**Educational Need/Practice Gap**

- **Practice Gap**
  - Less than 50% of persons with AD are diagnosed
  - We have the knowledge and ability to make this 100%
  - Less than 50% of those diagnosed are treated for AD
  - We have the knowledge and ability to make this 100%
  - The situation is even worse for other causes of dementia
  - We need to do much better than this

- **Practice Need**
  - The field is in dynamic change in regards to diagnosis and management
  - These changes are poorly understood by those that do not specialize in this area of care
  - Practice parameters need to be updated, but until then, programs like this are essential
  - Last updates for AAN practice parameters:
    - 2001 Early Detection of Dementia and Mild Cognitive Impairment
    - 2001 Diagnosis of Dementia
    - 2001 Management of Dementia

**Expected Outcome**

- Increased ability to recognize and diagnosis different causes of dementia even at the stage of mild cognitive impairment
- Development of a concise diagnostic algorithm that takes into account practical aspects of daily clinic flow
- Expand symptomatic targets for intervention and rationale therapeutic approaches to care of the patient with dementia

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**Objectives**

Upon completion of this educational activity, learners will be able to:

1. Review up to date criteria for the diagnosis of dementia by DSM-5 criteria
2. Describe diagnostic criteria for 4 major types of dementia
3. Discuss biomarker findings including: cognitive testing, structural & molecular imaging, and CSF in the context of the differential diagnosis of dementia
4. Explain how to develop a rationale plan for treatment of dementia and associated symptoms

**Case #1**

- 78 year old man referred for consultation of memory loss, accompanied by wife of 56 years
- Pt denies memory changes or functional decline
- Wife has noticed decline in his abilities to shop for a few items without a list, and notes intermittent repeating of questions
- She agrees that he is experiencing no functional decline and is still actively driving (without concerns on her part), managing finances (assembling tax information), and engaged socially (local rotary club & Church activities)
- He is also noted to be less "warm", more distanced emotionally, has behavioral change (telling grandson, age 10 dirty limericks), and has some early paranoid thoughts that his wife is having an affair
- They note imbalance in gait with some intermittent "shuffling"
- PMHx notable for: HTN, HLD, DM, CABG x 3
What is your pre-diagnostic differential?

1) Normal as there is no impact on his daily function
   ✓
2) Mild cognitive impairment (MCI) - no particular type specified
3) Alzheimer’s disease
4) Dementia with Lewy Bodies
5) Vascular dementia
6) Frontotemporal dementia

How does one get from here?

First step: Determine where on the cognitive spectrum a person may be?

Diagnostic Algorithm: cognitive continuum

- Memory complaint may be made by informant or participant (either or both)
- Neuropsych testing determines objective evidence for impairment
  - 1.5 s.d. below mean for new subjects or 1.0 s.d. below baseline for longitudinal participants
- Functional decline is measured on FAQ (CDR?)

Neuropsych testing

- Decline in cognition
- Decline in function

AAN Practice parameter: Medical w/u for reversible causes of dementia or MCI

- Labs: TSH, B12, folate, RPR if at risk
- V-subdural hematoma, reversible posterior leukoencephalopathy
- I-Syphils, HIV, PML
- T-trauma, NPH, drugs
- A-SLE, Sjogren's, MS
- M-Thyroid, Wernicke's, Wilson's, SCD
- I-Vasculitis, Hashimoto's
- N-neoplasms, limbic encephalitis
- S-nonconvulsive status (EPC)

Medical w/u is negative

So, it’s MCI! But what type?

1) Alzheimer’s disease
2) Dementia with Lewy Bodies
3) Vascular dementia
4) Frontotemporal dementia
5) Other
Alzheimer’s disease (NINDS-ADRDA)
- Dementia by DSM-III-R criteria
- Deficits in two or more areas of cognition
- Progressive worsening of memory and cognitive dysfunction
- Onset age 40-90
- Absence of other systemic/brain disorders

Dementia by DSM-III-R/V criteria
- Deficits in two or more areas of cognition
- Progressive worsening of memory and cognitive dysfunction
- Onset age 40-90
- Absence of other systemic/brain disorders

Vascular dementia (NINDS-AIREN)
- Dementia by DSM-III-R/V criteria
- Cerebrovascular disease present:
  a) focal neurologic signs (stroke)
  - history of stroke not necessary
  - CT or MRI evidence of stroke
  - Onset of dementia within 3 months of stroke, or abrupt deterioration of cognitive function or stepwise course

Dementia with Lewy bodies (3rd Int. Workshop on DLB)
- Dementia by DSM-III-R/V criteria
- Deficits in cognition may not be memory (usually attention/spatial)
- Parkinsonism
- Early hallucinations
- Fluctuations
- Supportive:
  - Depression
  - REM sleep behavior disorder

Frontotemporal dementia (NIH work group on FTD)
- Prominent behavioral disorder
- Loss of interpersonal skills
- Emotional blunting
- Perserveration or in persistance
- Language involvement
- Cognition typically preserved
- Can be associated with MND/ALS

Biomarkers of disease?

Biomarker use
- If available, these can be powerful tools to guide accurate biologic etiology

<table>
<thead>
<tr>
<th>Diagnostic category</th>
<th>Amyloid (PET or CSF)</th>
<th>Neuronal Injury (MRI, tau-PET, CSF)</th>
<th>Biomarker probability</th>
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<tr>
<td>Probable AD or MCI due to AD (clinical)</td>
<td>Not needed</td>
<td>Not needed</td>
<td>Not determined</td>
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<tr>
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<td>Positive</td>
<td>Negative or not done</td>
<td>Intermediate</td>
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<tr>
<td>Probable AD or MCI-AD</td>
<td>Positive</td>
<td>Positive</td>
<td>High likelihood</td>
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<tr>
<td>Probable AD or MCI-AD</td>
<td>Negative</td>
<td>Negative</td>
<td>Low likelihood</td>
</tr>
</tbody>
</table>

3rd Party payors including Medicare will cover?

