Diagnostic criteria for dementia include memory impairment plus impairment in at least one other cognitive function, including aphasia, apraxia, agnosia, or disturbance in executive functioning. These deficits must represent a decline from a previous level of functioning and be sufficiently severe to cause significant impairment in social or occupational performance. The diagnosis of dementia begins with a patient presenting with memory difficulties or other complaints. These can include apathy or lack of initiative, disorientation, sleep–wake cycle disturbance, aggression, disinhibition, agitation, depression, anxiety, or psychotic symptoms, as well as impairment in cognitive domains such as attention and concentration, language, motor coordination, recognition of objects, visuospatial skills, insight, and judgment. The patient may be self-referred or brought to the clinician’s attention by concerned family members, friends, neighbors, or health care professionals. While several decision trees for dementia exist, the process of differential diagnosis can be summarized in three questions (Table I):

- Does the patient have dementia?
- Does the patient have dementia alone or dementia comorbid with some other condition(s)?
- What is the etiology of the patient’s dementia?

A comprehensive work-up for dementia includes a thorough history, with reports from informants as well as the patient, a mental status evaluation, and physical, neurological, and neuropsychological examinations. Neuroimaging and specific laboratory tests are recommended, depending upon findings from the history and physical examination.

### Does the patient have dementia?

The first question requires the diagnostician to distinguish dementia from depression, delirium, intoxication, and other conditions such as mental retardation, schizophrenia, bipolar disorder, and malingering. Important issues for the clinician to consider at this stage include whether objective findings of impairment support a diagnosis of dementia, because memory complaints unaccompanied by objective impairment may indicate depression. Additionally, a cognitive profile suggestive of depression may include decreased working memory, psychomotor slowing, and responses that suggest lack of motivation or effort, as well as prominent mood symptoms or somatic complaints. Clear consciousness and a stable course would tend to rule out delirium, a potentially fatal condition that is often reversible when the cause (eg, medication or substance, nutritional deficiency, infection) is remedied. Substance use history, including use of alcohol and prescription medications, could suggest intoxication. An impairment of recent origin with a history of good premorbid functioning would likely rule out mental retardation and serious psychopathology, although new onset of psychotic disorders in middle to late life is more common than previously thought. Finally, the presence of secondary gain and inconsistent performance on neuropsychological testing (eg, poorer performance on easier items than on more difficult items) might suggest malingering.
Patients occasionally present with deficits in one cognitive domain only. Amnestic disorder is characterized by memory impairment in the absence of other cognitive deficits.\(^4\) Aphasia, apraxia, agnosia, and disturbance in executive functioning, without accompanying memory deficit, are classified as “cognitive impairment not otherwise specified.” The deficit may be caused by a focal lesion or may be the initial symptom of a dementing process. Longitudinal follow-up of the patient is essential.

**Does the patient have dementia alone or dementia comorbid with some other condition(s)?**

It is important to recognize that conditions that cause cognitive and functional impairment are not mutually exclusive; hence the question of whether the dementia is comorbid with another condition, such as delirium, depression, or substance abuse, or a medical condition, such as tumor or infection, must be addressed. Often, treatment of the coexisting condition can reduce the degree of impairment and improve the quality of life.

Dementia may also have multiple etiologies. For example, substance abuse and traumatic brain injury can contribute to dementia of other etiologies as well as cause dementia in their own right, eg, dementia due to head trauma, Korsakoff syndrome, or substance-induced persisting dementia. Anoxia, another common contributing factor, can result from heart attack, severe asthma, smoke or carbon monoxide inhalation, high altitude exposure, strangulation, anesthetic accidents, or poisoning. Because an older individual may present with a complex history and multiple medical comorbidities, it is important to diagnose the patient, not the disease.

**What is the etiology of the patient’s dementia?**

Finally, the clinician must determine the etiology of the dementia. Although there are innumerable causes of dementia, the initial diagnostic focus is usually on the conditions that are most common and those that are

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**Table I.** Diagnostic decision tree in dementia.

| A. Does the patient have dementia? |
|-----------------------------------|
| 1. Is there impairment in memory plus one of the following: aphasia, apraxia, agnosia, disturbance in executive functioning? |
| 2. Does it represent a decline from premorbid functioning? |
| 3. Does it interfere with social or occupational functioning? |
| 4. Differentiate from delirium, depression, intoxication, mental retardation, psychopathology, malingering |

| B. Does the patient have dementia alone or dementia with some other comorbid condition(s)? |
|-----------------------------------|
| 1. Delirium, depression, substance abuse, medical conditions in addition to primary etiology |
| 2. Head trauma, substance abuse, anoxia as contributing factors |

| C. What is the etiology of the patient’s dementia? |
|-----------------------------------|
| 1. Common causes of dementia: Alzheimer disease, vascular dementia, mixed dementia, frontotemporal dementia, Parkinson disease, human immunodeficiency virus (HIV) disease, Huntington disease |
| 2. Potentially modifiable causes of dementia: metabolic or toxic encephalopathies, central nervous system infections, neoplasms, normal pressure hydrocephalus |
| 3. Less common causes of dementia: systemic disorders, inflammatory disease, immune disorders, metabolic conditions, Wilson disease, Creutzfeldt-Jakob disease, progressive supranuclear palsy, epilepsy, demyelinating diseases |

