Dementia: Causes and Medical Interventions

Rodney Sepich, M.D., C.M.D.
Medical Director, Foxdale Village
State College, PA
Overview

- Causes of Dementia
- Medical Workup of Dementia
- Causes of Behavioral Changes
Are these people demented?
Definition of Dementia

- An acquired complex of intellectual deterioration which affects at least two areas of cognitive function.
- A syndrome, not a diagnosis.
- In the past, commonly referred to as senility or “hardening of the arteries”
- 34% of those over 85 have dementia.
DSM 5 eliminates “Dementia”

- The term “dementia” has been eliminated and replaced with major or minor neurocognitive disorder. It was believed that the word dementia was stigmatizing toward older individuals and not well accepted by younger individuals with HIV dementia.
a minor neurocognitive disorder is defined by the following:

- There is evidence of modest cognitive decline from a previous level of performance in one or more of the domains outlined above based on the concerns of the individual, a knowledgeable informant, or the clinician; and a decline in neurocognitive performance, typically involving test performance in the range of one and two standard deviations below appropriate norms (i.e., between the third and 16th percentiles) on formal testing or equivalent clinical evaluation.

- The cognitive deficits are insufficient to interfere with independence (e.g., instrumental activities of daily living, like more complex tasks such as paying bills or managing medications, are preserved), but greater effort, compensatory strategies, or accommodation may be required to maintain independence.

- The cognitive deficits do not occur exclusively in the context of a delirium.

- The cognitive deficits are not primarily attributable to another mental disorder (e.g., major depressive disorder, schizophrenia).
Major Neurocognitive Disorder

- A major neurocognitive disorder is defined by the following:
  - There is evidence of substantial cognitive decline from a previous level of performance in one or more of the domains outlined above based on the concerns of the individual, a knowledgeable informant, or the clinician; and a decline in neurocognitive performance, typically involving test performance in the range of two or more standard deviations below appropriate norms (i.e., below the third percentile) on formal testing or equivalent clinical evaluation.
  - The cognitive deficits are sufficient to interfere with independence (i.e., requiring minimal assistance with instrumental activities of daily living).
  - The cognitive deficits are not sufficient to interfere with independence.
  - The cognitive deficits are not primarily attributable to another mental disorder (e.g., major depressive disorder, schizophrenia).
  - Note that in diagnosing a minor neurocognitive disorder, one and two standard deviations below appropriate norms is required. In diagnosing a major neurocognitive disorder, two or more standard deviations below appropriate norms are required. This need for cognitive testing will add to patient cost since neither the Mini Mental State Examination nor the Montreal Cognitive Assessment, the common screening tools utilized by many clinicians, yields results in standard deviations. In addition, the requirement that the cognitive deficits are insufficient to interfere with independence is subjective and will cause additional confusion for both clinicians and patients.
  - Having determined whether a patient has a major or minor neurocognitive disorder, the healthcare professional making the diagnosis must then decide on the etiological subtype of the major or minor neurocognitive disorder. The subtypes that have been listed are neurocognitive disorder due to Alzheimer’s disease; vascular neurocognitive disorder; frontotemporal neurocognitive disorder; neurocognitive disorder due to traumatic brain injury, Lewy body dementia, Parkinson’s disease, or HIV infection; substance-induced neurocognitive disorder; neurocognitive disorder due to Huntington’s disease, Prion disease, or to another medical condition; and neurocognitive disorder not elsewhere classified.
Cognitive Functions

- Memory
- Orientation
- Language
- Judgment
- Perception
- Attention
- Ability to perform tasks in sequence
Many Causes of Dementia

- Alzheimer’s Dementia
Alzheimer’s Disease

- Most common dementia (64%)
- Affects twice as many women as men.
- Strikes at any age
- 10% of cases have genetic link
Alzheimer’s Dementia

