 10–30 times normal values were found in brain tissue of patients with Alzheimer's disease (Crapper *et al.*, 1976). Although an attempt to replicate these findings was unsuccessful, aluminum was demonstrated in the nuclear region of neurofibrillary tangles containing neuronal cells from Alzheimer's patients through the use of scanning electron microscopy and X-ray spectrometry (Perl and Brody, 1980). As noted previously (see the section on Pathology), injection of aluminum into animal brains causes neurofibrillary tangles, but these tangles are structurally different from the neurofibrillary tangles that occur in human beings. However,

identical immunostaining for Alzheimer's neurofibrillary tangles and aluminum-induced neurofibrillary tangles has been reported (Gambetti *et al.*, 1979). Since aluminum is ubiquitous in the environment, and there is no evidence that persons exposed to high levels of aluminum have a higher incidence of Alzheimer's disease (dialysis dementia, in which aluminum was implicated, has a different picture than Alzheimer's), it is generally believed that aluminum may be secondarily sequestered in diseased cells rather than being the causative agent of the dementia (Beck *et al.*, 1982).

Multiinfarct Dementia

Multiinfarct dementia is more common in men than in women, and most common between the ages of 40 and 60.

Multiple and extensive localized areas of softening characterize the brain with multiinfarct dementia. Cerebral and extracerebral vessels usually show hypertensive, atherosclerotic, or inflammatory abnormalities. Unlike Alzheimer's disease, multiinfarct dementia is a dementia secondary to vascular changes, and the etiology is that of the underlying vascular disease.

CLINICAL COURSE OF THE DEMENTIAS IN THE ELDERLY

The clinical course of dementia of the Alzheimer type is characterized by an insidious onset, with progression from Phase I, forgetfulness phase, through Phase II, confusional phase, to Phase III, dementia phase, with progressive confusion, memory loss, and behavioral problems including inappropriate behavior, loss of social judgment, and, at times, psychotic behavior. Originally, Alzheimer's dementia was considered to be a disease of the presenium (under age 65), but now there is believed to be no evidence that there is any difference, either clinically or pathologically, between Alzheimer's disease occurring in the presenium and that occurring at a more advanced age.

In multiinfarct dementia, the onset is usually rapid, often following a series of strokes, and the course often fluctuates, with episodes of confusion followed by relative remissions, and the personality tends to be better preserved than in dementia of the Alzheimer type. Multiinfarct dementia is often associated with hypertension and a series of cerebrovascular accidents.

Dementia is known to decrease life expectancy markedly. In one study, the average survival period was 2.6 years following diagnosis for demented men and 2.3 years for demented women, as compared to 8.7 years and 10.9 years for age-matched, nondemented men and women, respectively (Kay *et al.*, 1964).

MEMORY DYSFUNCTION IN THE ELDERLY

While dementia as a syndrome is not the norm in the elderly population, there is generally a decline in memory and intellectual function with advancing age (Corkin *et al.*, 1982). Cognitive decline with advancing age has also been demonstrated in other mammalian species, including mice, rats, and monkeys (Bartus et *al.*, 1982). Such decline in intellectual functioning may be associated with age-related loss of neurons as well as other degenerative changes in the brain.

As we discussed above, nearly all pathological changes that occur in Alzheimer's disease are also present in normal aging brain. Thus, it appears that the difference between the decline of intellectual function in the normal elderly and that of dementia is a matter of degree, perhaps correlated to the degree of pathological changes in the brain. On the other hand, it is possible that the senile plaques and neurofibrillary tangles, even if they are found in elderly persons without dementia, nonetheless represent pathological conditions.

EVALUATION OF ORGANIC BRAIN SYNDROMES

Biological Dimension

Organic brain syndrome, by definition, implies that there is a biological etiology to the syndrome that must be investigated. Careful medical history, physical examination, and laboratory tests are indicated in any patient with organic brain syndrome to identify the biological causative agent. Careful history for both licit and illicit drug use is an important aspect of history-taking.

If delirium is suspected, particular attention should be paid to conditions and diseases that cause metabolic changes in the brain—conditions that cause an alteration in the extracellular environment. These include, among others, endogenous and exogenous toxic states, fever, electrolyte imbalance, hypoxia, and drug-withdrawal states. Laboratory

tests are of utmost importance in evaluating delirium, since they are likely to provide information concerning the exact metabolic abnormality (e.g., uremia, hypokalemia). The confusion in vignette 3 was probably caused by uremia. The EEG is useful in documenting cerebral dysfunction when significant slowing is present. However, the EEG slowing may be only in relation to premorbid frequency, without reaching abnormal proportions.

