DEMENTIA

Dementia is chronic, global, usually irreversible deterioration of cognition. Diagnosis is clinical; laboratory and imaging tests are used to identify treatable causes. Treatment is supportive. Cholinesterase inhibitors can sometimes temporarily improve cognitive function.

Dementia may occur at any age but affects primarily the elderly (about 5% of those aged 65 to 74 and 40% of those > 85). It accounts for more than ½ of nursing home admissions. At least 5 million people in the US have dementia.

Dementias can be classified in several ways:

- Alzheimer's or non-Alzheimer's type
- Cortical or subcortical
- Irreversible or potentially reversible
- Common or rare

Etiology

Dementias may result from primary diseases of the brain or other conditions.

The most common types of dementia are Alzheimer's disease, vascular dementia, Lewy body dementia, frontotemporal dementias, and HIV-associated dementia. Dementia also occurs in patients with Parkinson's disease, Huntington's disease, progressive supranuclear palsy, Creutzfeldt-Jakob disease, Gerstmann-Sträussler-Scheinker syndrome, other prion disorders, and neurosyphilis. Patients can have > 1 type (mixed dementia).

Some structural brain disorders (eg, normal-pressure hydrocephalus, subdural hematoma), metabolic disorders (eg, hypothyroidism, vitamin B_{12} deficiency), and toxins (eg, lead) cause a slow deterioration of cognition that may resolve with treatment. This impairment is sometimes called reversible dementia, but some experts restrict the term dementia to irreversible cognitive deterioration.

Depression may mimic dementia (and was formerly called pseudodementia); the 2 disorders often coexist. However, depression may be the first manifestation of dementia.

Changes in cognition, including memory, occur with aging, but they are not dementia. The elderly have a relative deficiency in recall, particularly in speed of recall, compared with recall during their youth. However, this change does not affect daily function. Mild cognitive impairment is more severe than age-associated memory impairment; memory is impaired compared with that of age-matched controls, but other cognitive domains and daily function are not affected. Up to 50% of patients with mild cognitive impairment develop dementia within 3 yr.

Any disorder may exacerbate cognitive deficits in patients with dementia. Delirium often occurs in patients with dementia. Drugs, particularly benzodiazepines and anticholinergics (eg, some tricyclic antidepressants, antihistamines, antipsychotics, benztropine), may temporarily cause or worsen symptoms of dementia, as may alcohol, even in moderate amounts. New or progressive renal or liver failure may reduce drug clearance and cause drug toxicity after years of taking a stable drug dose (eg, of propranolol).

Symptoms and Signs

Dementia impairs cognition globally. Onset is gradual, although family members may suddenly notice deficits (eg, when function becomes impaired). Often, loss of short-term memory is the first sign. Although symptoms exist in a continuum, they can be divided into early, intermediate, and late.

Personality changes and behavioral disturbances may develop early or late. Motor and other focal neurologic deficits occur at different stages, depending on the type of dementia; they occur early in vascular dementia and late in Alzheimer's disease. Incidence of seizures is somewhat increased during all stages. Psychosis—hallucinations, delusions, or paranoia—occurs in about 10% of patients with dementia, although a higher percentage may experience these symptoms temporarily.

Early

Recent memory is impaired; learning and retaining new information become difficult. Language problems (especially with word finding), mood swings, and personality changes develop. Patients may have progressive difficulty with independent activities of daily living (eg, balancing their checkbook, finding their way around, remembering where they put things). Abstract thinking, insight, or judgment may be impaired. Patients may respond to loss of independence and memory with irritability, hostility, and agitation.

Functional ability may be further limited by the following:

- Agnosia: Impaired ability to identify objects despite intact sensory function
- Apraxia: Impaired ability to do previously learned motor activities despite intact motor function
- Aphasia: Impaired ability to comprehend or use language Although early dementia may not compromise sociability, family members may report strange behavior accompanied by emotional lability.