- Lose many neurons and neuronal connections
- Neuritic plaques in brains cells on autopsy. Plaques made of amyloid protein. Does the amyloid kill the cells?
- Acetylcholine neurotransmitter decreased in alzheimer’s patients.
Alzheimer’s Dementia

Amyloid Plaque

Farlow et al., 1994
Alzheimer’s Disease

Prevalence of AD Through 2030

Alzheimer’s Disease Prevalence

Alzheimer’s Disease Screening

1. Recent memory loss affecting job
2. Difficulty performing familiar tasks
3. Problems with language
4. Disorientation to time or place
5. Poor or decreased judgment
6. Problems with abstract thinking
7. Misplacing things
8. Changes in mood or behavior
9. Changes in personality
10. Loss of initiative

Alzheimer’s Association
Alzheimer’s Disease

How did your memory improvement class go last night?

I completely forgot about it!!
Alzheimer’s Dementia

“I’m stumped. We’ll have to wait for the autopsy.”
PROBABLE AD, VERY LATE STAGE
Lewy Body Dementia DSM5

- The individual meets criteria for major or minor neurocognitive disorder and meets a combination of core diagnostic features and suggested diagnostic features of Lewy body dementia.
- The individual experiences insidious onset and gradual progression.
- The symptoms are not better attributed to cerebrovascular disease, as evident on focal neurologic signs or on brain imaging.
- The symptoms are not better attributed to another physical illness or brain disorder.
- Providers must specify whether major or minor neurocognitive disorder is due to probable Lewy body dementia (requiring two core features or one suggestive feature with one or more core features) or possible Lewy body dementia (requiring one core feature or one or more suggestive features).
- Core diagnostic features of Lewy body dementia include the following:
  - fluctuating cognition with pronounced variations in attention and alertness;
  - recurrent visual hallucinations that are typically well formed and detailed; and
  - spontaneous features of Parkinsonism with onset at least one year later than the cognitive impairment.
- Suggestive diagnostic features of Lewy body dementia include the following:
  - rapid eye movement sleep behavior disorder;
  - severe neuroleptic sensitivity; and
  - low dopamine transporter uptake in basal ganglia demonstrated by SPECT or PET imaging.
Lewy Body Dementia

- Four symptoms reliably distinguish Lewy Body dementia from Alzheimer’s
  1. daytime drowsiness and lethargy despite sufficient sleep the night before
  2. napping two or more hours during the day;
  3. staring into space for long periods
  4. episodes of disorganized, incoherent speech

Journal of Neurology, Jan 27, 2004
Lewy Body Dementia

- Deposits in brain cells called Lewy Bodies.
- Lewy Body deposits made of protein called alpha-synuclein (this protein also has been linked to Parkinson’s)
- May account for up to 20% of total dementia cases.  Annals Int Med 1 Apr 2008
Lewy Body Dementia

- Visual hallucinations common
- Many times have similar symptoms to Parkinson’s (rigidity, bradykinesia, shuffling gait, tremor)
- Often have fluctuating cognition
- No specific treatment
- Limitations of antiparkinson or antipsychotic drugs.
Multiinfarct Dementia

VASCULAR DEMENTIA CHANGE ON THE MINI-MENTAL STATE EXAM OVERTIME

![Graph showing the change in score over average time of illness.](image)
"The computer says I need to upgrade my brain to be compatible with its new software."
Frontotemporal Dementia

- Onset often before age 60
- Language difficulties common.
- Prominent personality changes, behavioral disturbances, like hyperphagia, aggression, or prominent apathy. Memory may be preserved early
- Functional MRI with decreased activity in frontal and temporal lobes. 

Annal Int med 1 Apr. 2008
Causes of Dementia

- Degenerative diseases (MS)
- Normal Pressure Hydrocephalus
Causes of Dementia

- Tumors
Causes of Dementia

- Tumors
Causes of Dementia

- Huntington's
- Parkinson's
- Infections (HIV, Creutzfeldt-Jakob)
- Mixed
Causes of Dementia

- Trauma
I saw patient with know microvascular disease with SLUMS score of 21 out of 30.