When dementia is suspected, emphasis should be on identifying medical and neurological diseases that may cause structural or chronic metabolic changes in the brain. While dementia is usually a result of irreversible and widespread neuronal death, the progression of dementia may be halted and some of the lost functions may even be restored if the underlying medical condition is treated or controlled. Among such treatable causes of dementia are endocrinopathies (e.g., hypo- and hyperthyroidism, Addison's disease, Cushing's disease, parathyroid disease), metabolic diseases and nutritional deficiencies (e.g, diabetes mellitus, thiamine deficiency, vitamin B_{12} deficiency, pellagra), infections (e.g., brain abscess, neurosyphilis), neoplasms (e.g., meningioma), and vascular disorders (e.g., atherosclerosis, systemic lupus erythematosus, cerebrovascular accidents). Pseudodementia of depression is also often misdiagnosed as irreversible dementia (see below).

See Table 8 for a list of reversible causes of dementia (Beck *et al.*, 1982).

Unfortunately, primary progressive degenerative dementias, such as Alzheimer's disease and Pick's disease, account for more than 50% of dementias in persons over 65 years of age.

The most common dementing conditions of the elderly, Alzheimer's disease and multiinfarct dementia, account for some 75% of the dementias in the elderly.

Personal Dimension

Symptoms and signs in the personal dimension constitute the cardinal features of organic brain syndromes. Fluctuating levels of consciousness, perceptual changes, and impairment of attention and memory are characteristic features of delirium. Forgetfulness, decrease in intellectual ability, and personality change (exaggeration of premorbid personality traits such as querulousness, suspiciousness, and impulsivity) are prominent in dementia. Careful history-taking in the personal dimension will also provide information concerning the onset—rather rapid and fluctuating in delirium, and insidious and progressive in dementia.

Table 8. Reversible Causes of Dementia[a]

Depression ("pseudodementia")
Intoxication
Therapeutic drugs
Alcohol
Other substances (e.g., heavy metals, CO)
Metabolic-endocrine derangements
Renal failure
Hyponatremia
Volume depletion
Hypoglycemia
Hepatic failure
Hypothyroidism
Hyperthyroidism
Hypercalcemia
Cushing's syndrome
Hypopituitarism
Brain disorders
Stroke
Subdural hematoma
Infection (e.g., meningitis, neurosyphilis, abscess)
Tumors (primary or metastatic)
Normal-pressure hydrocephalus
Cardiopulmonary disorders (e.g., congestive heart failure, arrhythmias, chronic obstructive pulmonary disease)
Generalized infections (e.g., tuberculosis, endocarditis)
Deficiency states (e.g., vitamin B_{12}, folate, niacin)
Miscellaneous causes
Sensory deprivation (e.g., blindness, deafness)
Hospitalization (e.g., from isolation or anesthesia)
Fecal impaction
Anemia
Remote effects of cancer

[a]From Beck *et al.* (1982). Reprinted with permission.

Mental-status examination, described in detail in Chapter 13, documents the specific deficits in organic brain syndrome. Abnormalities in *appearance* may be present; a delirious or demented patient often appears cachectic because of the underlying disease. The *sensorium* is characteristically clouded in delirium. *Orientation* is impaired markedly in delirium, and progressively in dementia. *Speech and motor activity* are often impaired in delirium and dementia. *Cognitive processes, including memory, attention, concentration, logical thinking, abstraction, calculation, and judgment, are impaired in organic brain syndromes.* Of particular importance is the memory impairment, which is an early sign of dementia, and is

especially pronounced concerning recent events. For example, a patient who took a prescribed pill at 9 P.M. may not remember at 10 P.M. that he had already taken the medicine, so he may take an additional dose at 10. At 11 P.M. he may have again forgotten taking the pill at 10, and so on. Accidental overdoses of this kind are quite common among elderly patients with mild to moderate dementia (see vignette 2).

Perceptual abnormalities are common, particularly illusions and misperceptions, as well as frank hallucinations. In organic brain syndromes, *visual hallucinations* are quite common, in distinction to schizophrenia, in which auditory hallucinations are more characteristic.

The affective disturbance in organic brain syndromes is *lability*—the patient may cry one minute and then burst out laughing in a matter of seconds. There is also impairment in the modulation of affect, so that the patient may strike out in a fit of anger at the slightest provocation. When confronted with a cognitive deficit (e.g., not being able to do a simple calculation), the patient may show irritability, anger, or panic. This phenomenon has been called "catastrophic reaction" by Goldstein (1952). The sudden confrontation with an intellectual deficit may cause a collapse of the defense mechanism of denial (see Chapter 5), resulting in overwhelming anxiety. In interviewing patients with suspected dementia, the physician must use tact and gentleness to avoid a catastrophic reaction.