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Potentially modifiable. Dementia of the Alzheimer type is the most common form of dementia. Diagnostic criteria for Alzheimer disease include dementia with gradual onset and progressive decline that cannot be attributed to other conditions. Typically, the first symptom is an inability to learn new information. Other early symptoms include visuospatial deficits, decreased verbal fluency, and subtle personality changes. Vascular dementia has a variable onset, presentation, and course due to the heterogeneity of cerebrovascular insults that can result in cognitive impairment, although onset is often abrupt with a stepwise progression. Vascular dementia is diagnosed when focal neurological signs and symptoms or laboratory findings indicate the presence of cerebrovascular disease. Treatment of the underlying hypertension and vascular disease may prevent further progression of dementia. Dementia of combined vascular and Alzheimer etiology, or mixed dementia, may be more common than pure vascular dementia. Other common progressive dementing conditions include the frontotemporal dementias, such as Pick disease, in which patients often present initially with personality change rather than cognitive impairment, and Lewy body disease, including dementia due to Parkinson disease, which is associated with extrapyramidal signs. Symptoms of dementia due to the human immunodeficiency virus include forgetfulness, impairment in attention and concentration, psychomotor slowing, poor balance, and tremor. Symptoms of dementia due to Huntington disease, a condition caused by an autosomal dominant gene, include changes in behavior and personality, as well as characteristic choreiform movements. Potentially modifiable dementias include those due to metabolic or toxic encephalopathies, central nervous system infections, tumors, and normal pressure hydrocephalus. It is important to note that recovery of function following treatment for these so-called “reversible dementias” may be incomplete. Hypothyroidism, hypercalcemia, hypoglycemia, and nutritional deficiencies are among the more common metabolic causes of dementia. Deficiencies of vitamin B12, folic acid, and niacin can lead to dementias that are partially reversible with appropriate supplementation. Patients with dementia due to infectious agents may present with confusion along with impaired attention and arousal or signs of increased intracranial pressure, such as headache and nausea. Neoplasia-associated dementias have a variety of neurological signs and symptoms, as well as variability in course and onset, due to their heterogeneous etiology. Pathognomonic signs of normal pressure hydrocephalus include dementia, gait disturbance, and urinary incontinence. Treatment involves surgical shunting, which is most effective among patients with the complete triad including early gait disturbance. Other dementias are less common and typically not reversible. Systemic disorders such as cardiopulmonary failure, anemia, hepatic encephalopathy, and inflammatory disease can produce dementia, as can immune disorders such as temporal arteritis and systemic lupus erythematosus. Metabolic conditions with associated dementia include Kufs disease, adrenoleukodystrophy, and metachromatic leukodystrophy. Neurosyphilis and Lyme disease are chronic nervous system infections that can cause dementia. Hepatolenticular degeneration (Wilson disease) and dementias due to prion diseases such as Creutzfeldt-Jakob disease have a subacute course. Less common subcortical dementias with a chronic course and steady progression include those due to progressive supranuclear palsy, myoclonic epilepsy, and demyelinating diseases such as multiple sclerosis.

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A comprehensive biopsychosocial evaluation is important in the diagnosis and management of dementia. An accurate history with data from multiple sources is critical. Laboratory testing can help diagnose or rule out conditions like hypothyroidism, anemia, pulmonary dysfunction, hypoglycemia, renal dysfunction, and endocrinopathies. Neuroimaging is particularly important in the diagnosis of vascular dementia and neoplasms. Psychological counseling may help the individual grieve for lost functioning and learn compensatory strategies; work with caregivers is often helpful to alleviate burden. Appropriate social and environmental support may allow the person to remain independent as long as possible.

Last but not least, we should stress that, because of the difficulty of differential diagnosis and the frequency of comorbidity, the clinician must be prepared to keep an open mind and follow the patient longitudinally. For example, patients presenting with depression for the first time in late life frequently go on to develop dementia. The course of a progressive dementia such as Alzheimer disease will often distinguish it from impairment due to head injury or stroke.

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