Intermediate

Patients become unable to learn and recall new information. Memory of remote events is reduced but not totally lost. Patients may require help with basic activities of daily living (eg, bathing, eating, dressing, toileting). Personality changes may progress. Patients may become irritable, anxious, self-centered, inflexible, or angry more easily, or they may become more passive, with a flat affect, depression, indecisiveness, lack of spontaneity, or general withdrawal from social situations. Behavior disorders may develop: Patients may wander or become suddenly and inappropriately agitated, hostile, uncooperative, or physically aggressive.

By this stage, patients have lost all sense of time and place because they cannot effectively use normal environmental and social cues. Patients often get lost; they may be unable to find their own bedroom or bathroom. They remain ambulatory but are at risk of falls or accidents secondary to confusion. Altered sensation or perception may culminate in psychosis with hallucinations and paranoid and persecutory delusions. Sleep patterns are often disorganized.

Late (severe)

Patients cannot walk, feed themselves, or do any other activities of daily living; they may become incontinent. Recent and remote memory is completely lost. Patients may be unable to swallow. They are at risk of undernutrition, pneumonia (especially due to aspiration), and pressure ulcers. Because they depend completely on others for care, placement in a long-term care facility often becomes necessary. Eventually, patients become mute.

Because such patients cannot relate any symptoms to a physician and because elderly patients often have no febrile or leukocytic response to infection, a physician must rely on experience and acumen whenever a patient appears ill. End-stage dementia results in coma and death, usually due to infection.

Diagnosis

- Differentiation of delirium from dementia, mainly by mental status examination

- Identification of treatable causes clinically and by laboratory testing and neuroimaging
- Sometimes formal neuropsychologic testing

Recommendations about diagnosis of dementia are available from the American Academy of Neurology.

Distinguishing type or cause of dementia can be difficult; definitive diagnosis often requires postmortem pathologic examination of brain tissue. Thus, clinical diagnosis focuses on distinguishing dementia from delirium and other disorders and identifying the cerebral areas affected and potentially reversible causes.

Dementia must be distinguished from the following:

- Delirium: Distinguishing between dementia and delirium is crucial (because delirium is usually reversible with prompt treatment) but can be difficult. Attention is assessed first. If a patient is inattentive, the diagnosis is likely to be delirium, although advanced dementia also severely impairs attention. Other features that suggest delirium rather than dementia are determined by the history, physical examination, and tests for specific causes.
- Age-associated memory impairment: This impairment is not severe enough to affect daily function. If affected people are given enough time to learn new information, their intellectual performance is good.
- Mild cognitive impairment: Memory is impaired, but other cognitive domains and daily function are not affected.
- Dementia of depression: This cognitive disturbance resolves with treatment of depression. Depressed older patients may experience cognitive decline, but unlike patients with dementia, they tend to exaggerate their memory loss and rarely forget important current events or personal matters. Neurologic examinations are normal except for signs of psychomotor slowing. When tested, patients with depression make little effort to respond, but those with dementia often try hard but respond incorrectly. When depression and dementia coexist, treating depression does not fully restore cognition.

Clinical criteria

The best screening test for dementia is a short-term memory test (eg, registering 3 objects and recalling them after 5 min); patients with dementia forget simple information within 3 to 5 min. Another test assesses the ability to name objects within categories (eg, lists of animals, plants, or pieces of furniture). Patients with dementia struggle to name a few; those without dementia easily name many.

In addition to loss of short-term memory, diagnosis of dementia requires at least one of the following cognitive deficits:

- Aphasia
- Apraxia
- Agnosia
- Impaired ability to plan, organize, sequence, or think abstractly (executive dysfunction)

Each cognitive deficit must substantially impair function and represent a significant decline from a previous level of functioning. Also, the deficits must not occur only during delirium.

A formal mental status examination should be done. The Mini-Mental Status Examination is often used. When delirium is absent, the presence of multiple deficits, particularly in patients with an average or a higher level of education, suggests dementia.