Environmental Dimension

Information to be gained in the environmental dimension is essential in understanding organic brain syndromes. To begin with, because of the confusion and memory deficit so common among patients with delirium and dementia, the physician may be unable to obtain a reliable medical history from the patient. A spouse, relative, or friend may be indispensable not only in obtaining history, but also in providing objective information concerning the patient's performance—for example, was he able to shop, cook, get around town, and otherwise live independently? An assessment of the living conditions of the patient suspected of having organic brain syndrome is crucial—for example, does the apartment have an elevator and are there persons nearby who might be able to supervise the administration of the patient's prescribed drugs?

Environmental factors may precipitate or exacerbate an organic brain syndrome. Delirium may occur in states of sensory deprivation or overload, as in the intensive care unit psychosis (see Chapter 19). Other environmental factors that may contribute to organic brain syndromes include environmental toxins (e.g., heavy metals), extremes of temperature or noise, and infectious agents.

Many patients with organic brain syndrome maintain routine daily function as long as they are in a familiar environment. This is because their adaptational ability is not taxed through the need to learn new things (remote memory and routinized activities are not as impaired as recent memory and newly learned tasks). Once such a patient is removed from the familiar surroundings and placed in a strange and often confusing environment such as that in a hospital, sudden decompensation of the patient's defense mechanisms and personality may occur, with an exacerbation of the preexisting deficits as in vignette 4. Thus, a careful history concerning any recent changes in physical and social environment and in activities and routines may provide important information.

DIFFERENTIAL DIAGNOSIS OF ORGANIC BRAIN SYNDROMES

The syndromic diagnosis of delirium or dementia is only the first step in a differential diagnostic process that should lead to a definitive diagnosis of an underlying disease as outlined in the preceding section.

In this section, we will discuss the differential diagnosis of the organic brain syndromes from other psychiatric and behavioral syndromes.

Delirium should be differentiated from schizophrenia, acute mania, and other forms of "nonorganic" psychosis. While hallucinations, agitation, and disordered thinking and speech are common in both categories, clouding of sensorium is unlikely in schizophrenia, mania, and "nonorganic" psychoses. Visual hallucinations are more indicative of delirium than of schizophrenia. Laboratory abnormalities (e.g., electrolyte imbalance) as well as EEG slowing are helpful in establishing the diagnosis of delirium.

Dementia should be differentiated from "normal process of aging," schizophrenia, and depression. While there may be some deterioration in memory with aging, normal aging does not produce the degree of intellectual deterioration as in dementia to the extent that it interferes with social and occupational functioning. While chronic schizophrenia may be accompanied with some intellectual deterioration, it is rarely as progressive as in dementia. Schizophrenia cannot be diagnosed *de novo* in a patient over the age of 45 (that is, if the patient is over age 45, as most patients who are suspected of dementia are, the syndrome cannot be due to schizophrenia unless the patient had schizophrenic episodes

in the past). The identification of the underlying disease establishes the diagnosis of dementia.

Depression is an important syndrome to be differentiated from dementia. As discussed in Chapter 6, cognitive difficulties including inability to concentrate, indecisiveness, and slowed thinking processes are common in patients with the depressive syndrome. When these cognitive difficulties are pronounced in a patient with depression, this syndrome is sometimes referred to as "pseudodementia" of depression. The significance of this differentiation is that pseudodementia of depression abates when the depression is treated successfully. Patients with pseudodementia usually have other signs of depression. In general, patients with pseudodementia tend to have histories of previous depression, the onset of the cognitive difficulties is relatively more recent and abrupt, and the symptoms tend to be more fluctuating than in dementia patients. "I don't know" is a more frequent answer given by a pseudodementia patient, while "near-miss" answers are more likely given by the truly demented patient. EEG and CT scan abnormalities tend to support the diagnosis of true dementia, but in cases of serious doubt, a trial of antidepressant therapy may be necessary for a definitive differential (Beck *et al.*, 1982).

The patient described in vignette 5 was shown to have symptoms and signs of the depressive syndrome on careful examination. She had sleep disturbance (early morning awakening), anorexia, guilty ruminations, and suicidal ideation in addition to the apathy and forgetfulness. She would often reply "I don't know" to simple questions. An EEG and CT scan were normal. Under the presumptive diagnosis of pseudodementia of depression, she was given a course of desipramine, a tricyclic antidepressant (see Chapter 21). Within eight weeks of treatment, she showed a remarkable recovery from her cognitive and depressive symptoms.

