Dementia

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Organic brain disorders are dementia and delirium.
DEMENTIA is *chronic progressive encephalopathy*.

ETIOLOGIC CLASSIFICATION

A. **IRREVERSIBLE DEGENERATIVE causes** (NEURODEGENERATIVE DEMENTING DISEASES or PRIMARY ORGANIC DEMENTIAS) - incurable, invariably progressive, ultimately fatal.
   1) **degenerative**: Alzheimer's disease (AD), Pick's disease, asymmetrical cortical degeneration syndromes (ACDS), diffuse Lewy body dementia (DLBD), progressive supranuclear palsy (PSP), Huntington's disease (HD), Parkinson's disease (PD).
   2) **vascular**: multi-infarct dementia, Binswanger disease.
   3) **metabolic**: storage diseases, leukodystrophies, Wilson disease, aluminium (dialysis dementia).
   4) **neoplastic**: meningeal metastases, gliomatosis cerebri.
   5) **infectious** (in young patients!): prion diseases (Creutzfeldt-Jakob disease, etc.), HIV (!!!).
   6) **trauma**: dementia pugilistica.

N.B. DEGENERATIVE dementia implies disease ***progression over time***.

B. **POTENTIALLY REVERSIBLE NONDEGENERATIVE causes** (truly CHRONIC ENCEPHALOPATHIES or SECONDARY DEMENTIAS):
   1) **inflammatory**: chronic inflammatory meningoencephalitis (CIME), sarcoidosis, CNS vasculitides, CNS complications of SLE, paraneoplastic limbic encephalitis.
   2) **infectious**: chronic meningitis due to fungi, tuberculosis, *Listeria monocytogenes*, Lyme disease, neurosyphilis (general paresis), CNS Whipple's disease.
   3) **nutritional**: vitamin B_{12} deficiency (also folate, thiamine, nicotinic acid deficiencies).
   4) **metabolic**: hepatic, renal, pulmonary failures, hypercalcemia.
   5) **toxic**: drugs (barbiturates, digoxin, anticholinergics), alcohol.
      Gray SL "Cumulative Use of Strong Anticholinergics and Incident Dementia: A Prospective Cohort Study." JAMA Intern Med. 2015 Jan 26
      High cumulative anticholinergic use (e.g. low doses chronically) is associated with increased risk for dementia!
   6) **mass lesion**: subdural hematoma, normal-pressure hydrocephalus, meningioma and other tumors (esp. in frontal areas).
   7) complex partial **status epilepticus**.

Dementia is not part of normal aging and always represents PATHOLOGIC PROCESS!!!
Dementia is symptom – always has cause!

Of all dementias, 20% are potentially reversible!

NEURODEGENERATIVE DEMENTING DISEASES (irreversible chronic progressive encephalopathies) fall into three broad categories:

I. Cortical Dementia

1. **Alzheimer's Disease** – major cortical degenerative disease!
2. **Asymmetrical Cortical Degeneration Syndromes** (e.g. Pick's disease [frontotemporal dementia])
3. **ALS-Dementia Complex** - frontotemporal dementia with motor neuron disease (progression is more rapid than in AD - death within 3 to 5 years); some argue that it is not distinct etiologic entity.

II. Subcortical Dementia see Mov. Movement disorders >>

1. **Parkinson's Disease** with Dementia
2. **Huntington's Disease**
3. **Multiple System Atrophy**
4. **Progressive Supranuclear Palsy**

N.B. HIV encephalopathy (AIDS-dementia complex) is also subcortical dementia!

III. Mixed (Cortical-Subcortical) Dementia see Mov. Movement disorders >>

1. **Corticobasal Ganglionic Degeneration**
2. **Diffuse Lewy Body Disease**

EPIDEMIOLOGY

Dementia is **age-associated syndrome**:

prevalence 1% at age 60 → doubles every 5 years → prevalence 30-50% by age 85.

Etiology by frequency:

1. **Alzheimer's disease** accounts for 70% dementias
2. **Vascular dementia** accounts for 10-20% dementias.
3. **Alcoholism** (strong contributions from: associated nutritional deficiency, recurrent head trauma, chronic hepatic cirrhosis)
4. **Parkinson's disease**
5. **Chronic drug intoxications** (actually produce *confusional state*)
6. **Normal-pressure hydrocephalus** - 5% dementias in older age group.

CLINICAL FEATURES

Cognitive functions – processes by which knowledge is acquired, retained, and used.

DEMENTIA - ***acquired**** **impairment of multiple COGNITIVE domains** sufficient to interfere with previously successful daily activities.

DEMENTIA - **global intellectual deterioration** with clear consciousness (vs. delirium).

DEMENTIA - chronic and substantial decline in **≥ 2 areas of cognition**, i.e. **AMNESIA** + at least one of following: **APHASIA, APRAXIA, AGNOSIA, EXECUTIVE FUNCTION DISTURBANCE** (abstraction, judgment, complex problem solving, concept formation, planning, use of feedback to guide ongoing performance).

* vs. ***mental retardation*** - ***developmental*** (present since early childhood).

- dementia is continuum that starts with ***subjective cognitive impairment (SCI)*** and moves to ***mild cognitive impairment (MCI)***, culminating in full-blown ***dementia***.
- dementia is not homogeneous clinical syndrome - unlimited range of specific presentations that depend on which particular abilities are compromised.