History and physical examination should then focus on signs of treatable disorders that cause cognitive impairment.

Laboratory testing

Tests should include thyroid-stimulating hormone and vitamin B_{12} levels. Routine CBC and liver function tests are sometimes recommended, but yield is very low. If clinical findings suggest a specific disorder, other tests (eg, for HIV or syphilis) are indicated. Lumbar puncture is rarely needed but should be considered if a chronic infection or neurosyphilis is suspected. Other tests may be used to exclude causes of delirium.

Neuroimaging

CT or MRI should be done in the initial evaluation of dementia or after any sudden change in cognition or mental status. Neuroimaging can identify potentially reversible structural disorders (eg, normal-pressure hydrocephalus, brain tumors, subdural hematoma) and certain metabolic disorders (eg, Hallervorden-Spatz disease, Wilson's disease). Occasionally, EEG is useful (eg, to evaluate episodic lapses in attention or bizarre behavior). Functional MRI or single-photon emission CT can provide information about cerebral perfusion patterns and help with differential diagnosis (eg, in differentiating Alzheimer's disease from frontotemporal dementia and Lewy body dementia).

Neuropsychologic testing

If the diagnosis remains in doubt, patients should be referred for formal neuropsychologic testing, which evaluates mood as well as all mental functions and takes 1 to 3 h. It is done or supervised by a neuropsychologist. Such testing helps primarily in differentiating the following:

- Age-associated memory impairment, mild cognitive impairment, and dementia, particularly when cognition is only slightly impaired or when the patient or family members are anxious for reassurance
- Dementia and focal syndromes of cognitive impairment (eg, amnesia, aphasia, apraxia, visuospatial difficulties) when the distinction is not clinically evident

Testing may also help characterize specific deficits due to dementia.

Prognosis

Dementia is usually progressive. However, progression rate varies widely and depends on the cause. Dementia shortens life expectancy, but survival estimates vary.

Treatment

- Measures to ensure safety
- Provision of appropriate stimulation, activities, and cues for orientation
- Elimination of drugs with sedating or anticholinergic effects
- Possibly cholinesterase inhibitors
- Assistance for caregivers
- Arrangements for end-of-life care

Recommendations about treatment of dementia are available from the American Academy of Neurology. Measures to ensure patient safety and to provide an appropriate environment are essential to treatment, as is caregiver assistance. Several drugs are available.

Patient safety

Occupational and physical therapists can evaluate the home for safety; the goals are to prevent accidents (particularly falls), to manage behavior disorders, and to plan for change as dementia progresses.

How well patients function in various settings (ie, kitchen, automobile) should be evaluated using simulations. If patients have deficits and remain in the same environment, protective measures (eg, hiding knives, unplugging the stove, removing the car, confiscating car keys) may be required. Some states require physicians to notify the Department of Motor Vehicles of patients with dementia because, at some point, such patients can no longer drive safely. If patients wander, signal monitoring systems can be installed, or patients can be registered in the Safe Return program. Information is available from the Alzheimer's Association. Ultimately, assistance (eg, housekeepers, home health aides) or a change of environment (living facilities without stairs, assisted-living facility, skilled nursing facility) may be indicated.

Environmental measures

Patients with mild to moderate dementia usually function best in familiar surroundings. Whether at home or in an institution, the environment should be designed to help preserve feelings of self-control and personal dignity by providing the following:

- Frequent reinforcement of orientation
- A bright, cheerful, familiar environment
- Minimal new stimulation
- Regular, low-stress activities

Large calendars and clocks and a routine for daily activities can help with orientation; medical staff members can wear large name tags and repeatedly introduce themselves. Changes in surroundings, routines, or people should be explained to patients precisely and simply, omitting nonessential procedures. Patients require time to adjust and become familiar with the changes. Telling patients about what is going to happen (eg, about a bath or feeding) may avert resistance or violent reactions. Frequent visits by staff members and familiar people encourage patients to remain social.

