Approach to Patients with Memory Disorders

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What do we mean by “memory disorders”?

• “Memory” describes our ability to RETAIN AND RECALL information

• It is only one part of COGNITION
  – Attention
  – Concentration
  – Memory
  – Language
  – Visuospatial function
  – Executive function
  – Mood
  – Hallucinations / Delusions
Maybe my patient is just getting old?

Yes...but that’s not a good excuse!

<table>
<thead>
<tr>
<th>Normal Aging</th>
</tr>
</thead>
<tbody>
<tr>
<td>“Retrieval deficits” with memory</td>
</tr>
<tr>
<td>Insight retained</td>
</tr>
<tr>
<td>Little to no change in ADLs</td>
</tr>
<tr>
<td>Minor delay in word finding</td>
</tr>
<tr>
<td>Normal visuospatial function</td>
</tr>
<tr>
<td>Normal social engagement</td>
</tr>
</tbody>
</table>
Can my patient have “pre-dementia”? 

Sort of...

- “Mild Cognitive Impairment” (MCI)
  - Cognitive complaint, cognitive decline or impairment
  - Objective evidence of impairment in cognitive domains: memory, executive function/attention, language, or visuospatial skills
  - Essentially normal functional activities

- “Cognitive Impairment Not Demented” (CIND)
  - Participant or informant-reported decline in cognition or function; 
  - Physician-detected significant impairment in cognition
  - Cognitive test score(s) at least 1.5 SD below the mean
  - No clinically important impairment in ADLs
Mild Cognitive Impairment

**Epidemiology**
--Prevalence 15-20% > 60 yo – increases with age (30-40% > 80 yo)
--Cumulative incidence of progression to dementia over 6 years ~80%
--Other estimates of 6%-15% per year progress
--But with 20% “reversion to normal”

**Clinical classification**
1) MCI amnestic – single and multiple domain
   More likely to progress to AD
2) MCI nonamnestic – single and multiple domain
   More likely to progress to non-AD dementia (VaD, FTD, DLB)

**Management**
--Rule out reversible causes
--Serial evaluations
--No clear role for AchE inhibitors
--Screening for and treatment of vascular risk factors
# Mild Cognitive Impairment

<table>
<thead>
<tr>
<th>Variable</th>
<th>Amnestic</th>
<th>Non-amnestic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Etiology</td>
<td>Neurodegenerative disease</td>
<td>Vascular damage</td>
</tr>
<tr>
<td></td>
<td>APOE ε4</td>
<td>Cerebrovascular disease</td>
</tr>
<tr>
<td>Pathology</td>
<td>Neurodegenerative</td>
<td>Cerebrovascular</td>
</tr>
<tr>
<td></td>
<td>Amyloid β plaques</td>
<td>Cortical infarctions</td>
</tr>
<tr>
<td></td>
<td>Neurofibrillary tangles</td>
<td>Subcortical infarctions</td>
</tr>
<tr>
<td></td>
<td>Hippocampal atrophy</td>
<td>White matter hyperintensities</td>
</tr>
<tr>
<td></td>
<td>Reduced brain volume</td>
<td></td>
</tr>
<tr>
<td>Presentation</td>
<td>Memory impairment present</td>
<td>Impairment in non-memory domains</td>
</tr>
<tr>
<td>Long term outcomes</td>
<td>Alzheimer’s dementia (AD)</td>
<td>Non-Alzheimer dementias:</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Vascular dementia</td>
</tr>
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<td></td>
<td></td>
<td>Lewy body, Frontotemporal</td>
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</tbody>
</table>

Clin Geriatr Med. 2013 Nov; 29(4)
Where is the transition from MCI to dementia?

Risk factors for progression

• age, severity of deficits
• ?apo e4
• ?increased CSF tau
• amount and progression of MTL atrophy

<table>
<thead>
<tr>
<th>Dementia</th>
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</thead>
<tbody>
<tr>
<td>“Amnestic deficits” with memory</td>
</tr>
<tr>
<td>Insight lost</td>
</tr>
<tr>
<td>Significant change to ADLs</td>
</tr>
<tr>
<td>Anomia</td>
</tr>
<tr>
<td>Poor visuospatial function</td>
</tr>
<tr>
<td>Apathy, withdrawal</td>
</tr>
</tbody>
</table>
Progression of cognition...