MANAGEMENT OF ORGANIC BRAIN SYNDROMES

Biological Dimension

Accurate diagnosis of the underlying biological condition is essential in the successful management of organic brain syndromes. In the case of delirium, this is particularly important, since there is no such thing as "primary or idiopathic delirium." Delirium is always secondary to a metabolic derangement in the brain. A corollary of this is that the

treatment of delirium must always be directed to the underlying biological condition. Treatment or management of the diagnosed medical or surgical disease, toxic state, drug-withdrawal state, or laboratory abnormality, then, is the definitive treatment of delirium.

There is no effective drug treatment for delirium per se, with the exception of drug-withdrawal states. In fact, discontinuation of nonessential drugs should be considered, since delirium is often caused by the toxic or idiosyncratic effect of a drug. In delirium caused by withdrawal of CNS depressant drugs (e.g., delirium tremens), other CNS depressant drugs such as benzodiazepines are effective. Small doses of antipsychotic drugs may be tried for severe agitation in delirious patients if the agitation renders the patient unmanageable. This is no substitute, however, for identification and treatment of the underlying etiological condition.

In dementia, identification and treatment or control of the underlying disease should be attempted whenever possible. One should recognize that there are a number of treatable and reversible diseases that cause dementia. Etiological treatment is not possible, however, for the primary degenerative diseases such as Alzheimer's disease.

Drug Therapy for Elderly Patients and Patients with Irreversible Dementia

General Principles. Americans aged 65 and older receive 22% of all drug prescriptions (Rabin, 1972). Nearly two thirds of the elderly use drugs on a regular basis, using more than 13 prescriptions per year. Less than 5% of the aged population abstain from all drugs (Salzman, 1982).

Since most patients with irreversible dementia are elderly, special consideration should be given to the age-related changes in drug metabolism. Elderly patients, in general, have diminished hepatic and renal function; thus, the blood level of a dose of drug may be higher than in a younger person because of the prolonged half-life. Drugs should be started at a very small dose and increased very gradually if necessary. On the other hand, concomitant medications (the elderly tend to take more than one drug—an average of 5–12 medications a day [Salzman, 1982]) may delay the absorption of some drugs (antacids and milk of magnesia often do this) or cause undesirable interactions.

Since memory deficit is a prominent feature of patients with dementia, compliance with a verbally given drug regimen cannot be assured. Whenever possible, medications should be dispensed by someone other than the patient—spouse, relative, friend, or a visiting nurse. As much as possible, drugs should be dispensed in individual containers that specify the dates and times when the drugs are to be taken.

See Table 9 for a list of age-related biological changes and their clinical and pharmacological consequences.

Table 9. Age-Related Biological Changes and Their Clinical and Pharmacological Consequences

Factor	Change	Consequence
Absorption	1. May be delayed due to antacids, milk of magnesia, or anticholinergic drugs	1. These changes are not specific for the elderly, but are more likely to occur in the elderly patient who takes these drugs. 2. Delayed passive absorption of chlordiazepoxide
Distribution	1. Increase in fat/muscle ratio, which leads to increased apparent volume of distribution of lipid-soluble drugs	1. All psychotropic drugs except lithium are lipid-soluble. Clinical consequences of increased volume of distribution are uncertain in elderly patients; may prolong clearance.
Plasma albumin levels	1. Decrease	1. Hypoalbuminemia has been associated with increased psychotropic drug toxicity in the elderly.
First-pass effect	1. Decreases with age and congestive heart failure 2. Decreased by propranolol and cimetidine	1. Theoretically would increase the fraction of unmetabolized psychotropic drugs with high or intermediate extraction such as imipramine, desipramine, and nortriptyline.
Hepatic metabolism	1. Decreased demethylation	1. May be responsible for increased plasma levels and prolonged excretion half-lives of imipramine, amitriptyline, chlordiazepoxide, and diazepam, depending on exact site of methyl removal. Decreases thioridazine metabolism.
	2. Decreased hydroxylation	2. Impaired or delayed production of hydroxy metabolite of tricyclic antidepressants, leading to higher blood levels of above drugs and nortriptyline. 3. Prolongation of time to reach steady-state levels of above drugs
Excretion	1. Gradual age-related decrease in renal blood flow; reduction in drug clearance; decline in glomerular filtration rate, reabsorptive capacity, and excretory capacity of tubules	1. Decreased lithium clearance; prolongation of time to reach steady state of lithium.
Receptor-site sensitivity	1. Conflicting reports about age-related CNS toxicity of lithium	1. Increased confusion with lithium in the elderly.
	2. Increased CNS sensitivity to benzodiazepines	2. Age-related increase in sedation, disinhibition, and confusion with chlordiazepoxide, nitrazepam, and flurazepam.
	3. Decrease in nigrostriatal dopamine	3. Increase in extrapyramidal side effects with neuroleptics.
	4. Decrease in CNS cholinergic functioning	4. Increased sensitivity to anticholinergic properties of psychotropic drugs; increase in toxic confusional states with tricyclics.