The room should be reasonably bright and contain sensory stimuli (eg, radio, television, night-light) to help patients remain oriented and focus their attention. Quiet, dark, private rooms should be avoided.

Activities can help patients function better; those related to interests before dementia began are good choices. Activities should be enjoyable, provide some stimulation, but not involve too many choices or challenges. Exercise to reduce restlessness, improve balance, and maintain cardiovascular tone should be done daily. Exercise can also help improve sleep and manage behavior disorders. Occupational and music therapy helps maintain fine motor control and provides nonverbal stimulation. Group therapy (eg, reminiscence therapy, socialization activities) may help maintain conversational and interpersonal skills.

Drugs

Eliminating or limiting drugs with CNS activity often improves function. Sedating and anticholinergic drugs, which tend to worsen dementia, should be avoided.

The cholinesterase inhibitors donepezil, rivastigmine, and galantamine are somewhat effective in improving cognitive function in patients with Alzheimer's disease or Lewy body dementia and may be useful in other forms of dementia. These drugs inhibit acetylcholinesterase, increasing the acetylcholine level in the brain.

Memantine, an NMDA (*N*-methyl-D-aspartate) antagonist, may help slow progression of moderate to severe dementia and can be used with a cholinesterase inhibitor.

Other drugs (eg, antipsychotics) have been used to control behavior disorders. Patients with dementia and signs of depression should be treated with nonanticholinergic antidepressants, preferably SSRIs.

Caregiver assistance

Immediate family members are largely responsible for care of a patient with dementia. Nurses and social workers can teach them and other caregivers how to best meet the patient's needs (eg, how to deal with daily care and handle financial issues); teaching should be ongoing. Other resources (eg, support groups, educational materials, Internet web sites) are available.

Caregivers may experience substantial stress. Stress may be caused by worry about protecting the patient and by frustration, exhaustion, anger, and resentment from having to do so much to care for someone. Health care practitioners should watch for early symptoms of caregiver stress and burnout and, when needed, suggest support services (eg, social worker, nutritionist, nurse, home health aide). If a patient with dementia has an unusual injury, the possibility of elder abuse should be investigated.

End-of-life issues

Because insight and judgment deteriorate in patients with dementia, appointment of a family member, guardian, or lawyer to oversee finances may be necessary. Early in dementia, before the patient is incapacitated, the patient's wishes about care should be clarified, and financial and legal arrangements (eg, durable power of attorney, durable power of attorney for health care) should be made. When these documents are signed, the patient's capacity should be evaluated, and evaluation results recorded. Decisions about artificial feeding and treatment of acute disorders are best made before the need develops. In advanced dementia, palliative measures may be more appropriate than highly aggressive interventions or hospital care.

ALZHEIMER'S DISEASE

Alzheimer's disease causes progressive cognitive deterioration and is characterized by senile plaques, β-amyloid deposits, and neurofibrillary tangles in the cerebral cortex and subcortical gray matter.

Alzheimer's disease is the most common cause of dementia; it accounts for > 65% of dementias in the elderly. The disease is twice as common among women as among men, partly because women have a longer life expectancy. Alzheimer's disease affects about 4% of people aged 65 to 74 and 30% of those > 85. Prevalence in industrialized countries is expected to increase as the proportion of the elderly increases.

Etiology

Most cases are sporadic, with late onset (≥ 60 yr) and unclear etiology. However, about 5 to 15% are familial; 1/2 of these cases have an early (presenile) onset (< 60 yr) and are typically related to specific genetic mutations.