**Normal Aging**: Everyone experiences slight cognitive changes during aging.

**Preclinical**
- Silent phase: brain changes without measurable symptoms.
- Individual may notice changes, but not detectable on tests.
- “A stage where the patient knows, but the doctor doesn’t.”

**MCI**
- Cognitive changes are of concern to individual and/or family.
- One or more cognitive domains impaired significantly.
- Preserved activities of daily living.

**Dementia**
- Cognitive impairment severe enough to interfere with everyday abilities.

From UC Irvine ADRC
Considerations of causes of dementia

Localize and use diagnostic parsimony...
• Start by figuring out what they don’t have
• Then better characterize what they likely have

– Normal
– “Pseudodementia”
– Vitamin deficiencies
– Systemic diseases
– Other brain lesions
– Mild cognitive impairment
– Alzheimer’s disease
– Vascular dementia
– Dementia with Lewy bodies
– Fronto-temporal dementia
– Secondary dementias
How do we sort this out?

• **Examining** memory, mood, & physical abilities

• Look for **reversible causes**
  – Blood tests
  – Urine tests
  – Brain imaging (CT, MRI, PET)

• **Meds & interdisciplinary care**

• **Clinical trials**

• **Progression and planning**
Classification of the dementias
What is Alzheimer’s disease?

Named after Dr. Alois Alzheimer

1) Progressive worsening of memory and at least one other area of cognition (attention, language, executive, apraxia)

2) No disturbance of consciousness

3) Onset ages 40 – 90, usually > 65

4) Absence of other systemic disorders that can account for the symptoms

• 10% of age >65, 40-50% of age >85
Alzheimer’s Disease

**Amyloid hypothesis**

- $\alpha$-secretase
- $\beta$-secretase
- $\gamma$-secretase
- APP
- 83-res frag
- 99-res frag
- non-toxic fragment
- $\text{A}\beta_{40}$ (more common)
- $\text{A}\beta_{42}$ (more toxic)

**Cholinergic hypothesis**

- Neuronal degeneration in nucleus basalis of Meynert and diagonal band of Broca
- Result is decreased acetylcholine activity in the cortex
- Cholinergic tone thought to be important for memory function
- Reason for using AchE inhibitors
Alzheimer’s Disease

**Genetics** (4 main genes – 1,14,19, 21)

<table>
<thead>
<tr>
<th>Chromosome</th>
<th>Gene</th>
<th>% of AD</th>
<th>Age at onset</th>
</tr>
</thead>
<tbody>
<tr>
<td>21</td>
<td>APP</td>
<td>&lt;1% (&lt;10% fAD)</td>
<td>49-60</td>
</tr>
<tr>
<td>14</td>
<td>PS-1</td>
<td>1-5% (&gt;50% fAD)</td>
<td>30-60</td>
</tr>
<tr>
<td>1</td>
<td>PS-2</td>
<td>&lt;1% (&lt;1% fAD)</td>
<td>50-65</td>
</tr>
<tr>
<td>19</td>
<td>ApoE</td>
<td>50-60% (sporadic)</td>
<td>60+</td>
</tr>
</tbody>
</table>

**Amyloid Precursor Protein** (APP, chr 21) – Mutations may alter the ratio of its proteolytic products, resulting in accumulation of more toxic Aβ42. Thought to be responsible for AD neuropathologic changes seen in Down’s syndrome.

**Presenilin 1** (PS1, chr 14), **Presenilin 2** (PS2, chr 1) – the PSs function as cofactors or catalytic components of the γ-secretase metalloprotease complex.

**Apolipoprotein E** (ApoE, chr 19) – accounts for majority of sporadic, late-onset AD. Involved in deposition / clearance of Aβ in the brain. e4 allele = most risk.
What happens to the brain in Alzheimer’s disease?