[a] From Salzman (1982). Reprinted with permission.

Table 10. Routine Screening Procedures Recommended for Elderly Patients in Whom Use of Psychotropic Drugs Is Being Considered[a]

History
- Is a medical illness causing the "psychiatric" symptoms?
- Is a drug the patient is currently taking causing the psychiatric symptoms?
- Has the patient had these or other psychiatric symptoms in the past? If so, what was the diagnosis and what medication, if any, was therapeutically effective? What side effects, if any, developed?

Physical examination
- Is there evidence of neurological, renal, hepatic, or other medical disease that would further increase the elderly patient's risk for side effects?

Mental status
- Is there a psychiatric illness of recent onset?
- Is there evidence of dementia or delirium?

Laboratory studies
- Is there evidence of decreased hepatic synthesizing function (i.e., decreased serum albumin) or decreased renal function (i.e., decreased creatinine clearance)?

Drug interactions
- What adverse drug interactions might develop if the psychotropic drug was added to medications the patient is currently taking?

[a] From Thompson *et al.* (1983). Reprinted with permission.

Psychotropic Drugs. At least one third of elderly patients hospitalized for medical or surgical illness in a general hospital received at least one psychotropic drug according to one report (Salzman and van der Kolk, 1980). About half of patients receiving a psychotropic drug report that the drug is essential for their daily functioning (Kalchthaler *et al.*, 1977).

Caution is necessary if elderly patients are to be treated effectively with psychotropic drugs without subjecting them to unnecessary polypharmacy, psychological dependence on drugs, and the side effects of potent drugs. Thompson *et al.* (1983) proposed a routine screening procedure prior to the institution of a psychotropic drug regimen for the elderly, which is presented in Table 10. In general, psychotropic drugs should be started in smaller doses (30–50% of normal adult starting dose) and increased very gradually. The dosage should be titrated against therapeutic effect and side effects. The physician should periodically attempt to taper off the medication. Psychotropic drugs should not be continued indefinitely in the absence of any clear-cut improvement in target symptoms. If in doubt, discontinue the medication (Thompson *et al.*, 1983).

Drugs for Anxiety, Agitation, and Psychosis. Benzodiazepines are useful for mild to moderate anxiety states in the elderly. The longer-acting benzodiazepines have the advantage of being able to be administered

Table 11. Selected Benzodiazepines: Pharmacological Factors of Special Relevance for the Elderly[a]

Drug	FDA-approved use	Half-life	Usual initial dose for the elderly
Flurazepam	Hypnotic	50–100 hours (major metabolite)	15 mg at bedtime
Temazepam	Hypnotic	5–15 hours	15 mg at bedtime
Oxazepam	Anxiolytic	5–20 hours	10 mg three times a day
Diazepam	Anxiolytic	20–100 hours (major metabolite)	2 mg per day or twice a day
Lorazepam	Anxiolytic	10–20 hours	0.5–2 mg per day

[a] From Thompson *et al.* (1983). Reprinted with permission.

only once a day, but the disadvantage of potential cumulative effects. There is evidence that the elderly, compared to younger patients, are more sensitive to benzodiazepines, due partly to increased target-organ sensitivity and partly to impairment of the drug metabolism (Thompson *et al.*, 1983). Antianxiety drugs should be used only for short-term relief of anxiety and not for long-term coping with stresses of life, for which psychotherapy or counseling is more appropriate (Thompson *et al.*, 1983). In using benzodiazepines, one should be aware that they are CNS depressants, that they potentiate the effect of alcohol, and that they are habit-forming.

See Table 11 for a list of benzodiazepines and their relevant attributes in the treatment of the elderly.

Antipsychotic drugs, in small doses, are effective in controlling severe agitation and confusion. These drugs, of course, are also used in treating coexisting psychosis. Antipsychotic drugs should be used only as a temporary measure and in the smallest effective doses in treating agitation and confusion because of the risk of tardive dyskinesia, a chronic and often irreversible movement disorder.

