What do you expect? I am 80.

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DISCLOSURE

- None

LECTURE OUTLINE

- Introduction
- Diagnostic criteria for Mild Cognitive Impairment (MCI) and Dementia
- Overview the key components to the outpatient clinic evaluation of memory loss
- Review the pharmacologic and non-pharmacologic management of MCI and Dementia
- Q&A

CAUSE OF ALZHEIMER’S DISEASE

THE CAUSE OF ALZHEIMER’S DISEASE IS NOT KNOWN
- DIFFERENT THEORIES
- GENETICS
- AGE
- EDUCATIONAL STATUS
- ENVIRONMENTAL FACTORS
- LIFESTYLE FACTORS


NEJM 2003; 348:1356
STATE OF ALZHEIMER’S DETECTION

- Cognitive impairment unrecognized in 27-81% of affected patients in primary care
  - Cordell Alz and Dementia 2013
- Diagnostic Sensitivity among PCPs
  - Mild dementia (0.41) vs. moderate dementia (0.59) vs. severe dementia (0.95)
  - Borson Int J Geriatr Psychiatry 2006
- Diagnosis of Alzheimer’s Disease delayed by months to years

IS SCREENING GOOD MEDICINE?

2014 US Preventative Services Task Force (USPSTF)

- Purpose: Systematically review the diagnostic accuracy of brief cognitive screening instruments and the benefits/harms of medication and non-medication interventions for early cognitive impairment.
- Limitation: Limited studies in persons with dementia other than AD and sparse reporting of important health outcomes.
- Conclusion: Brief instruments to screen for cognitive impairment can adequately detect dementia, but there is no empirical evidence that screening improves decision making.

SHOULD WE SCREEN FOR ALZHEIMER’S DEMENTIA

- Under current Medicare Pay for Performance, PQRI measure 133: “Whether or not patient (>65 yo) was screened for cognitive impairment using a standardized tool”
- Affordable Care Act require clinicians to assess for cognitive impairment as part of annual wellness visit

RATIONALE FOR TIMELY DETECTION?

- Improve quality of life
- Identify reversible causes
- Maximize treatment response
- Prevent diagnosis during crises
- Identify strategies for medication adherence
- Promote independence, lifestyle changes
- Reduce cost of care by decreasing hospitalizations, ER visits, and nursing home placement.
- Clarify advance directives while patient still competent.
- Begin discussion about alternatives to driving, housing alternatives.
- Prevent financial victimization or self neglect; remove firearms
- Participate in research

PROVIDER’S PERSPECTIVE

- “Avoiding detection of a serious and life changing medical condition just because there is no cure or ‘ideal’ medication therapy seems, at worst, incredibly unethical, and, at best, just bad medicine.”
  - George Schoephoerster, MD
  - Family Practice Physician

DIAGNOSTIC CHALLENGES

- Attribution error:
  - “What do you expect? She is 80 years old.”
- Limited time
  - Subjective impressions fail to detect dementia in early stages
- Many patients unaware, do not self-identify problems
  - CULTURE / STIGMA / AGEISM
- Heterogeneous baseline
  - Easy to be fooled by a sense of humor, reliance on old memories, or quiet/affable demeanor
- Fear of giving wrong diagnosis
- Skepticism, lack of knowledge re: treatment options/efficacy
NORMAL CHANGES WITH AGING

• Slowing in rate at which information can be received and processed
• Reduction in “explicit memory” (e.g., the ability to recall a specific name, number, or location on demand)
• Not progressive
• Does not interfere with daily function or independence

RED FLAGS

– Repetition (not normal in 7-10 min conversation)
– Tangential, circumstantial responses
– Losing track of conversation

Raise your expectation of older adults

• ANY instances whatsoever or getting lost while driving,
• Trouble following a recipe
• Asking same questions repeatedly,
• Mistakes paying bills

COGNITIVE CONTINUUM

Preclinical • Normal Cognitive Function
Minor Neurocognitive Disorder • MCI
Major Neurocognitive Disorder • Dementia