<table>
<thead>
<tr>
<th></th>
<th>With progression...</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amyloid</td>
<td>Normal (&amp; a-MCI?)</td>
</tr>
<tr>
<td>Inflammation</td>
<td></td>
</tr>
<tr>
<td>Tau deposition</td>
<td></td>
</tr>
<tr>
<td>Free radical toxicity</td>
<td>MCI</td>
</tr>
<tr>
<td>Poor calcium homeostasis</td>
<td></td>
</tr>
<tr>
<td>Synaptic loss</td>
<td></td>
</tr>
<tr>
<td>Cholinergic dysfunction</td>
<td>Mild to Moderate AD</td>
</tr>
<tr>
<td>Neuronal loss</td>
<td></td>
</tr>
<tr>
<td>Norepinephrine dysfunction</td>
<td></td>
</tr>
<tr>
<td>Serotonin dysfunction</td>
<td>Moderate to Severe AD</td>
</tr>
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</table>
What happens to the brain in Alzheimer’s disease?

Neuritic plaques (amyloid)  
Neurofibrillary tangles (tau)

Images courtesy of WikiCommons
What happens to the brain in Alzheimer’s disease?

- Normal aging brain
- Alzheimer’s disease
Tests in Alzheimer’s disease?
MRI
Tests in Alzheimer’s disease? MRI

Rapid atrophy of medial temporal lobe in AD

At presentation
MMSE 23

7 years later
MMSE 13

Image source: http://www.medsci.ox.ac.uk/optima/old-page/selected-highlights/neuroimaging
Tests in Alzheimer’s disease?

PET

Image source: http://www.canadian-universities.net/News/health-science/bilingualism-can-delay-onset-of-alzheimer%e2%80%99s/
Tests in Alzheimer’s disease?
PiB / Amyloid
Alzheimer’s disease risk factors

- Age
- Family history / genetics
- Head trauma
- Blood vessel health
  - High blood pressure
  - Diabetes
  - Cholesterol
  - Diet
Most families are looking for a medication...

- Memory drugs improve the symptoms but are NOT neuroprotective or disease modifying
  - Aricept® (donepazil)
  - Exelon ® (rivastigmine)
  - Razadyne ® (galantamine)
  - Namenda ® (memantine)

- Consider clinical trials
- Other drugs for mood and attention may help
- Also can treat psychosis if it worsens
Your patients WILL ask Dr. Google

Improve Your Memory With Supplements
www.webmd.com/vitamins.../fortifying-your-memory-with-supplement...
As we age, we all want to avoid memory loss. Can supplements like ginkgo and ginseng help?

Vitamins for Memory - Which are the Best?
www.memory-improvement-tips.com/vitamins-for-memory.html
Should you take vitamins for memory improvement? This page provides a quick primer about the facts.

WATCH: The Best Vitamin Supplement For Memory, From Dr. Oz
www.huffingtonpost.com/.../mondays-with-marlo-best-vitamins-for...
Aug 13, 2012 – Dr. Oz, the Emmy Award-winning doctor, television host and author, recently joined me on Mondyas with Marlo, and I just had to ask him what...

Can B Vitamins Boost Your Memory?
www.huffingtonpost.com/.../b-vitamins-memory-boost-older-adults-f...
Jan 6, 2012 – By Kerry Grens NEW YORK (Reuters Health) - Older adults who took vitamin B12 and folic acid supplements for two years had greater ...

Vitamins for memory - what vitamins will help you to improve memory?
wannabeinstein.com/vitamins-memory/
Read this article about vitamins for memory. Learn what food contain vitamins important to your memory. Prevent memory loss!

5 Foods and Vitamins to Sharpen Your Memory and Prevent ...
www.realage.com » Anti-Aging
Jan 19, 2012 – Fond of your memory? Treasure your brain? Don't want to lose them to Alzheimer's? Take these six simple but powerful steps to prevent ...

The Best Vitamins For Memory | LIVESTRONG.COM
www.livestrong.com » ... » Vitamin Basics » Best Vitamins
Mar 28, 2011 – The Best Vitamins For Memory. There are three types of memory: sensory, short-term and long-term. Many factors affect memory, such as age ...
What supplements the medications

• Cognitive exercise
• Physical exercise
• “Nutriceuticals”...
  – coenzyme Q10
  – alpha lipoic acid
  – ginkgo biloba
  – phosphatidylserine
  – acetyl-L-carnitine
  – tumeric
  – coconut oil
  – DHA

*But remember...*

Any statements or reviews made by this site have not been evaluated by the Food and Drug Administration. These products are not intended to diagnose, treat, cure or prevent any disease. Results will vary on an individual basis.
HELP – I have an overwhelmed caregiver!