- Stopped Ambien given by another physician
- Score on SLUMS increased to 27 out of 30.
Diagnostic evaluation

- History (Trauma, Stroke, Drugs, Alcohol)
- Physical
- Labs: B12, Thyroid, Complete Metabolic Panel, CBC, Urinalysis, Sed Rate, RPR
Diagnostic Evaluation

- Consider CT scan of brain (or MRI). Most helpful if less than 3 years duration, early age of onset, rapid progression, focal neurologic deficits, atypical symptoms or know vascular risk factors.

- Consider HIV, Toxicology, Heavy metals, Folate, Chest xray, Urinalysis
Maybe they are stubborn
Cholinesterase Inhibitors: Aricept, Exelon, Razadyne

Cholinesterase inhibitors work by decreasing breakdown of acetylcholine, which is neurotransmitter thought to be important for alertness, memory, thought, and judgment

Most common side effects: nausea, diarrhea, urinary incontinence
Do they work?

- Lancet study 2004: (*The Lancet* (vol 363, p 2105) not underwritten by Pfizer
- 565 pts mild to moderate dementia
- ½ treated with aricept: 42% ended up in nursing facility at three years.
- ½ not treated with aricept: 44% ended up in nursing facility in three years.
- Equal numbers in both groups disabled.
Donepezil also failed to improve behavioral and psychological symptoms, the amount of time needed from caregivers, or adverse events or death.

- Pfizer says not enough patients in trial (565)
- Alzheimers Assn. raises issues with study but according to NYTimes, they receive 5% of their funding from the pharmaceutical companies.
Over 900 people with vascular dementia enrolled for the drug trial. Just under 650 took Aricept once a day for 24 weeks and 326 received a placebo. Eleven people in the group taking Aricept died compared with no deaths in the group taking placebos.

Eisai Co. Ltd 3/18/2006
What is the point?

- The results are conflicting on cholinesterase inhibitors. Be aware of bias in the studies that are reported.
- They have statistical effect on some rating scales, but clinical effect may not be that great.
- If you are seeing side effects, ask if it's worth staying on the medicine.
Alzheimer’s Medications

- Namenda
- Works by regulating glutamate, which is thought to be involved in memory.
- Approved for moderate to severe dementia
- May be used with Cholinesterase inhibitors
Alzheimer’s medications

- Avoid in uncontrolled asthma, closed angle glaucoma, sick sinus syndrome without pacemaker, or left bundle branch block.

Vitamin E not helpful and may increase mortality.  NEJM 1997:336:1216-22

Ginko Biloba not supported by evidence at this time  Curr Alzheimer Res 2005;2:541-551
Treating multiinfarct dementia

- *Hypertension Research* (2011) 34, 74–78; doi:10.1038/hr.2010.179; published online 23 September 2010

- High plasma aldosterone concentration is a novel risk factor of cognitive impairment in patients with hypertension
Prevention

1. Treating Hypertension reduces risk by half roughly half [Lancet 1998;352:q347-1351]
   - Ace inhibitors may be particularly effective
2. Hyperlipidemia and diabetes associated with dementia.
   - Taking statins reduces dementia risk 29% [Mayo Clinic Proceedings, 10/1/2013]
   - Fish Oil may be helpful to prevent dementia [J Alzheimers Dis. 2011;24(3):485-93. doi: 10.3233/JAD-2011-101524.]

Incidence of dementia is increased in type 2 diabetes and reduced by the use of sulfonylureas and metformin.
Prevention

3. Avoid trauma
4. Avoid cigarettes
5. Exercise, but avoid head trauma
6. Screening with MMSE or SLUMS
HOW FAST YOU WALK IN MIDDLE AGE MAY PREDICT DEMENTIA RISK

"I wish I never knew that..."