Dementia:
Focus on Alzheimer’s Disease

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Disclosures

- Site Investigator for Myriad (R-Flurbiprofen study)
- Site Principal Investigator for Novartis (Excelon Patch study)
DEMENTIA DIAGNOSIS
When to Check?

- Complaint of chronic memory loss (AD) or changes in thinking, behavior.
- Screening checks every 6 months to a year in the elderly are also recommended, especially those 75 years or older.
- Consider screening at earlier ages for those with a strong family history of dementia (multiple first degree relatives with dementia or a first degree relative with early onset dementia).
But my practice is busy…

- What you need is a short screening test that is 100% sensitive for Mild Cognitive Impairment and Alzheimer’s Disease (and probably even good for Frontal-Subcortical dementias).
- Is there such a test?
- Yes. The Montreal Cognitive Assessment.
- Sensitivity 100%
- Specificity 89%
- Takes about 10 minutes.
- Available for free clinical use at http://www.mocatest.org/
- Available in multiple languages, including Spanish.
- Site provides instructions and normative data.
- 30 point scale, 26 and above normal.
MoCA 26 or above…

- Patient is probably Normal cognitively, no further work-up necessary at that time.
- Give reassurance.
- Consider rechecking in 6 months to a year.
- If the patient still wishes further investigation, consider referral to a neuropsychologist for further testing (if there’s a problem, its subtler than what you will pick up in the clinic).
MoCA 25 or below

- If only a little low (24 – 25) may still be normal, but now you need to evaluate. Remember to ask if the patient has less than a high school education (they get a point added, so a 25 becomes a 26 for them).

- Also, if the patient missed 3 or more on the delayed recall for the five words, do the optional cuing (you will need to know if memory improves with cuing, as lack of improvement with cuing is a hallmark of Alzheimer’s Disease).
Warning! Some dementia patients have anosognosia and will not be able to answer these questions. Wherever possible try and ask family or friends as well!
Onset and Course

- Onset and Course
  - Anything happen at start?
  - Sudden or Gradual?
  - Getting better, worse, fluctuating, or staying the same?
  - Order of symptom onset?

- AD should have gradual onset and slowly getting worse.
A note on duration…

- If the patient has had a significant cognitive and functional decline within less than six months, you may wish to stop there and consult a memory specialist if patient can be seen expeditiously, as it will likely be complicated.
Symptoms (remember, these are changes from previous function!)

- Forgetting things (necessary for AD dx)
- Changes in language expression or comprehension (check for hearing loss)
- Weakness, numbness, vision loss on one side of body (CVA)
- Early hallucinations (suggests Lewy Body Dementia)
- Early slowing down, gait change, falls, tremor (Parkinsonian symptoms)
- Urinary Incontinence (determine if stress or urge)
- Paranoia (thinks things are stolen or spouse cheating)
- Poor judgment (too generous, buys into get rich quick schemes)
- Disinhibited behavior (inappropriate language, too outgoing)
- Strange new food cravings (suggestive of Frontotemporal Dementia)
A comment on timing of Symptoms

- Note that most mention ‘early’ appearance in trying to differentiate different dementia syndromes.
- As dementias progress, one can see all of these sorts of symptoms arise in AD as well as other dementias.
Also screen for:

- Depression
- Ask about driving (may need driving retirement or driver’s evaluation course)
- Check Independent ADLs, ADLs
  - Able to manage finances, bills?
  - Able to shop for self?
  - Cooking and cleaning for self?
  - Bathing and dressing self okay?
  - Etc.
Example Functional Assessment:

Add Score. 9 or More is consistent with Dementia

- **SCALE:** (if the patient never did this, use best guess as to how patient would do)
  - 0: Can do this without help.
  - 1: Has some difficulty, but can do this without help.
  - 2: Need help with this.
  - 3: Can't do this.

- In the past four weeks, did the patient have any difficulty or need help with:
  - Writing checks, paying bills, or balancing a checkbook.
  - Assembling tax records, business affairs, or other papers.
  - Shopping alone for clothes, household necessities, or groceries.
  - Playing a game of skill, working on a hobby.
  - Heating water, making a cup of coffee, turning off the stove.
  - Preparing a balanced meal.
  - Keeping track of current events.
  - Following a TV show, book, or magazine and being able to discuss with acquaintances.
  - Remembering appointments or remembering to take medications.
  - Keeping track of recent conversations, recent events, and the date.
  - Driving, traveling out of the neighborhood, or arranging to take public transportation.