• Biggest support is the interdisciplinary team
• Stabilize the living arrangement
• Get help from friends, family, & professionals
• Work with attorneys and social workers for long term planning
• Join a support group
• Encourage them to take care of themselves!
Specific needs for “next generation” care for Alzheimer’s disease and dementia

- Alzheimer’s disease is the #1 neurodegenerative disease in U.S.
- 5 million in the U.S. have Alzheimer’s
- 83,000 in Louisiana have Alzheimer’s
- 10% of those > 65 yrs, 40% of those aged >85
- 6th leading cause of death in the U.S.
- U.S. cost of Alzheimer’s in 2012 was $183 billion
- By 2050 16 million Americans will have AD.
- AD mortality rates are increasing by 66%
Specific needs for “next generation” care for Alzheimer’s disease and dementia

• Rural, less educated patients have greater problems with medication non-adherence\(^1\) and there is an association between rurality and prevalence of AD (OR = 1.50, 90% CI 1.33–1.69) – a “hard to reach” demographic\(^6\)

• Improved lifestyle with Mediterranean style diet and/or avoidance of high saturated fats can improve outcome in AD \(^2,3,4\)

• Wandering patients are a problem – 40% of people with dementia get lost at some point, 5% get lost repeatedly, and ½ of missing dementia patients > 24 hours are seriously injured or die. \(^5\)

• Improved “cognitive lifestyle” may help mitigate aging and prevent dementia \(^7\)

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3) J Neurol Neurosurg Psychiatry. Published online May 13, 2013.
4) JAMA Neurol. Published online June 17, 2013.
5) BMJ 2013;346:f3603
7) Biol Psychiatry 2012 May 1; 71:783.
Specific needs for “next generation” care for Alzheimer’s disease and dementia

• Fall prevention

• Delirium prevention

• Caregiver burden and mitigation

• Driving risk

• Lost productivity for office visits

• Incurable disease needing research
Alzheimer's: The disease that could bankrupt Medicare

By Sandee LaMotte, CNN

Updated 12:26 PM ET, Tue March 7, 2017

Importance of Neuroscience

What do we mean by "memory disorders"?
Importance of Neuroscience

Interdisciplinary treatment model

Ochsner Brain Health and Cognitive Disorders Program

Program Coordinator and Psychometrist

Patient referrals:
- Risk Factor +
- >50
- ? Primary Care Champions, Women’s Health

Brain Health

- Brain Health Intervention Series (bi-weekly, running on quarters)
- Research

Cognitive Disorders

Memory Assessment and Treatment Clinic

General Outpatient Neuropsych

Aim: Preventing and reducing risk for cognitive decline

Aim: Optimal assessment and management of cognitive/memory disorders.

Patient referrals:
- + Cognitive Complaints
- From Neurology or Primary Care?
Questions?

THANK YOU!
APPENDIX
Vascular Dementia

**Epidemiology**
-- 2nd most common cause of dementia after AD in clinical series
-- 3rd after AD / DLB in autopsy studies using pure vascular pathology
-- After stroke, 20-25% of patients are demented

**Clinical Features**
-- 3 basic requirements: dementia, evidence of cerebrovascular disease, and a temporal relation between the vascular changes and dementia

* Hachinski Ischemic Score (sensitivity/specificity= 89% to distinguish from AD)
  → 2 points for: abrupt onset, fluctuating course, history of strokes, focal neurologic symptoms, and focal neurologic signs
  → 1 point for: **Stepwise deterioration**, nocturnal confusion, relative preservation of personality, depression, somatic complaints, emotional incontinence, HTN, evidence of associated atherosclerosis
  TOTAL ≤ 4 = primary degenerative dementia, ≥ 7 = VaD.