At least 5 distinct genetic loci, located on chromosomes 1, 12, 14, 19, and 21, influence initiation and progression of Alzheimer's disease. Mutations in genes for the amyloid precursor protein, presenilin I, and presenilin II may lead to autosomal dominant forms of Alzheimer's disease, typically with presenile onset. In affected patients, the processing of amyloid precursor protein is altered, leading to deposition and fibrillar aggregation of *β*-amyloid. *β*-Amyloid may lead to neuronal death and formation of neurofibrillary tangles and senile plaques, which consist of degenerated axonal or dendritic processes, astrocytes, and glial cells around an amyloid core.

Other genetic determinants include the apolipoprotein (apo) E alleles (ε). Apo E proteins influence *β*-amyloid deposition, cytoskeletal integrity, and efficiency of neuronal repair. Risk of Alzheimer's disease is substantially increased in people with 2 ε4 alleles and may be decreased in those who have the ε2 allele. Variants in *SORL1* may also be involved; they are more common among people with late-onset Alzheimer's disease. These variants may cause the gene to malfunction, possibly resulting in increased production of *β*-amyloid.

The relationship of other factors (eg, low hormone levels, metal exposure) and Alzheimer's disease is under study, but no definite causal links have been established.

Pathophysiology

Typically, extracellular β-amyloid deposits, intracellular neurofibrillary tangles (paired helical filaments), and senile plaques develop, and neurons are lost. Cerebrocortical atrophy is common, and use of cerebral glucose is reduced, as is perfusion in the parietal lobe, temporal cortices, and prefrontal cortex.

Other common abnormalities include increased brain and CSF concentrations of the tau protein (a component of neurofibrillary tangles and β-amyloid) and reduced levels of choline acetyltransferase and various neurotransmitters (eg, somatostatin).

Symptoms and Signs

Symptoms and signs of Alzheimer's disease are similar to those of other dementias, with early, intermediate, and late stages. Loss of short-term memory is often the first sign. Cognitive deficits tend to involve multiple functions. The disease progresses gradually but may plateau for periods of time. Behavior disorders (eg, wandering, agitation, yelling, persecutory ideation) are common.

Diagnosis

- Similar to that of other dementias
- Formal mental status examination
- History and physical examination
- Laboratory testing
- Neuroimaging

Generally, diagnosis is similar to that of other dementias (see Delirium and Dementia: Diagnosis). Clinical criteria (including a thorough history and standard neurologic examination) are 85% accurate in establishing the diagnosis and differentiating Alzheimer's disease from other forms of dementia, such as vascular dementia and Lewy body dementia.

Traditional diagnostic criteria for Alzheimer's disease include all of the following:

- Dementia established clinically and documented by a formal mental status examination
- Deficits in ≥ 2 areas of cognition
- Gradual onset and progressive worsening of memory and other cognitive functions
- No disturbance of consciousness
- Onset after age 40, most often after age 65
- No systemic or brain disorders that could account for the progressive deficits in memory and cognition

However, deviations from these criteria do not exclude a diagnosis of Alzheimer's disease, particularly because patients may have mixed dementia.

Differential diagnosis

Distinguishing Alzheimer's disease from other dementias is difficult. Assessment tools can help distinguish vascular dementia from Alzheimer's disease. Fluctuations in cognition, parkinsonian symptoms, well-formed visual hallucinations, and relative preservation of short-term memory suggest Lewy body dementia rather than Alzheimer's disease. Patients with Alzheimer's disease are often better-groomed and neater than patients with other dementias.

Prognosis

Although progression rate varies, cognitive decline is inevitable. Average survival from time of diagnosis is 7 yr, although this figure is debated. Average survival from the time patients can no longer walk is about 6 mo.

Treatment

- Generally, similar to that of other dementias
- Possibly cholinesterase inhibitors and memantine

General treatment is the same as that of all dementias.

Cholinesterase inhibitors modestly improve cognitive function and memory in some patients. Four are available; generally, donepezil, rivastigmine, and galantamine are equally effective, but tacrine is rarely used because of its hepatotoxicity. Donepezil is a first-line drug because it has once/day dosing and is well-tolerated. The recommended dose is 5 mg once/day for 4 to 6 wk, then increased to 10 mg once/day. Treatment should be continued if functional improvement is apparent after several months, but otherwise it should be stopped. The most common adverse effects are GI (eg, nausea, diarrhea). Rarely, dizziness and cardiac arrhythmias occur. Adverse effects can be minimized by increasing the dose gradually.