Dementia Essential PMH Questions

If you already know most of these for the patient, you can simply review records.
Previous Medical Conditions

- Strokes & stroke risk factors:
  - Atrial Fibrillation
  - Hyperlipidemia
  - Hypertension
  - Diabetes Mellitus
  - Sleep Apnea

- Parkinson’s Disease
- Seizures
- Head Injury
- Thyroid Disease
- Organ failure (Kidney, Lung)
- Autoimmune Diseases
- Infections (Syphilis, HIV, Meningitis)
- Cancers
- Vitamin Deficiencies (B-1, B-12, etc)
Previous Surgeries

- CABG
- Knee Surgery
- Any major surgery
- Some patients develop cognitive problems after surgery, be aware!
Medications (problems)

- Check for meds that cause confusion!
- Anti-cholinergics (including bladder control drugs)
- Hypnotics
- Sedatives/Anxiolytics
- Narcotics
- Anti-Epileptic Drugs
- Chemotherapy
Family History

- Check for first degree relatives with history of dementia, and if possible find out what type of dementia, age of onset, and duration of dementia in those family members.
- Check also for family with ALS, PD, and other neurodegenerative disorders.
- Check for family with early strokes.
Social History

- How did the patient do in school? Repeat any grades, have any learning disabilities? (pre-existing learning problems may throw off test results and require more formal testing).
- Highest level of education achieved?
- Alcohol (a glass a day is good, heavy drinking is a cause), Smoking, etc.
Dementia Essential Physical Examination
General Examination

- General appearance (signs of jaundice, etc).
- Vision and Hearing.
- Cardiovascular: Check for elevated blood pressure, carotid bruits, irregular heart rhythms, signs of peripheral vascular disease (poor distal pulses).
Neurological Examination

- Complete the MMSE (note that you can carry over the serial sevens and orientation questions from the MoCA to shorten this). Note time finished and ten minutes later ask patient to draw the figure from the MMSE again from memory.
- Note language ability on MoCA and MMSE.
- Have patient name as many animals as possible in a minute’s time (compare this result to the single letter fluency in the MoCA). Most normal people should get around 18.
- Extraocular movements (gaze palsy suggests PSP, especially on downgaze).
- Facial Expression.
Neurological Examination Cont.

Remember to check both hands on these!

- Ideomotor Praxis (have patient pantomime such actions as using scissors, screwdriver).
- Graphesthesias (write letters or numbers in palms of hands for patient to identify).
- AD patients will sometimes have graphesthesias or apraxias, usually in left hand.
Neurological Examination Cont.

- Strength (brief overview unless specific weakness reported)
- Tone (at neck as well as in arms, and use activation)
- Speed, dexterity, coordination (finger tap, foot tap, finger to nose)
- Transitions, Posture, Gait (patient able to stand from sitting sans assist, does patient have abnormal gait such as in PD, NPH, etc?)
- Tremor (Resting? Unilateral?)
Abnormal Motor activity
- Alien Hand
- Myoclonus
- Chorea (if you see this, send them to a movement disorders specialist, it's something weird)
- Fasciculations

Reflexes and Babinski
Dementia Imaging

- MRI Brain (more sensitive than CT for vascular lesions and atrophy patterns, though CT can be obtained if patient can’t have MRI)
- Caveat Emptor! MRI readings are variable.
- All patients with a cognitive abnormality deserve structural imaging!
Dementia Labs (review or order)

- CBC
- CMP
- TFT
- B12 (check Folate too) B12 below 400 can be a cause of cognitive problems!
- B1
- TPPA (RPR is inadequate!)
- Lipid Panel
- Hgb A1C
Sleep Study with CPAP fitting

- If the patient has symptoms suggestive of Obstructive Sleep Apnea, send for sleep study with CPAP fitting. This will help control vascular risk, and improved sleep may help those with mild cognitive problems secondary to sleep deprivation.
Other tests for dementia risks and diagnosis...

- **Carotid U/S and Echocardiogram**
  - If there is evidence for strokes on MRI.

- **PET scan**
  - Works in distinguishing FTD from AD in research, clinical PET less certain. FDA indication only for trying to distinguish the two. If you think you need a PET, probably need to consult a memory specialist.

- **EEG**
  - Good if there is a suspicion from history for seizures. Otherwise nonspecific.