MILD COGNITIVE IMPAIRMENT

AKA: Minor neurocognitive disorder

• Patients are not functionally impaired enough to meet criteria for dementia but still show cognitive decline from their baseline.
• Two Types:
  – Amnestic MCI
  – Non-amnestic MCI

MCI PROGRESSION TO ALZHEIMER’S DISEASE

At rate of about 7-15% per year

Conversion rate (%)

0 1 2 3 4 5 6 7
Duration (years)

DIAGNOSTIC CRITERIA

DSM-5
Introducing the term Neurocognitive Disorders

• Delirium
• Neurocognitive disorders (Not delirium)
  – Minor
  – Major
• Further subdivision based on etiology
**Cognitive Domains**

1. Complex attention
2. Executive function
3. Learning and memory
4. Language
5. Perceptual-motor
6. Social cognition

**Diagnosis of Alzheimer’s**

Alzheimer’s disease is diagnosed by exclusion.

Steps in the diagnostic process:
- Medical history –
- Physical exam –
- Neurological examination –
- Neuroimaging: Brain scan, EEG, or an MRI
- Psychological examination – via psychiatrist

The only positive diagnosis is made with microscopic examination of the brain tissue. This can only be done on autopsy.

**Features Inconsistent with Alzheimer’s Dementia**

- Sudden onset
- Focal neurological findings
- Frequent symptom fluctuation (decreased/shifting attention)
- Seizures
- Early marked changes in personality/behaviors
- Gait disorder early in disease
- Perceptual disturbances (illusions or misinterpretations 30%)
- Hallucinations
- Tremors/asterixis

**History Pearls**

- Medical conditions
- Social history
- Family history
- Medications
- Quality of onset and temporal nature of cognitive decline
- Evaluate for delirium/depression
- Collaborative history is key

**POOH Corner Rx**

- Patient: Mr. John Doe
  - Symptoms: Drowsy
  - Prescriptions: Albuterol
- Patient: Ms. Jane Smith
  - Symptoms: Anxiety
  - Prescriptions: Cymbalta

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AGS Beers Criteria 2019
POTENTIALLY REVERSIBLE DEMENTIAS

- DRUGS 16
- HYPOTHYROID 7
- HYPERPARATHYROID 3
- B12 DEFICIENCY 2
- SUBDURAL HEMATOMA 2
- OTHER 3
- TOTAL 31 (10%) (Larson et al, Ann Intern Med 1984;100:417-23. 107 cognitively impaired outpatients)

REVERSIBILITY OF DRUG INDUCED DEMENTIA

- >50% who stop medication will improve
- Often a single medication implicated
- Patients with drug-induced cognitive impairment were also 3 times more likely to fall
- Most offending drugs taken for several years prior to diagnosis


DRUGS IMPAIRING COGNITION

- Anticholinergics (eg, diphenhydramine, trihexyphenidyl, oxybutynin, etc)
- Anticonvulsants (phenytoin, gabapentin, valproate)
- Muscle relaxers (carisoprodol [Soma], cyclobenzaprine [Flexeril])
- Antiemetics (prochlorperazine, metoclopramide)
- Digoxin, clonidine, amantadine, amiodarone
- Benzodiazepines, antipsychotics
- Everything we prescribe ... except acetaminophen and docusate

SCREENING TOOL SELECTION

- Montreal Cognitive Assessment (MoCA)
  www.mocatest.org
  Sensitivity: 90% for MCI, 100% for dementia
  Specificity: 87%
- St. Louis University Mental Status (SLUMS)
  30 point; includes cutoffs for education/MCI
  Sensitivity: 92% for MCI, 100% for dementia
  Specificity: 81%
  http://medschool.slu.edu/agingsuccessfully/pdf surveys/slumsexam_05.pdf
- Mini-Mental Status Exam (MMSE)
  12-item, 30-point tool administered in 10-15 minutes
  Sensitivity: 18% for MCI, 78% for dementia
  Specificity: 100%