- **memory loss** alone does not equal dementia, even though it may be *heralding symptom* and is *most commonly impaired* cognitive domain among all dementia syndromes (cortical and subcortical).
- in addition, alterations of **mood** (shallow labile affect) and **personality** are present.

N.B. **consciousness & perception are intact**!!!

CORTICAL vs. SUBCORTICAL dementia

- distinction is not absolute:
  - most diseases are not limited to either cortical or subcortical regions.
  - differences are matters of degree and proportion rather than strict dichotomies.
- differences are more distinct in early, mild stages.

CORTICAL DEMENTIA SYNDROME – global declarative **memory loss** + elements of **aphasia**, **apraxia**, **agnosia, acalculia**.

SUBCORTICAL DEMENTIA SYNDROME:

1) movement disorders (e.g. **bradykinesia**)
2) slowed thought (**bradyphrenia**)
3) **disproportionate memory problems**
   - severely affected *working* memory, *reasoning*, *procedural* memory, and *strategic* memory (e.g. recall);
   - deficits in nondeclarative memory (vs. remain intact in cortical dementia).

PSEUDODEMENTIA - treatable / psychiatric disorder that mimics dementia (most common is **depression**!!!).

- purely depressed patients perform better on declarative memory tests than genuinely demented patients, but depressed patients tend to complain of memory loss disproportionately.
- depressed patients demonstrate little effort at tasks and answer "I don't know" to direct questions (vs. demented patients are cooperative and struggle to perform various tasks).

DIAGNOSIS

Assume confusion is due to acute illness until proved otherwise!

Depends on **CLINICAL EXAMINATION:**

1. **HISTORY** (usually requiring informant – friend, relative, etc).
   - always consider defects of daily activities (e.g. Katz's Scale for Activities of Daily Living).
2. **NEUROPSYCHOLOGICAL TESTING** – impairment in **all cognitive areas** (except *attention* - able to repeat digits forward and backward in normal fashion).
   - core psychological features of dementia involve impairments of **memory** and **intelligence** (IQ↓ in comparison to premorbid levels).

Exclude:

1. ***Other causes for widespread cognitive failure*** - diminished arousal / wakefulness, acute confusional states (e.g. drug intoxication).
2. ***More circumscribed deficits*** (such as aphasia or amnesia – patients may appear superficially as widespread disorder of cognition).

Differentiate:

REVERSIBLE FORMS OF DEMENTIA often have following: hypersomnolence, (sub)acute deterioration, fluctuating severity, severe EEG abnormalities, visual hallucinations, tremulousness, unsteadiness.

N.B. **depression** should be considered in any diagnostic evaluation (e.g. Geriatric Depression Scale).

IRREVERSIBLE FORMS OF DEMENTIA - more slowly progressive (more than year or two), fluctuate much less, have recognizable clinical / cognitive profiles.

LABORATORY EVALUATION is directed toward ***elimination of reversible causes***:

1. ***Chest x-ray, ECG, urinalysis, CBC, chemistry profile*** (electrolytes, calcium, fasting blood glucose, renal and liver function tests, lipid panel, serum iron)
2. **Thyroid** function studies
   thyroid peroxidase antibodies – if positive, may mean steroid responsive encephalopathy and not a degenerative dementia (H: trial of oral prednisone).
3. **Vitamin B_{12}** deficiency tests
4. **SEROLOGICAL TESTS** for:
   1) *syphilis* (now rare cause of dementia), *Lyme disease*, *HIV*
      In any young adult with dementia, HIV titer should be considered!
   2) various *connective tissue disease*
   3) *paraneoplastic* (in prior or known provocative malignancies - oat cell lung cancer, ovarian cancer).
5. **Small bowel biopsy** (CNS Whipple's disease).
6. **EEG**:
   – should be ≈ normal in *neurodegenerative dementias*.
   – many ***reversible*** *chronic progressive encephalopathies* produce severe dysrhythmic slowing (nonspecific loss of alpha rhythm).
      N.B. ***normal EEG in no way excludes dementia***, but diffusely abnormal record supports diagnosis of dementia as opposed to pseudodementia.
   – EEG may suggest cause of dementia (e.g. focal structural lesion, Creutzfeldt-Jakob disease or subacute sclerosing panencephalitis).
7. **CSF examination** should include microbiological, cytological, and immunological studies (elevated IgG index and synthesis rate, oligoclonal bands - suggest intrathecal inflammatory reaction).
8. **MRI without contrast** (rarely is contrast helpful) – first neuroimaging for demented patient!
9. **CT**
10. Overnight **oximetry** (screening for obstructive sleep apnea).
11. Cerebral **angiography**
12. Meningeal & brain **biopsy**
13. Empirical therapeutic trial of ***prednisone*** (to exclude steroid-responsive type of chronic inflammatory meningoencephalitis [CIME]).
14. Empirical therapeutic trial of ***antidepressants*** (to exclude pseudodementia).

Main role of **neuroimaging** is to exclude treatable causes (e.g. hematomas, neoplasms, hydrocephalus); **MRI** / **CT** are recommended at least once in clinical course, repeated only if intercurrent disease is suspected.

N.B. loss of brain substance is normal function of aging - does not correlate either with changes in brain metabolism (as measured with PET) or with cognitive impairment - best described as brain parenchymal *volume loss* rather than *atrophy*.

BIBLIOGRAPHY see p. S11 >>