-- Forgetfulness tends to be minor and easily overcome with cues in VaD
Vascular Dementia

**Pathophysiology**: multiple etiologies
--Chronic hypoperfusion of white matter
--Multiple lacunar infarctions (Binswanger’s disease)
--Large artery disease,
  --Also consider ICH (hypertensive or amyloid angiopathy), vasculitis, or CADASIL.

**MRI**: Periventricular WM disease, lacunes, atrophy, hydrocephalus ex vacuo

**PET / SPECT**: Irregular patterns of hypoperfusion / hypometabolism

**Treatment**
--AChEIs shown to be efficacious in RCTs
--Neurostimulants (Ritalin, Bromocriptine, Modafinil)
--Treat underlying vascular disease, modify vascular risk factors
Vascular Dementia

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Dementia with Lewy Bodies

**Epidemiology**
--2nd most common cause of dementia next to AD in autopsy series
--3rd behind AD and VaD clinically
--Sporadic >> familial
--Makes up 20% of clinical dementia cases

**Clinical Features** → *Parkinsonian dementia syndrome*
--Fluctuations in attention and alertness (can lead to false dx of VaD)
--Visual hallucinations (seen in up to 80%), well-formed and detailed
--Parkinsonism

*Supportive*: falls, syncope, LOC, *neuroleptic sensitivity*, delusions, and other hallucinations.

** Two features = probable DLB, one feature = possible DLB

--REM behavioral disorder may be seen early in DLB.
Dementia with Lewy Bodies

**Genetics**
--Familial DLB exists, but not assoc with α-synuclein gene mutations

**Pathophysiology**: synucleinopathy (along with MSA and PD)

**MRI**: Atrophy, hydro ex vacuo

**PET / SPECT**: Temporo-parieto-occipital hypometabolism / dysfunction

**Pathology**: Ubiquitin- & α-synuclein-positive Lewy bodies / Lewy neurites in cortex / brainstem / SN

**Treatment**
--AChEIs benefit for cognitive aspects of the disease
--Neuroleptics help cognition, worsen extrapyramidal (prefer Seroquel).
--Dopamine / DA improve parkinsonism, worsen hallucinations
Dementia with Lewy Bodies

Micro pathology

Lewy bodies in the cortex (in non-pigmented cells)
Frontotemporal Dementia

**Epidemiology:** 8–17% of patients who die of dementia prior to age 70

**Clinical subtypes** (Neary-refined, Lund-Manchester classification):
--Frontal variant FTD (fvFTD) – apathy, disinhibition, poor hygiene, personality change, poor executive function
--Nonfluent primary progressive aphasia (PPA) – *think Broca’s*: effortful nonfluent speech, anomia, phonologic errors.
--Semantic dementia (SD) - *think Wernicke’s*: fluent aphasia with poor comprehension, anomia, and/or associative agnosia (impaired understanding of visual percepts). Can lead to prosopagnosia.

--Onset in 50s, relatively spared memory
--Can be associated with motor neuron disease

**Personality changes**
1) Disinhibition, reckless behavior
2) Stereotyped, ritualized behaviors
3) “Gramophone” (catch-phrase) syndrome
4) Preference for sweet foods
5) Item hoarding

**Non-dominant features**
1) Disinhibition (orbitofrontal)
2) Apathy (medial frontal)
3) Lack of empathy (temporal)
Frontotemporal Dementia

**Genetics**
- 40% of FTD is familial
- 30% familial/10% sporadic FTD due to mutations in MAPT gene (chr 17q)
- Recently recognized mutation in progranulin gene (chr 17q; AD)
- FTDP-17 is FTD with Parkinsonism linked to tau on chromosome 17.