Memantine, an *N*-methyl-D-aspartate receptor antagonist, appears to slow the progression of Alzheimer's disease. The dose is 5 mg po once/day, which is increased to 10 mg po bid over about 4 wk. For patients with renal insufficiency, the dose should be reduced or the drug should be avoided. Memantine can be used with a cholinesterase inhibitor.

Efficacy of high-dose vitamin E (1000 IU po once/day or bid), selegiline, NSAIDs, *Ginkgo biloba* extracts, and statins is unclear. Estrogen therapy does not appear useful in prevention or treatment and may be harmful.

Prevention

Preliminary, observational evidence suggests that risk of Alzheimer's disease may be decreased by the following:

- Continuing to do challenging mental activities (eg, learning new skills, doing crossword puzzles) well into old age
- Exercising
- Controlling hypertension
- Lowering cholesterol levels
- Consuming a diet rich in ω-3 fatty acids and low in saturated fats
- Drinking alcohol in modest amounts

However, there is no convincing evidence that people who do not drink alcohol should start drinking to prevent Alzheimer's disease.

VASCULAR DEMENTIA

Vascular dementia is acute or chronic cognitive deterioration due to diffuse or focal cerebral infarction that is most often related to cerebrovascular disease.

Vascular dementia is the 2nd most common cause of dementia among the elderly. It is more common among men and usually begins after age 70. It occurs more often in people who have vascular risk factors (eg, hypertension, diabetes mellitus, hyperlipidemia, smoking) and in those who have had several strokes. Many people have both vascular dementia and Alzheimer's disease.

Vascular dementia occurs when multiple small cerebral infarcts (or sometimes hemorrhages) cause enough neuronal or axonal loss to impair brain function. Vascular dementias include the following:

- **Lacunar disease:** Small blood vessels are affected.
- **Multi-infarct dementia:** Medium-sized blood vessels are affected.
- **Strategic single-infarct dementia:** A single infarct occurs in a crucial area of the brain (eg, angular gyrus, thalamus).
- **Binswanger's dementia (subcortical arteriosclerotic encephalopathy):** This uncommon variant of small-vessel dementia is associated with severe, poorly controlled hypertension and systemic vascular disease. It involves multiple lacunar infarcts in deep hemispheric white and gray matter.

Symptoms and Signs

Symptoms and signs are similar to those of other dementias. However, because infarction is the cause, vascular dementia tends to progress in discrete steps; each episode is accompanied by intellectual decline, sometimes followed by modest recovery.

As the disease progresses, focal neurologic deficits often develop:

- Exaggeration of deep tendon reflexes
- Extensor plantar response
- Gait abnormalities
- Weakness of an extremity
- Hemiplegias
- Pseudobulbar palsy with pathologic laughing and crying
- Other signs of extrapyramidal dysfunction

However, because small-vessel ischemic damage tends to cause small, incremental deficits, the decline appears to be gradual.

Cognitive loss may be focal. For example, short-term memory may be less affected than in other dementias. Patients with partial aphasia may be more aware of their deficits; thus, depression may be more common than in other dementias.

Diagnosis

Diagnosis is similar to that of other dementias. If focal signs or evidence of cerebrovascular disease is present, a thorough evaluation for stroke should be done.

CT and MRI may show bilateral multiple infarcts in the dominant hemisphere and limbic structures, multiple lacunar strokes, or periventricular white-matter lesions extending into the deep white matter. In Binswanger's dementia, imaging shows leukoencephalopathy in the cerebrum semiovale adjacent to

the cortex, often with multiple lacunae affecting structures deep in the gray matter (eg, basal ganglia, thalamic nuclei).