- **Lumbar Puncture**
  - For unusual cases or ruling out neurosyphilis. Also for trial of treatment in NPH. May need to consult a memory specialist if this the case is complicated enough to warrant CSF examination.
Dementia Differential Diagnosis
Depression can be a mimic of AD and other dementias. Screen for it, and if present, treat. If the cognitive complaint goes away, probably Pseudodementia of Depression....

BUT Depression can also be a harbinger of Depression, sometimes appearing before full blown depression. Even if patient gets better, follow over time.

Depression is also a symptom commonly seen in Dementias.
Remove medications that can be causing problems. This in and of itself may correct some problems.

If correctable or treatable lab abnormalities found, correct underlying disease and reassess.

If patient continues to decline even after successful treatment, may be dealing with something else.
Normal Pressure Hydrocephalus

- Problem with the reabsorption of CSF fluid. History of Meningitis or Subdural Hemorrhage puts at greater risk.
- Classic Triad of Gait Apraxia, Urinary Incontinence, Confusion.
- MRI findings of ventriculomegaly out of proportion to any sulcal atrophy, subependymal leakage sometimes seen as bright on MRI.
- Treatment is placement of Lumboperitoneal Shunt. Should halt progression, and may reverse symptoms.
- Good prognostic indicators; presence of classic triad, short duration (several months as opposed to years), significant improvement after large volume LP.
Vascular Cognitive Impairment
- Cognitive complaint and dysfunction on exam but preserved function with MRI evidence of vascular damage.

Mild Cognitive Impairment
- Cognitive complaint and dysfunction on exam but preserved function with no other etiology.
Patients with MCI with a memory component have a greater risk for developing Alzheimer’s Disease, about 10-15% per year compared to 2% per year for the general population.
A note on MCI in people younger than 55 years old.

- In prospective studies following people younger than age 55 at time of diagnosis with MCI, the rate of conversion to dementia after a 10 year period was... 
  - None.
- We don’t know yet about the 20 year period, but this does imply that diagnosing MCI in people younger than 55 may not be prognostically useful at this time.
Alzheimer’s Disease

- Most common Dementia age 60 and older.
- Up to 50% by some studies have it by their 80s!
- First and Worst: Memory! Specifically memory that doesn’t improve with cuing.
- Should have at least one more cognitive domain involved.
- Animal fluency worse than letter fluency.
- Should have some functional impairment in real life.
- MRI may show atrophy, particular in the hippocampal regions.
- Other causes excluded.
Some FDA indications make reference to stage of severity in AD. This is where your MMSE score is useful.

Roughly MMSE scores:
- Above 20 = ‘Mild’
- 20 – 10 = ‘Moderate’
- Below 10 = ‘Severe’

May also use functional information to determine where patients fall in the spectrum.

Though flawed, the MMSE actually follows progression in AD (not necessarily other dementias, though) reasonably well.

General recommendation is follow-up visits every 6 months.
Vascular Dementia

- **Multiple Infarct Dementia easy to identify**
  - Stepwise deterioration
  - Focal symptoms & signs
  - Strokes on MRI

- **Subcortical Dementia harder**
  - Gradual and/or stepwise decline
  - No memory problem or better with cuing
  - Letter fluency worse than animal fluency
  - MoCA may be much worse than MMSE
  - Lacunes and/or White Matter Changes on MRI
Both Alzheimer’s Disease and Vascular Dementia are common in the elderly, so it is not surprising to find that they also co-occur. Also share as a risk factor Diabetes! Patients with a Hgb A1C 7.5 or greater have about ten times the risk of developing AD. Treat both the vascular and the AD components.
Lewy Body Dementia

- Same pathology as Parkinson Disease, but in the cortex.
- Has slightly less problems with memory, more with executive function.
- Early hallucinations, rigidity, falls, and fluctuating level of consciousness suggest LBD.
- Patients should have visuospatial dysfunction, otherwise it is very unlikely to be LBD.
Parkinson Disease Dementia

- Parkinson Disease patients get subtle cognitive problems, and about a third go on to develop full Dementia.
- Memory is less of a problem, more likely to be down on things like letter fluency and MoCA than animal fluency and MMSE.
- There is overlap between PDD, LBD, and AD (including pathological overlap.)
Parkinsonian Syndromes
(don’t usually respond to dopaminergic tx)

- **Progressive Supranuclear Palsy**
  - Gaze palsies, especially on downgaze.
  - Early parkinsonism, especially falls and rigidity, less so tremor. More subcortical abnormalities.

