treatment of risk factors for vascular disease—blood pressure control, smoking cessation, diet modification, and anticoagulation (in select settings such as atrial fibrillation)—is mandatory and may be of benefit.

Frontotemporal Dementias

Patients with the behavioral variant of frontotemporal dementia (FTD) are frequently socially disinhibited, but they may also be lethargic and lack motivation and spontaneity. Patients with the progressive nonfluent aphasia variant of FTD have loss of speech fluency with poor articulation and syntactic errors but relative preservation of comprehension. Those with the semantic dementia variant of FTD remain fluent with normal phonation but have progressive difficulty with naming and word comprehension. Memory and spatial skills and praxis are relatively preserved early on in all of these forms, whereas executive function, emotional regulation, and conduct are relatively impaired.

There are several frontotemporal lobar degenerations (FTLDs), including Pick's disease (now referred to as FTLD-tau). In some families, a mutation in the microtubule-associated protein tau gene *(MAPT)* on chromosome 17 causes tau-positive frontotemporal dementia with parkinsonism (FTDP-17). Transactive response DNA-binding protein (TDP-43) pathology accounts for 40% of FTD with or without motor neuron disease. Although mutations in the fused in sarcoma gene *(FUS)* had previously been identified as a cause of familial amyotrophic lateral sclerosis (ALS), some also give rise to 5% to 10% of clinically diagnosed FTD (typically the behavioral variant). Hexanucleotide repeat expansions in *C9orf72* cause neurodegeneration in FTD and ALS. RNA processing is abnormal in both conditions.

As in AD, all forms of FTD progress for years. No intervention slows the inevitable decline of these patients. Approximately 50% of patients have a family history of the disease.

Parkinson's Disease

Almost 50% of patients with Parkinson's disease (see Chapter 114) become demented by the time they reach the age of 85 years. The dementia of Parkinson's disease affects executive function out of proportion to its impact on language and visuospatial processing. Thought processes appear to slow down (i.e., bradyphrenia), analogous to the slowing of movement (i.e., bradykinesia).

Because dementia occurs relatively late in the progression of Parkinson's disease, most patients are taking drugs to improve their movement disorder by enhancing dopaminergic neurotransmission. These drugs can induce psychosis. Dose reductions should be attempted before the diagnosis of underlying dementia is made for these patients. Acetylcholinesterase inhibition has been helpful for patients with dementia caused by Parkinson's disease, and the FDA has specifically approved rivastigmine for this indication.

Normal-Pressure Hydrocephalus

The triad of dementia (typically subcortical), gait instability, and urinary incontinence suggests the possibility of normal-pressure hydrocephalus. These patients appear to walk with their feet stuck to the floor, without lifting up the knees and with a broad base. Symptoms evolve over the course of weeks to months, and brain imaging reveals ventricular enlargement out of proportion to the degree of cortical atrophy.

Numerous diagnostic tests have been described, including radionuclide cisternography and MRI flow studies. The most important test remains the clinical response to removal of large volumes of CSF through serial lumbar punctures or the temporary placement of a lumbar drain, followed by examination of the patient's gait and cognitive function. Neurosurgical placement of a permanent ventriculoperitoneal shunt may correct the problem. Patients likely to benefit from shunt placement have a clear response to the removal of 30 to 40 mL of spinal fluid, with improved gait and alertness within minutes to hours of the procedure. The cause of normal-pressure hydrocephalus is a derangement of the CSF hydrodynamics. Shunt placement is most likely to be effective if normal-pressure hydrocephalus occurs after severe head trauma or subarachnoid hemorrhage.

Prion Infection, Chronic Meningitis, and Dementia Related to Acquired Immunodeficiency Syndrome

Creutzfeldt-Jakob disease (CJD) is a subacute, dementing, transmissible illness with typical onset between 40 and 75 years of age and an incidence of one case per 1 million people (see Chapter 90). The disease causes spongiform degeneration and gliosis in widespread areas of the cortex. Clinical variants of the disorder are differentiated by the relative predominance of cerebellar symptoms, extrapyramidal hyperkinesias, or visual agnosia and cortical blindness (i.e., Heidenhain variant).

Ninety percent of patients with CJD have myoclonus, compared with 10% of patients with AD. Patients with all forms of the disease share a relentlessly progressive dementia and disruption of personality over weeks to months. The electroencephalogram shows characteristic abnormalities, including diffuse slowing and periodic sharp waves or spikes.

The transmissible agent, a prion protein, is invulnerable to routine modes of antisepsis. CSF can be tested for the 14-3-3 protein, although this test is not as sensitive or specific for CJD as once hoped (see Chapter 90). Diffusion-weighted MRI images show characteristic cortical ribbon changes.

Certain infectious agents can cause the subacute or chronic development of subcortical dementia. These chronic meningitides are discussed in Chapter 90.

Human immunodeficiency virus accesses the central nervous system through monocytes and the microglial system and causes associated neuronal cell loss, vacuolization, and lymphocytic infiltration. The dementia associated with this infection is characterized by bradyphrenia and bradykinesia. Patients have executive dysfunction, impaired memory, poor concentration, and apathy. Treatment of the underlying viral infection with protease inhibitors and reverse transcriptase inhibitors may slow the progression of the dementia (see Chapter 90).

OTHER MEMORY DISTURBANCES

Structure of Memory

Memory function is divided into introspective processes (i.e., declarative, explicit, aware memories) and processes that are not accessible to introspection (i.e., nondeclarative, implicit, procedural memories). Short-term memory (e.g., words on a list) is