**Pathophysiology**: tau-mediated grouping of microtubule-associated proteins [also are ubiquitin+, tau-negative inclusions (more common)]

**Micro**
- Clinical FTD has been shown pathologically to be 60-63% DLDH, 15-20% classic Pick’s disease, and 0-22% CBGD, and 0-20% AD
- Increasingly, the use of ”Pick’s disease” restricted to pathological findings
- Classic Pick’s disease pathology features ubiquitin- and tau-positive argyrophilic intracytoplasmic round inclusions (Pick bodies) in limbic/paralimbic cortices, and swollen, achromatic neurons (a.k.a. ballooned neurons or “Pick cells”) in areas with gross pathology

**EM**: Paired helical filaments of hyperphosphoryl tau within Pick bodies
**Frontotemporal Dementia**

**MRI:**
--“Knife-edge” gyral atrophy in frontal and temporal lobes, hydrocephalus ex vacuo. Atrophy is unilateral in 70% of cases.
--Nonfluent PPA: widening of Sylvian fissure, and atrophy of the insula, inferior frontal lobes, and superior temporal lobes.
--SD: temporal atrophy involving the polar region, fusiform and inferolateral gyri.

**PET / SPECT:** Frontotemporal hypometabolism / dysfunction

**Treatment**
--For disinhibition: SSRIs
--For aggression: Try anticonvulsants or neuroleptics
--AChEIs relatively contraindicated due to exacerbation of aggression, worse in fvFTD than others
Frontotemporal Dementia

Micro pathology

Pick bodies and a few tangles (silver stain)
Frontotemporal Dementia

- Knife-edge atrophy
Frontotemporal Dementia

Notice that the areas circled in red have less white area compared with the other areas. This indicates loss of brain tissue (atrophy).

Frontotemporal Dementia (FTD)

Semantic Dementia (SD)

Progressive Non-Fluent Aphasia (PNFA)
Creutzfeld-Jacob Disease

**Epidemiology**
--Worldwide incidence of 1 in 1,000,000 per year (sporadic form)

**Clinical Features of CJD**
--Rapidly-progressive dementia with startle myoclonus
--Duration of illness typically 4 months
--Onset typically age > 55
* Heidenhein variant = parieto-occipital involvement with visual disturbances before dementia (field defects, cortical blindness, visual hallucinations, Balint’s syndrome, oculomotor palsies, nystagmus, impaired saccades)

**Clinical features of nvCJD**
--Early ataxia, neuropsych and pyramidal symptoms *before* dementia
--Duration of illness typically 14 months
--Onset typically age < 55
Creutzfeld-Jacob Disease

Genetics
--85% sporadic, 15% familial (mutations PrPC, chr 20p)
--A small number of cases of CJD occur iatrogenically (corneal transplants, neurosurgical EEG electrodes, pooled human growth hormone, dura mater transplants)
--nvCJD = ingestion of BSE-infected beef

Pathophysiology
--Normal prion protein (PrPC) exists in α-helical conformation
--Infectious prion protein (PrPSC) exists in a β-pleated sheet conformation and catalyzes PrPC to PrPSC
--PrPSC is protease-resistant and accumulates in plaques → toxic

Micro
--Spongiform changes, kuru-type amyloid plaques, loss of neurons, and a conspicuous absence of inflammation
Creutzfeld-Jacob Disease

**MRI**
--CJD = T2-hyperintensities and DWI+ “cortical ribboning” & basal ganglia changes
--nvCJD = pulvinar T2-hyperintensities

**LP**: 14-3-3 > 95% sensitive and specific in appropriate clinical setting

**EEG**: periodic sharp-wave complexes in CJD resembling triphasics

Tonsillar biopsy for cases of suspected nvCJD.

**Prognosis**: uniformly fatal
Creutzfeld-Jacob Disease

Micro pathology

Spongiform changes (H&E)
Creutzfeld-Jacob Disease

Kuru-type plaques, aka “spiky ball”
Creutzfeld-Jacob Disease

MRI
Creutzfeld-Jacob Disease

From UCSF Memory and Aging Center website
Subcortical Dementias

**Clinical Features** *(symptoms less specific)*
--Psychomotor slowing
--Impaired concentration
--Impaired reading
--General forgetfulness
--Apathy and depression are prominent
--Cortical symptoms (aphasia, agnosia, apraxia) unusual

**Etiologies**
--Normal pressure hydrocephalus
--Pseudodementia of depression
--Progressive supranuclear palsy and parkinson’s disease
--Multiple sclerosis
--HIV-associated dementia complex
--Subcortical vascular dementia / Binswanger’s disease