See Table 12 for a list of antipsychotic drugs with special relevance to the elderly patient.

Hypnotic Drugs. The elderly constitute about 11% of the whole population, but they are reported to receive almost 40% of all sedative-hypnotic prescriptions in the United States (Solomon *et al.*, 1979). There is a sleep-pattern change as well as a reduction in the total sleep time with age (see Figure 21 [Chapter 11]). There is often a disturbance in sleep

Table 12. Selected Antipsychotics: Pharmacological Factors of Special Relevance for the Elderly[a]

Agent	Relative potency[b]	Predominant side effects	Usual initial daily dose for the elderly
Chlorpromazine	100	Sedating, anticholinergic	10–25 mg two or three times a day
Thioridazine	95–100	Sedating, anticholinergic	10–25 mg two or three times a day
Thiothixene	5	Extrapyramidal	2–3 mg
Haloperidol	2	Extrapyramidal	0.5–2 mg
Fluphenazine	2	Extrapyramidal	0.5–2 mg

[a]From Thompson *et al.* (1983). Reprinted with permission.
[b]Chlorpromazine was arbitrarily assigned a potency of 100, for the sake of comparison with other agents. Thus, 100 mg of chlorpromazine approximately equals 2 mg of fluphenazine.

continuity in elderly persons. Napping is also common, which may reduce the amount of nighttime sleep.

In general, hypnotic drugs are not indicated for elderly patients, except on a temporary basis for relatively severe difficulty in falling asleep. Persistent sleep disturbances and early morning awakening should alert the physician to the possibility of a medical disease or the depressive syndrome.

When a hypnotic drug is indicated, benzodiazepines such as flurazepam and temazepam may be used (see Tables 11 and 23).

Barbiturates should be avoided in elderly patients, since these drugs are particularly prone to cause paradoxical excitement, suppression of rapid eye movement (REM) sleep (Chapter 11), and rebound nightmares and insomnia (Kales and Kales, 1974).

Antidepressant Drugs. Depression is an important syndrome that often mimics (pseudodementia) or coexists with dementia in the elderly. Clinically significant depression is considered to be present at any given time in at least 10% of the elderly population (Thompson *et al.*, 1983). Recognition and treatment of the depressive syndrome, then, is an important aspect of managing the elderly patient with dementia. (See Chapter 6 for further discussion of the depressive syndrome.)

Antidepressant drugs are effective when used in combination with psychotherapy and social support. Tricyclic antidepressants are most commonly used in elderly patients. Special attention should be paid to the anticholinergic and hypotensive effects of antidepressant drugs. Tricyclic antidepressants also have quinidinelike antiarrhythmic action, which may interact with other antiarrhythmic drugs, or cause heart block in patients with preexisting bundle-branch block.

Table 13. Selected Antidepressants: Pharmacological Factors of Special Relevance for the Elderly[a]

Agent	Category	Relative anticholinergic effects	Relative sedative effects	Usual initial daily dose for the elderly
Amitriptyline	Tricyclic tertiary amine	6+	5+	10 mg three times a day and possibly 20 mg at bedtime
Doxepin	Tricyclic tertiary amine	3+	6+	25–50 mg
Imipramine	Tricyclic tertiary amine	4+	3+	30–40 mg
Nortriptyline	Tricyclic secondary amine	3+	2+	25–50 mg
Desipramine	Tricyclic secondary amine	1+	2+	25–50 mg
Maprotiline	Tetracyclic	3+	3+	25 mg per day or twice a day
Amoxapine	Dibenzoxazepine	3+	3+	25 mg three times a day
Trazodone	Triazolopyridine	1+	3+	50–100 mg

[a]From Thompson *et al.* (1983) Reprinted with permission.

See Table 13 for a list of antidepressant drugs with special relevance to elderly patients (Thompson *et al.*, 1983).

Drugs to Improve Memory. There is as yet no demonstrably and consistently effective drug for the memory problems in elderly or demented patients. The search for drugs that may prevent or reverse intellectual deterioration is continuing along various lines (Giacobini, 1990). Among others, they include (1) agents that augment cholinergic function in the brain, (2) CNS stimulants, (3) drugs that affect dopaminergic, GABAergic, and peptidergic neurotransmission, (4) metabolic enhancers, (5) cerebral vasodilators, (6) drugs that affect autooxidation (e.g., Coenzyme Q), and (7) drugs that affect immune and autoimmune mechanisms.

Some promising results have been obtained with the administration of dietary lecithin, a choline precursor.

