CHAPTER 14

DEMENTIA

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GENERAL CONSIDERATIONS

1. How is dementia defined? How do definitions vary?

Dementia is generally regarded as an acquired loss of cognitive function due to an abnormal brain condition. The National Institutes of Health criteria (formerly NINCDS-ADRDA criteria) for the diagnosis of Alzheimer's disease (AD) stress that there must be progressive loss of cognitive function, including but not limited to memory loss. The DSM-IV general criteria for dementia include the requirement of functional decline that interferes with work or usual social activities in addition to cognitive decline.

American Psychiatric Association: Diagnostic and Statistical Manual of Mental Disorders, 4th ed. Washington, D.C., American Psychiatric Association, 1994.

McKhann G, Drachman D, Folstein M, et al.: Clinical diagnosis of Alzheimer's disease: Report of the NINCDS-ADRDA Work Group under the auspices of Department of Health and Human Services Task Force on Alzheimer's disease. Neurology 34:939-944, 1984.

2. What is senility? Is it normal?

Senility is an outdated term. It used to mean cognitive impairment due to aging, which was assumed to be normal. Although memory, learning, and thinking change with age in subtle ways, memory loss and cognitive impairment are not features of normal aging.

3. What is pseudodementia?

Pseudodementia has many meanings. It refers to depressed patients who are cognitively impaired and often have psychomotor slowing but do not have one of the well-defined dementia syndromes. The term does not mean that the patient is consciously simulating dementia (malingering) or is cognitively intact but believes himself or herself to be demented (Ganser's syndrome). Some researchers believe that pseudodementia may be a precursor to dementia.

4. What features are characteristic of pseudodementia associated with depression?

Patients with pseudodementia may or may not have a history of depressive or vegetative symptoms. They tend to have flat affect, to give up easily when mental status is examined, or to say that they cannot perform a task without even trying it. They often respond surprisingly well when given extra time and encouragement, but they may deny their success. Results of mental status examination are inconsistent; for example, they may fail a simple task but perform a similar, more difficult one correctly. Or they may have variable strengths and weaknesses over repeated testing sessions.

5. What is Ganser's syndrome?

It is an involuntary and unconscious simulation of altered mental status (confusion or dementia) in a patient who is not malingering and believes in the validity of his or her symptoms.

6. What is delirium?

Delirium is an acute confusional state.

7. What features distinguish delirium from dementia?

Although this distinction cannot always be made with certainty, several features are helpful. Sudden onset suggests delirium, as do findings of altered consciousness, marked problems with attention and concentration out of proportion to other deficits, cognitive fluctuations (e.g., lucid intervals), psychomotor and/or autonomic overactivity, fragmented speech, and marked hallucinations (especially auditory or tactile). Chronically demented patients may develop delirium in addition to dementia, which will change the clinical picture.

8. Do all patients with dementia develop psychotic features?

No. Psychosis is a variable finding in all types of dementia and is not even clearly related to the stage or severity of dementia.

9. Which screening instruments are commonly used in diagnosing dementia?

The Folstein Mini-Mental Status Examination (MMSE), Short Blessed dementia scale, and Mattis Dementia Rating Scale are commonly used clinically and in experimental studies to screen for dementia and to rate severity of dementia.

10. What are the limitations of the MMSE in the assessment of dementia?

Besides the fact that it has both false-positive (usually depression) and false-negative results (usually early dementia in highly functioning patients), the MMSE also has limitations based on its lack of comprehensiveness.

11. At what point is a patient too demented to require an evaluation?

No patient is too demented to be evaluated. The need to rule out reversible causes and structural lesions always remains. Neurologic and psychometric examinations can be tailored to the level of even the most profoundly demented patients. Further, even severely demented patients may respond to treatments.

12. What are the most common causes of dementia or conditions resembling dementia?

Alzheimer's disease is the most common form of dementia in adults (>80% in most series). Depression with pseudodementia is a frequent cause of cognitive loss and must be ruled out in all patients. Other important causes include multi-infarct or vascular dementia, dementia with Lewy bodies, frontotemporal dementia, and dementia-like syndromes due to alcohol or chronic use of certain prescription drugs.

13. What uncommon causes of dementia must be considered in the differential diagnosis *of every patient with dementia?*

1. Toxins (lead, organic mercury)
2. Vitamin deficiencies (B_{12}, B_1, and B_6, in particular)
3. Endocrine disturbances (hypothyroidism or hyperthyroidism, hyperparathyroidism, Cushing's disease, and Addison's disease)
4. Chronic metabolic conditions (hyponatremia, hypercalcemia, chronic hepatic failure, and renal failure)
5. Vasculopathies affecting the brain
6. Structural abnormalities (chronic subdural hematomas, normal-pressure hydrocephalus, and slow-growing tumors)
7. Central nervous system (CNS) infections (including acquired immune deficiency syndrome [AIDS], Creutzfeldt-Jakob disease, and cryptococcal or tuberculous meningitis).

14. How often is a Wernicke's diagnosis missed and what are the consequences?
Wernicke's encephalopathy is correctly diagnosed in 1 of 22 patients. The classic features of confusion due to encephalopathy, variable ophthalmoplegia, and ataxia may be complete or only one or two of the features may be present. Untreated, patients can become comatose and death can result.