1. MRI scans
2. FDG-PET for diagnosis of any dementia
3. CSF for amyloid and tau
4. Amyloid-PET
5. Tau-PET

Diagnosis using MRI: Visual Rating System (VRS)
- MRI Characteristics
  - T2 weighted 3D Echo sequence such as MP-RAGE or similar in the CORONAL PLANE

Stage 0
- ENTO RHINAL CORTEX
- RATING = 0
  - NO ATROPHY
  - NORMAL THICKNESS
  - NO WIDENING OF COLLATERAL SULCUS
Mr. ER is a 78 yo male evaluated for the first time in 2005. He presented with mild cognitive deficits predominantly in short term memory and word finding difficulties. He also had mild symptoms of depression that required the use of an antidepressant.
Now what’s your diagnosis?

1) Alzheimer’s disease
2) Dementia with Lewy Bodies
3) Vascular dementia
4) Frontotemporal dementia
5) Other

Algorithm for Dx

Drugs to use...

- AChEi- effective in AD, DLB, & VaD, 50/50 in FTD?
- Memantine- effective in AD & DLB, possible in VaD, in question in FTD
- SSRIs & other antidepressants- effective across the board
  - Select based on side effect profile
- Benzodiazepines- can help at times but at a cost?
  - Anti-hypertensives- α-antagonists like prazosin may help, but watch BP
  - Stimulants- of active interest, but as of yet have not shown benefit and may have some risk
- Antipsychotics- 2.6 to 4.5% increase (OR 1.7) in pneumonia and CVD events
Back to our patient...

The primary issue at hand is his delusional thoughts about his wife having an affair

✓ Try an AChEI?
  • Try memantine?
  • Try an SSRI?
  • Try a Benzo?
  • Try Prazosin?
  • Try a stimulant?
  • Try an anti-psychotic?

You put him on an AChEI

He responds with improvement in cognition and resolution of his delusions.

What else should you do?
Where do you turn for help managing the behavioral, psychiatric, and caregiving issues?
What about disease-modifying therapies?

Long-term Effects of Donepezil on Cognition: ADAS-Cog Mean Change From Baseline

Increased benefit in mod-severe AD adding memantine to AChEI

The debate over combination therapy?

Do new higher dose formulations help?

• Modifications of existing drugs can lead to longer patent protection, but do they really help?
• Remember, these drugs help symptoms but do not change course of disease
• If they do not add benefit, why invest the time or money?
**Aricept 23mg?**

Farkas et al., Clin Ther. 2010 Jul;32(7):1234-51

**Namenda XR 28mg?**

Data derived from FDA package inserts

**Exelon patch 13.3mg?**

Cummings et al., Dement Geriatr Cogn Disord. 2012;33(5):341-53

**Extending patent life...**

Let’s assume that 3 million of the over 5 million persons with AD are taking an AD drug

A brand name AD drug typically costs $450/mos

Total costs over 12 months at $450/mos = $5,400/year

Market $ for an AD drug/year = $16,200,000,000

**There are 81 countries in the world with smaller GNP than this!**

Notable countries include: Georgia, Jamaica, North Korea, Iceland, Greenland, Armenia, and much of the entire continent of Africa, among others

**Comprehensive care throughout the continuum of decline**

• Reach out to the Alz Assoc for support groups and resources
• Refer to the senior center for resources
• Refer to day care programs
• Utilize non-pharmacologic interventions as a 1st line
• Call us at SBCoA (859) 323-5550
  • We may be able to help you identify the resources in your area!
• If it’s a tricky case or nothing you do seems to help?
  • Refer on to a specialist
• Done everything and the family wants more?
  • Consider clinical trial opportunities

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**Namenda vs Placebo vs AChEI**

- Namenda 10mg
  - 5.7 point difference in SIB
  - Placebo vs Namenda
- Namenda XR 28mg
  - 2.6 point difference in SIB
  - AChEI vs Namenda/AChEI
Final word on driving issues in dementia

- At least texting isn’t a major problem here
- Non-memory domain involvement may be more an issue than STM alone
- Managing driving cessation with respect is key
- Often direct confrontation is the only way

Factors that may add to unsafe driving practices...

In addition to cognitive loss:
- Vision loss
- Hearing loss
- Loss of sensation in feet
- Slow reaction time
- Medications

AAN Practice parameter on driving in dementia

If driving is an issue, how you may be able to help?

- Directly state the issues
- Order a formal driving evaluation
  - Preferably through a rehab facility rather than DMV assessment (up to 76% pass even though actuarial stats demonstrate poor driving safety)
- Support family intervention
- Be the “bad guy/gal”
- Write a Rx

Follow state laws on reporting unsafe driving

- All states have laws for persons with lapses of consciousness (seizures, syncope...etc)
- Reporting laws vary between states
  - In KY there is no mandate to report, but a letter to DMV frequently solves the matter
  - Other states may have reporting requirements
    - States whose licensing laws specifically mention Alzheimer’s disease include CA and PA.
    - OR laws refer to individuals with cognitive impairment
    - FL, GA, IA, KS, KY, NE, NV, ND, RI, SC, UT, VA, & DC reference the need to monitor people with mental disease or impairment.