Earlier reports of promising results with the stimulant dihydroergotoxin mesylate (Hydergine) have not been confirmed (Thompson *et al.*, 1990). In aged rats, it has been shown that piracetam, a stimulant, and choline act synergistically in improving memory retention (Roberts, 1982). Although the results have not been striking, dihydroergotoxine

mesylate may be used in the dose range of 3–6 mg orally per day for mild to moderate memory deficit in the elderly patient (Salzman, 1982).

Personal Dimension

Patients with acute delirium are typically confused, bewildered, and often frightened. A reassuring and nondemanding approach by health-care personnel will tend to reduce the patient's anxiety. Because of the impaired memory, concentration, and attention span, formal psychotherapy has no place in the treatment of a delirious patient. Once delirium has cleared, patients often need psychotherapeutic help to integrate the frightening experience (which is often described as being dreamlike) into their ongoing life. Letting patients tell the clinician, when they wish, about the frightening thoughts, hallucinations, and other experiences, and letting them know that these are common phenomena caused by transient toxic influences on the brain, can help patients overcome their fears (e.g., of recurrence, of being "crazy") and continue with their normal lives.

Patients with progressive dementia may require supportive psychotherapy to help them cope with daily stresses and directive counseling in managing their lives. This kind of support can be given by the patient's significant other, such as spouse or friend, as well as by health-care personnel. The purpose of psychotherapy or counseling for the dementia patient is to supplement the declining problem-solving ability and memory while providing a sense of being cared for. Scheduling and routinizing daily activities to reduce demands for new learning is also an important part of treatment in the personal dimension.

Environmental Dimension

When a pathogenic environment is identified, removal of the patient from the environment (e.g., transfer of the patient out of the intensive care unit in cases of ICU psychosis) or stabilization of the environment may be effective in managing the patient with organic brain syndrome. Night-lights, a calendar, and familiar objects (such as photographs of family) from home can stabilize and familiarize a strange environment. The staff should orient the patient repeatedly, since the patient may not remember the date or the place even if the nurse has told the patient what they are only a few hours previously.

Hospitalization should be considered for patients who have acute delirium, either alone or superimposed on dementia, since delirium is usually reversible if the cause is identified and treated vigorously.

Hospitalization also provides a protective environment for the severely agitated or confused patient.

Many patients with dementia require the help of another person in supervising their medication regimens and, eventually, for daily living and personal hygiene. Visiting nurse or homemaker service may be necessary.

Usually, nursing home placement is eventually necessary for patients with such progressive dementias as Alzheimer's disease. Families of patients who must be admitted to nursing homes often require counseling and reassurance, since they tend to feel guilty and anxious. It is useful for the families to know that in end-stage dementia, the suffering of the significant other is usually greater than that of the patient.

SUMMARY

Organic brain syndromes are characterized by cognitive dysfunction due to a metabolic or structural brain dysfunction. Major areas of deficit include sensorium, orientation, attention, memory, concentration, logical thinking, abstraction, and judgment. Lability of affect is also present, and perceptual abnormalities such as illusions and hallucinations may occur.

In delirium, clouding of sensorium is characteristic, the onset is usually rapid, and the course is fluctuating and usually reversible. Delirium is caused by a metabolic derangement of the neurons secondary to alterations in the neuronal environment, e.g., toxins, electrolyte imbalance, or drug withdrawal. Delirium is always secondary to an underlying organic condition, and laboratory findings are helpful in identifying and monitoring the metabolic alteration. Treatment of delirium should always be geared to the underlying metabolic cause.

Dementia refers to a syndrome of acquired loss of intellectual abilities to the extent that social and occupational function is impaired. There is often progressive loss of memory and impairment of abstract thinking and judgment. Personality change is also common. Dementia tends to occur more commonly in the elderly. The onset and course of dementia depend on the underlying cause. There are many reversible or treatable causes of dementia, including vitamin deficiency syndromes (e.g., thiamine, B_{12}, niacin), endocrinopathies, and metabolic disorders. Alzheimer's disease and multiinfarct dementia account for approximately 75% of dementia in the elderly. Alzheimer's disease is the most common cause of senile dementia, and is characterized microscopically by large

numbers of neurofibrillary tangles, senile plaques, and granulovacuolar degeneration in the brain. There may be a selective involvement of cholinergic neurons in Alzheimer's disease. Aluminum, found in the neurofibrillary tangles, has also been implicated. Genetic factors, viruses, and immunological factors have also been implicated in the pathogenesis of Alzheimer's disease. All Down's syndrome patients who survive long enough develop Alzheimer changes in the brain. CT scan of Alzheimer's disease patients usually reveals evidence of cortical atrophy and enlarged ventricles.