**Treatment**
--Aimed at specific symptoms
Normal Pressure Hydrocephalus

**Epidemiology**  ~1/25,000 – true incidence/prevalence not known

**Clinical Features** → common triad (usually appearing in this order):
--Gait apraxia *
--Dementia (subcortical features)
--Incontinence

*Remember: Wacky, Wobbly, Wet*

* gait apraxia = foreshortened steppage and shuffling quality, “magnetic,” preserved arm swing and posture (i.e., not parkinsonian)

**Pathophysiology**: changes in CSF flow dynamics; ventricular CSF pressure > subarachnoid CSF pressure

50% is idiopathic, 50% is secondary (SAH, meningitis, trauma, surgery)
Normal Pressure Hydrocephalus

**LP:** look for improvement in gait after large-volume tap (30-50 cc); may consider B-wave monitoring (short pulsations of CSF pressure)

**MRI and/or CT:** hydrocephalus with ventriculomegaly out of proportion to cortical atrophy; MRI more sensitive for transependymal flow, corpus callosal thinning

**Treatment**

VP shunt placement – Cochrane review in 2002 found “no good evidence to support…”

**Predictors of good response** (from Geoff Aguirre talk, unknown source)

-- Dementia < 2 years
-- Gait disturbance first symptom
-- No history of EtOH abuse
-- History of a secondary cause for hydrocephalus (subarachnoid hemorrhage, meningitis, etc.)
-- Improvement in gait following large-volume tap
B12 Deficiency

Clinical features:
--Inattention/confusion
--Somnolence
--Apathy
--Delirium

--Dementia due to pure B12 deficiency is rare; B12 deficiency causing only dementia without myeloneuropathy is rare.
--Optic neuropathy, subacute combined degeneration, and axonal neuropathy are other manifestations.
--CNS damage may be irreversible after 6 months of symptoms.
--Non-neurologic: pernicious anemia, smooth sore tongue, yellowish skin, diarrhea, fatigue.

Dx: Methylmalonic acid and homocysteine levels are high to confirm a borderline B12 level.

Treatment: 1000 μg IM qd X 1wk, then weekly x 1 mo, then monthly for life vs. oral supplementation
Neurosyphilis

Clinical features
--Personality changes (apathy, withdrawal, irritability), psychosis
--Dementia with impaired judgment and confusion
--Periodic convulsions, vegetative (“general paresis of the insane”), vision changes, headache, stroke

• Tertiary syphilis results from chronic inflammatory process that, years to decades after initial infection, presents with meningitis, endarteritis or parenchymal involvement

• Dementia paralytica is a chronic meningoencephalitis presenting 20-30 years after infection

Diagnosis: CSF with > 10 WBCs, elevated protein, + CSF VDRL
Treatment: Treat with PCN G, 2-4 million units IV q4 hours for 10-14 days
--may see Jarisch-Herxheimer reaction (give steroids)

Monitor: Retreat if RPR titers don’t drop by >2 dilutions after 3 months; CSF VDRL may take years to normalize, CSF pleocytosis should respond
Hypothyroidism

Cardinal features
-- Slowed memory retrieval
-- Psychomotor slowing
-- Impaired construction and visuoperceptual abilities

- Primary hypothyroidism is common in the elderly

- Look also for general depression, pathologically slowed deep tendon reflexes, swelling of hands and face, muscle cramps

- Cognitive impairments may not be fully reversible, but can arrest decline with treatment
Wernicke’s/Korsakoff’s

Clinical Features
• Altered mental status, ataxia, and ophthalmoplegia.
• Korsakoff amnestic syndrome → amnesia and confabulation
• Seen in alcoholics, also malnutrition (AIDS, HD, hyperemesis, malignancy, bariatric surgery)

Pathophysiology: Decreased thiamine (needed for carb metabolism)
Pathology: Punctate hemorrhages, atrophy of mammillary bodies

Diagnosis: Clinical diagnosis
• On MRI, FLAIR demonstrates increased signal in mamillary bodies and peri-aqueductal gray matter; associated abnormal enhancement on T1-weighted images

Treatment: IV thiamine (before glucose-containing fluids)
Wernicke’s Encephalopathy

Gross Pathology

Punctate hemorrhages and atrophy in the mamillary bodies