Prognosis

The 5-yr mortality rate is 61%, which is higher than that for most forms of dementia, presumably because other atherosclerotic disorders coexist.

Treatment

Generally, treatment is the same as that of other dementias (see Delirium and Dementia: Treatment). However, vascular dementia may be preventable, and its progression may be slowed by BP control, cholesterol-lowering therapy, regulation of plasma glucose (90 to 150 mg/dL), and smoking cessation.

The efficacy of cholinesterase inhibitors and memantine is uncertain. However, because many patients also have Alzheimer's disease, these drugs may have some benefit. Adjunctive drugs for depression, psychosis, and sleep disorders are useful.

LEWY BODY DEMENTIA

Lewy body dementia is chronic cognitive deterioration characterized by cellular inclusions called Lewy bodies in the cytoplasm of cortical neurons.

Lewy body dementia is the 3rd most common dementia. Age of onset is typically > 60.

Lewy bodies are spherical, eosinophilic, neuronal cytoplasmic inclusions composed of aggregates of α-synuclein, a synaptic protein. They occur in the cortex of some patients with primary Lewy body dementia. Neurotransmitter levels and neuronal pathways between the striatum and the neocortex are abnormal.

Lewy bodies also occur in the substantia nigra of patients with Parkinson's disease, and patients with Parkinson's disease may develop Lewy body dementia. Thus, some experts think that Parkinson's disease and Lewy body dementia may be part of a more generalized synucleopathy affecting the central and peripheral nervous systems. Lewy bodies sometimes occur in patients with Alzheimer's disease, and patients with Lewy body dementia may have neuritic plaques and neurofibrillary tangles. Lewy body dementia, Parkinson's disease, and Alzheimer's disease overlap considerably. Further research is needed to clarify the relationships among them.

Symptoms and Signs

Initial cognitive deterioration resembles that of other dementias. Extrapyramidal symptoms occur. However, unlike in Parkinson's disease, in Lewy body dementia, cognitive and extrapyramidal symptoms usually begin within 1 yr of each other. Also the extrapyramidal symptoms differ from those of Parkinson's disease: In Lewy body dementia, tremor does not occur early, rigidity of axial muscles with gait instability occurs early, and deficits tend to be symmetric. Repeated falls are common.

Fluctuating cognitive function is a relatively specific feature of Lewy body dementia. Periods of being alert, coherent, and oriented may alternate with periods of being confused and unresponsive to questions, usually over a period of days to weeks but sometimes during the same interview. Memory is impaired, but the impairment appears to result more from deficits in alertness and attention than in memory acquisition; thus, short-term recall is affected less than digit span memory (ability to repeat 7 digits forward and 5 backward). Patients may stare into space for long periods. Excessive daytime drowsiness is common. Visuospatial and visuoconstructional abilities (tested by block design, clock drawing, or figure copying) are affected more than other cognitive deficits. Thus, Lewy body dementia

may be difficult to distinguish from delirium, and all patients presenting with these symptoms and signs should be evaluated for delirium.

Visual hallucinations are common and often threatening, unlike the benign hallucinations of Parkinson's disease. Auditory, olfactory, and tactile hallucinations are less common. Delusions occur in 50 to 65% of patients and are often complex and bizarre, compared with the simple persecutory ideation common in Alzheimer's disease.

Autonomic dysfunction is common, and unexplained syncope may result. Autonomic dysfunction may occur simultaneously with or after onset of cognitive deficits. Extreme sensitivity to antipsychotics is typical. Many patients have rapid eye movement (REM) sleep behavior disorder, a parasomnia characterized by vivid dreams without the usual physiologic paralysis of skeletal muscles during REM sleep. As a result, dreams may be acted out, sometimes injuring the bed partner.

Lewy body dementia progresses; prognosis is poor.

Diagnosis

- Clinical criteria
- Neuroimaging to rule out other disorders

Diagnosis is clinical, but sensitivity and specificity are poor.