Pseudodementia of depression is frequently misdiagnosed as Alzheimer's disease. Coexisting symptoms and signs of depression, past history of depression, and relatively rapid and fluctuating symptomatology should alert the physician concerning the possibility of pseudodementia, which is quite reversible with successful treatment of depression.

While there seems to be a mild generalized reduction in memory function and intellectual ability with aging, dementia is not a normal concomitant of aging. Some 80–90% of the elderly population do not develop dementia.

The evaluation of organic brain syndromes should be comprehensive, with particular attention to the clinical manifestations by careful mental-status examination, to the underlying biological condition through physical examination and laboratory tests, and to the precipitating environmental factors.

Treatment of organic brain syndromes should always be directed to the underlying cause. Antipsychotic drugs may be used in small doses to control severe agitation or psychotic symptoms, but never as a substitute for definitive treatment of the underlying disease. Nightlights, familiar objects, and repeated orienting stimuli help reduce disorientation and confusion. In irreversible dementia, supportive and protective environment, counseling, and symptomatic drug treatment may be indicated.

Drug therapy for elderly patients requires special considerations. Drug metabolism is usually delayed in older persons due to decreases in hepatic and renal function. Thus, drug blood levels and half-lives are often drastically increased in the elderly. Since elderly patients usually use more than one drug on an ongoing basis, the physician must consider the interactions of the drugs the patient is taking. Elderly patients may be particularly sensitive to benzodiazepines, and paradoxical agitation may occur with CNS depressant drugs. In general, drug therapy should be instituted with caution, for specific target symptoms or goals, and drugs should be started at a very low dose and increased very gradually.

For patients with major memory problems, drugs should be dispensed by someone other than the patient to avoid confusion and accidental overdose. Drugs should be dispensed in individual containers with clear markings for the time and date of ingestion.

IMPLICATIONS

For the Patient

Delirium is a common experience for acutely ill patients. The experience of acute confusion, disorientation, agitation, illusions, and hallucinations is frightening to patients. Explanations concerning the transient and toxic nature of these symptoms may be particularly reassuring.

Suspected dementia is frightening to the patient because of the implications, and naturally generates severe anxiety. Patients should be educated that there are many reversible causes of memory loss. When irreversible progressive dementia has been diagnosed, supportive and protective measures should be undertaken (e.g., writing down daily schedule, supervised medication regimen).

For the Physician

Since organic brain syndrome is one of the most common psychiatric conditions on nonpsychiatric services in the general hospital, the physician should be alert to the possibility of its presence whenever he or she encounters a patient who seems confused or agitated or whose behavior or personality seems to have changed somehow. Careful mental-status examination will document the presence or absence of organic brain syndrome. In performing the mental-status examination (see Chapter 13), the physician should be gentle and supportive and avoid "catastrophic reaction."

If delirium is present, the physician should promptly identify the underlying metabolic abnormality through appropriate examinations and laboratory tests. Effective and speedy treatment of the underlying cause is important, since delirium, if prolonged, may cause irreversible neuronal death, resulting in dementia.

The physician should take careful drug history and drug screens on patients with delirium, since drug intoxication and withdrawal are common causes of delirium.

The physician should be aware that significant memory loss and confusion are abnormal even in the elderly, and should be alert to the

possibility that the patient may have dementia that may be secondary to potentially reversible causes, which should be investigated vigorously.

In managing a patient with severe memory deficits, the physician should not rely on verbal instructions. Step-by-step, written instructions, preferably given to a caretaking person as well as the patient, will ensure compliance with the regimen. The physician should be aware of the special considerations in the drug treatment of the elderly described in this chapter.

For the Community and the Health-Care System

Illicit drug use, a social problem, is a common cause of delirium in the younger population. Society should be educated concerning the dangers of delirium that often results from either intoxication or withdrawal from drugs such as phencyclidine, amphetamines, and barbiturates.

Dementia is a disorder of epidemic proportions in the elderly population. Dementias related to vascular problems (e.g., multiinfarct dementia) may be prevented by better control of hypertension and atherosclerosis through early detection, treatment, and judicious diet.

Alzheimer's disease patients are eventually institutionalized. Since the elderly population is increasing, there is a need to provide more and better facilities for those who are afflicted with this disease as well as other conditions requiring protective environments.

Medical schools should educate future physicians concerning the special considerations in evaluating and managing elderly patients, as well as facilitate research into the mechanisms of age-related changes in intellectual function.

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