Torvik A, et al.: Brain lesions in alcoholics: A neuropathological study with clinical correlations. J Neruol Sci 56:233-248, 1982.

15. Which dementia syndromes are associated with alcohol?
The DSM-IV includes alcohol amnestic syndrome (Korsakoff's syndrome), in which the amnestic disorder predominates, as well as a more generalized dementia associated with alcoholism. Both are associated with some degree of visuospatial impairment; neither includes aphasia. Patients with or without dementia may experience an acute, alcohol-related delirium known as Wernicke's encephalopathy (usually with confusion, eye movement abnormalities, and ataxia).

ALZHEIMER'S DISEASE

16. How is AD diagnosed?
First, the presence of dementia must be established clearly by clinical criteria and confirmed by neuropsychological testing. The clinical manifestations must include impairment of memory and at least one other area of cognition. There must be no evidence of other systemic or brain disease sufficient to cause the dementia, and the National Institutes of Health (NIH) criteria suggest basic laboratory studies (which are not all-inclusive) to exclude other disease. The diagnosis is both a diagnosis of exclusion and a diagnosis based on the establishment of certain characteristic features.

Knopman DS, DeKosky ST, Cummings JL, et al.: Practice parameter: Diagnosis of dementia. Neurology 56:1143-1153, 2001.

McKhann G, Drachman D, Folstein M, et al.: Clinical diagnosis of Alzheimer's disease: Report of the NINCDS-ADRDA Work Group under the auspices of Department of Health and Human Services Task Force on Alzheimer's disease. Neurology 34:939-944, 1984.

17. How are the alcohol-related dementias differentiated from AD?
No absolute features distinguish these conditions. If the patient has a systemic disorder (such as alcoholism) that, in the clinician's opinion, is sufficient to cause dementia, the diagnosis should not be probable AD. Possible AD may be used if underlying AD is suspected in an actively drinking patient. The patient should stop drinking with the help of appropriate rehabilitative services. If the dementia improves and the improvement continues or persists for 1 year or more, the diagnosis is not likely to be AD.

18. Which blood tests are typically ordered in a patient with suspected AD to rule out other causes or contributing factors?
1. Chemical analysis (including sodium, blood sugar, calcium, liver enzymes, and renal function)
2. Complete blood count with differential
3. Thyroid function tests
4. Venereal Disease Research Laboratory or equivalent test for syphilis
5. Vitamin B_{12}
6. Antinuclear antibody (extractable nuclear antigen panel, if positive)
7. Sedimentation rate

Additional tests:

Folate
Serum homocysteine
Serum methylmalonic acid

Serum arterial ammonia
Parathyroid hormone
Serum protein electrophoresis
Cortisol levels
Serum (and urine) drug screens
Hexosaminidase levels
Human immunodeficiency virus (HIV)

19. **What blood tests can be done to assess the risk for AD?**
Glucose, cholesterol, and homocysteine elevations are risk factors for developing AD, as is an ApoE4 genotype.

20. **Which ancillary studies (in addition to blood tests) are useful to evaluate patients with suspected AD?**
An imaging study (magnetic resonance imaging [MRI] or computed tomography [CT] with contrast) and neuropsychological testing to confirm dementia are necessary. Electroencephalography (EEG), single-photon emission CT (SPECT), or positron emission tomography (PET) studies and lumbar puncture (LP) may be useful or even necessary. Also consider an electrocardiogram (ECG) (to look for evidence of cardiovascular disease) and chest radiograph.

21. **When is LP necessary in the diagnostic work-up?**
When symptoms are of short duration (<6 months) or have atypical features, such as rapid progression or severe confusion, an LP should be performed early. It also should be done if clinical or laboratory features suggest a specific etiology that is an indication for LP, such as CNS meningitis or CNS vasculitis.

22. **What are typical symptoms of early AD?**
Early symptoms of AD include forgetfulness for recent events or newly acquired information, often causing the patient to repeat himself or herself. Other early features are disorientation, especially to time, and difficulty with complex cognitive functions such as mathematical calculations or organization of activities that require several steps.

23. **What are typical symptoms of moderately advanced AD?**
Advanced AD includes a history of progression of pervasive memory loss sufficient to impair everyday activities, disorientation to place and/or aspects of person (e.g., age), inability to keep track of time, and problems with personal care (such as forgetting to change clothes). Behavioral changes, such as depression, paranoia, or aggressiveness, are more likely in these stages.

24. **Does progression of AD follow a consistent pattern?**
Definitely not. Salient symptoms and rates of progression vary tremendously.

25. **What language disturbances do patients with AD experience?**
Early in the disease, most patients have word-finding difficulties that may cause pauses in spontaneous speech or may be detected by asking the patient to name objects (particularly objects with low frequency in the language). As AD progresses, most patients develop problems with comprehension with intact repetition (similar to transcortical sensory aphasia); then repetition becomes affected while speech remains fluent (similar to Wernicke's aphasia). Ultimately, some patients develop expressive speech problems in addition to the above symptoms, or they may just stop talking secondary to inanition and apparent lack of anything to say.

26. **Does the presence or absence of insight differentiate AD from other dementias?**
Lack of insight into their memory disorder (or anosognosia) occurs in some patients with AD as well as in patients with other dementing disorders. It does not appear to correlate with disease severity and is not useful in differential diagnosis.