Diagnosis is considered probable if 2 of 3 features—fluctuations in cognition, visual hallucinations, and parkinsonism—are present and possible if only one is present. Supportive evidence consists of repeated falls, syncope, and sensitivity to antipsychotics. Overlap of symptoms in Lewy body dementia and Parkinson's disease may complicate diagnosis. When motor deficits (eg, tremor, bradykinesia, rigidity) precede and are more severe than cognitive impairment, Parkinson's disease is usually diagnosed. When early cognitive impairment and behavioral disturbances predominate, Lewy body dementia is usually diagnosed.

CT and MRI show no characteristic changes but are helpful initially in ruling out other causes of dementia. Positron emission tomography with fluorine-18-labeled deoxyglucose and single-photon emission CT (SPECT) with ^{123}I-FP-CIT (N-w-fluoropropyl-2b-carbomethoxy-3b-[4-iodophenyl]-tropane), a fluoroalkyl analog of cocaine, may help identify Lewy body dementia but are not routinely done. Definitive diagnosis requires autopsy samples of brain tissue.

Treatment

Treatment is generally supportive. Rivastigmine 1.5 mg po bid, titrated upward as needed to 6 mg bid, may improve cognition. Other cholinesterase inhibitors may also be useful. In about ½ of patients, extrapyramidal symptoms respond to antiparkinsonian drugs, but psychiatric symptoms may worsen. If such drugs are needed, levodopa is preferred.

Traditional antipsychotics, even at very low doses, tend to acutely worsen extrapyramidal symptoms and are best avoided.

HIV-ASSOCIATED DEMENTIA

HIV-associated dementia is chronic cognitive deterioration due to brain infection by HIV.

HIV-associated dementia (AIDS dementia complex) may occur in the late stages of HIV infection. Unlike almost all other forms of dementia, it tends to occur in younger people. Purely HIV-associated dementia is caused by neuronal damage by the HIV virus. However, in patients with HIV infection, dementia may result from other infections, such as secondary infection with JC virus causing

progressive multifocal leukoencephalopathy. Other opportunistic infections (eg, fungal, bacterial, viral, protozoan) may also contribute.

In purely HIV-associated dementia, subcortical pathologic changes result when infected macrophages or microglial cells infiltrate into the deep gray matter (ie, basal ganglia, thalamus) and white matter.

Prevalence of dementia in late-stage HIV infection ranges from 7 to 27%, but 30 to 40% may have milder forms. Incidence is inversely proportional to $CD4^+$ count.

Symptoms and Signs

Symptoms and signs may be similar to those of other dementias. Early manifestations include slowed thinking and expression, difficulty concentrating, and apathy; insight is preserved, and manifestations of depression are few. Motor movements are slowed; ataxia and weakness may be evident. Abnormal neurologic signs may include paraparesis, lower-extremity spasticity, ataxia, and extensor-plantar responses. Mania or psychosis is sometimes present.

Diagnosis

Generally, diagnosis of dementia in patients with HIV infection is similar to that of other dementias. However, when patients present with an acute change in cognitive function, the cause must be identified as soon as possible.

CT or MRI should be done to check for signs of CNS infection (eg, toxoplasmosis). MRI is more useful than CT because it can exclude other CNS causes of dementia (eg, progressive multifocal leukoencephalopathy, cerebral lymphoma). Late-stage findings of HIV dementia may include diffuse nonenhancing white matter hyperintensities, cerebral atrophy, and ventricular enlargement. If no contraindication is identified by neuroimaging, lumbar puncture is done to rule out infection.

Prognosis and Treatment

Patients with HIV infection and untreated dementia have a worse prognosis (average life expectancy of 6 mo) than those without dementia.

The primary treatment is highly active antiretroviral therapy, which increases $CD4^+$ counts and improves cognitive function. Supportive measures are similar to those for other dementias.