- **Corticobasal Degeneration**
  - Unilateral Ideomotor Apraxia, Agraphesthesia, Astereognosis
  - Alien Hand Syndrome
  - Myoclonic Jerks
  - Some parkinsonism
  - Gait is often preserved until late. MRI may show asymmetric atrophy in one hemisphere
Frontotemporal Lobar Degeneration (Category)

- Includes Frontotemporal Dementia, Progressive Nonfluent Aphasia, Semantic Dementia.
- Earlier onset seen than AD. Can start as early as the 40s, in the 50s is as common as early onset AD.
- There is overlap in patients and in families in the occurrence of FTLD and ALS.
Frontotemporal Dementia

- Early odd and inappropriate behavior, food cravings, poor judgment, loss of insight and empathy.
- May test out perfectly normal on simple tests like MMSE.
- MRI may show more atrophy in right frontal and temporal lobes.
Primary Progressive Aphasia

- **Progressive Nonfluent Aphasia**
  - Patient losses fluency and language expression early.
  - MRI may show increased atrophy in left frontal and temporal lobe.

- **Semantic Dementia**
  - Language is fluent but patient losses the meaning of things, may lose empathy.
  - Some memory problems seen.
  - MRI may show increased atrophy in bilateral anterior temporal lobes.
The FTLD-CBGD-PSP overlap

- All of these diseases overlap to varying degrees in symptoms and in underlying pathology.
- None have been shown to respond to Acetylcholinesterase Inhibitors (small study in FTD did suggest rivastigmine might help).
- A specialist familiar with these should be consulted.
DEMENTIA TREATMENT
Fine Tune the Brain

- Remove medications that may add to confusion.
- Reverse any reversible causes.
- Correct vitamin deficiencies.
- Start or Maintain healthy physical exercise program. Literature suggests that physical exercise also improves cognitive function.
- Keep intellectually challenged.
A note on cognitive exercise

- An area still needing a great deal of research. However, Finney’s Rule of Thumb.
- Practice what you want to preserve!
- If you want to maximally stimulate the brain, try learning something completely new.
- Dementia patients can learn with enough repetition!
Control Vascular Risk Factors

- CPAP for OSA
- Statins for hyperlipidemia
- ACE-Is for essential hypertension (some hint in literature that those that cross the blood brain barrier may be better for dementia – lisinopril, monopril, fosinopril, perindopril, trandolopril cross the blood brain barrier)
- Smoking Cessation
- Tight Diabetes Control (preferably Hgb A1C below 6.5)
- Antiplatelet agent for stroke risk reduction (Aggrenox best, but both baby aspirin and Plavix close seconds)
- Anticoagulation for Atrial Fibrillation
- Folic Acid for Homocysteinemia.
Acetylcholinesterase Inhibitors

- Three commonly used in the United States
  - Donepezil
  - Rivastigmine
  - Galantamine
- Main side effects GI related, other side effects include bradycardia, vivid dreaming/sleep disturbance, and muscle cramps.
- Gradual titration helps limit side effects.
- Taking oral forms with a large, hearty meal helps lower risk of GI side effects.
- Taking medication earlier in the day may help if patients have dream/sleep side effects.
- If a patient cannot tolerate one AChE-I, try another.
Donepezil (Aricept)

- FDA Indications for
  - Mild, Moderate, and Severe Dementia
  - Evidence in Literature for some effect in
    - Vascular Dementia/VCI
    - Lewy Body Dementia
    - Parkinson Disease Dementia
    - Mild Cognitive Impairment
  - Once daily medication, begin with dose of 5 mg, may increase to 10 mg, both doses have clinical efficacy.
Rivastigmine (Excelon)

- **FDA Indications for**
  - Mild to Moderate Alzheimer’s Disease
  - Mild to Moderate Parkinson Disease Dementia
- **Evidence in Literature for some effect in**
  - Lewy Body Dementia
  - Vascular Dementia
  - A very small open label study in FTD
- **Available in Oral and Patch forms**
  - Very slow titration (about 3 months) for oral form, only therapeutic last month of titration.
  - Oral effective doses are 4.5 mg BiD and 6 mg BID. 6 mg superior to 4.5 mg dose.
  - Patch form has two doses, 5 mg and 10 mg. The 10 mg dose is equivalent in efficacy to the 6 mg PO BiD form. Titrate over one month.
Galantamine (Razadyne, Reminyl)

- FDA Indications for
  - Mild to Moderate Alzheimer’s Disease
- Evidence in literature for some effect in
  - Vascular Dementia
- Avoid use in MCI for now! One study of Galantamine and MCI showed higher mortality rate in those treated with Galantamine.
- Galantamine comes in oral form. Originally BiD dosing but also has extended release version (Razadyne ER).
  - About two month titration (8mg, then 16 mg, stop at 24 mg). 16 mg and 24 mg doses therapeutic. 24 mg dose superior to 16 mg dose.
Memantine (Namenda)  
(weak NMDA antagonist)

- FDA Indication for
  - Moderate to Severe Alzheimer’s Disease
- Evidence in literature for some effect in
  - Mild Alzheimer’s Disease
  - Vascular Dementia
- Little information in
  - Mild Cognitive Impairment
  - Lewy Body Dementia (and some reports of worsening)
  - A small case series in FTD
Ergoloid Mesylates (Hydergine) 
(sympatholytic, metabolic ‘enhancer’)

- Third category of drug recognized by CMS for dementia.
- FDA indication in
  - Idiopathic cognitive decline in the elderly
- Some evidence in literature for effect in
  - Vascular Dementia
  - Alzheimer’s Disease (less certain)
- Beers Report suggested it is not proven useful.
- Comes in 1 mg oral form. Original FDA indicated dose 1 mg PO TiD, but most studies suggesting efficacy have doses of 4.5 mg/day or higher.
- Main side effects of bradycardia, feeling of stuffy nose.
Treating Urge Urinary Incontinence

- Try to avoid using medications.
- Behavioral management such as regularly scheduled toileting can help.
- If must medicate, try trospium (Sanctura). It is an anti-muscarinic that does not cross the blood brain barrier and early studies have suggested that it has less cognitive side effects than other agents.
Treating Sleep in Dementia

- Try to avoid sedatives and hypnotics.
- Use good sleep hygiene (no napping during day, regular bedtime every night).
- Remember the no napping (or just cat-naps)! Patients who get their sleep-wake cycles reversed may be more likely to sundown (get confused at night).
- Patients with PDD and LBD often have REM sleep disturbances. A dopaminergic drug at bedtime may help.
Depressive symptoms common in Dementia, don’t forget to treat!

- Re-uptake inhibitors best bet.
- Avoid tricyclic antidepressants in the elderly.
Treatment for Agitation and Aggression in Dementia

- Don’t argue with the demented, it exacerbates the situation.
- Use redirection and distraction where possible.
- If this is new disruptive behavior, check for signs of infection or metabolic disturbance, as an overlying delirium can easily occur.
- If there is an indication for it such as in AD, make certain the patient is first on an acetylcholinesterase inhibitor and memantine, as both of these have positive behavioral effects and less side effects.
- If all the above done, may try symptomatic treatment, but most have side effects that counter most of benefit.
- Avoid anti-dopaminergic neuroleptics in PDD patients, but especially in those with Lewy Body Dementia who are often quite sensitive to them.
A note on wandering…

- Dementia patients can have wandering behavior, which is both stressful and dangerous.
- Most dementia patients who wander off if not found in the first 24 hours are found dead!
- Sign your dementia patients up for Safe-Return or similar programs.
Morbidity and Mortality rates are high in the caregiver population. Make certain to remind caregivers to take care of themselves!

An excellent resource for caregivers is the Alzheimer’s Association.
### Appendix A: Useful ICD-9 Codes

Avoid 290 Mental Health Codes, they reimburse 50% less for same disease!

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<tr>
<th>Code</th>
<th>Diagnosis</th>
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<tr>
<td>331.0</td>
<td>Alzheimer's disease</td>
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<tr>
<td>331.11</td>
<td>Pick's disease</td>
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<td>Other Frontotemporal dementia</td>
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<td>331.2</td>
<td>Senile degeneration of the brain</td>
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<td>Communicating hydrocephalus</td>
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<td>Obstructive hydrocephalus</td>
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<td>331.7</td>
<td>Cerebral degeneration in diseases classified elsewhere</td>
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<td>(code first underlying disease as:)</td>
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<td>Dementia with Lewy Bodies/Dementia with Parkinsonism</td>
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<td>Agraphia, Apraxia, Acaculia, Agnosia</td>
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The Godfather, Kenneth M. Heilman