MINI-COG SCREENING

- Figure 1. The Mini-Cog scoring algorithm. The Mini-Cog uses a three-item recall test for memory and the intuitive clock-drawing test. The latter serves as an "informative distractor," helping to clarify scores when the memory recall score is intermediate.
- Recall = 0 DEMENTED
- Recall = 1-2 NONDEMENTED
- Recall = 3 DEMENTED
- Clock Abnormal
- Clock Normal
**LAB WORK UP**

- All patients:
  - CBC
  - Electrolytes
  - Creatinine
  - Glucose
  - TSH
  - Vitamin B12

- Selected cases:
  - HIV serology
  - RPR
  - Heavy metal screening
  - LFTs
  - MMA

**INCIDENCE AND CAUSES OF DEMENTIA**

- Record review of 560 consecutive patients newly diagnosed with dementia
- No cases of dementia due to NPH, subdural hematoma, B12 deficiency, hypothyroidism, or neurosyphilis
- Conclusion: “None of the patients with dementia reverted to normal with treatment of the putative reversible cause.”

(Knopman et al, Arch Neurol 63:218, 2006)

**NEUROLOGIC IMAGING**

- Focal neurologic deficit
- History of head trauma
- History of strokes
- Symptoms of normal pressure hydrocephalus
- Unexpected course/progression

**NEUROLOGIC IMAGING**

Report of the Quality Standards Subcommittee of the American Academy of Neurology

- Structural neuroimaging with either a noncontrast CT or MR scan in the initial evaluation of patients with dementia is appropriate. (Guideline)"
- “Screening for depression, B12 deficiency, and hypothyroidism should be performed (Guideline).”


**STAGES OF ALZHEIMER’S DISEASE**
**EARLY STAGE**

- This stage can last for two to four years
- A person in this stage may be aware that something is wrong
- A person in the early stage may still be able to participate in decisions affecting their future

**MIDDLE STAGE**

- This stage may last from two to ten years
- Continued memory lapses
- Assistance required for daily tasks
- Appetite fluctuations
- Personality changes
  - Confusion
  - Anxiety
  - Pacing
  - Wandering
  - Suspicions
  - Sadness/depression
  - Hostility
- Caregiver may have difficulty as care becomes more difficult

**NEUROPSYCHIATRIC SYMPTOMS**

- 60% of community dwelling patients with dementia
- > 80% of nursing home residents with dementia
  - Hoarding
  - Wandering
  - Sun downing
  - Psychoses (delusions, hallucinations)
  - Sleep disturbances
  - Aggression, agitation
  - Hypersexuality

**LATE STAGE**

- This stage usually lasts from one to three years
- The person will need 24-hour a day care
  - Loses ability to speak
  - Becomes incontinent
  - Inability to swallow
  - May become unresponsive (coma)
  - Ends in death

**MANAGEMENT**

- No way to cure Alzheimer's disease or stop its progression.
- Goal: Enhance quality of life and maximize functional performance
  - Pharmacological
  - Non pharmacological
  - Specific symptoms management
  - Resources.

**PREVENTION**

Exercise your mind and body?

- 170 participants with MCI in randomized, controlled, 24-week trial of home-based physical activity intervention (70,000 steps/week) vs "usual care" showed modest improvement in cognition

(JAMA. 2008;300:1027-1037.)
NON PHARMACOLOGICAL MANAGEMENT

- Patient/Family education on the disease
- Utilize external memory aids (calendars, lists, whiteboards...)
- Regular appointments
- Attention to safety
- Focus on keeping a routine
- Maintain positive activities (church choir, handbell choir, Senior social dances, etc.)
- Participation in socially and cognitively stimulating activities
- Aerobic exercise

Key to Success!

NON PHARMACOLOGICAL MANAGEMENT

- Validation Therapy
- Structured Areas for Mobility
- Provides avenue for social interaction
- Provides a medium for verbal/non-verbal expression
- Dancing allows for intimacy between spouses
- Caring for physical needs
- Maintain integrity of the skin
- Utilize touch: holding hands, hugging, rocking, hand on shoulder, etc.
- Do not criticize or correct
- Offer a guess
- Limit distraction

PHARMACOLOGICAL MANAGEMENT

- There are NO FDA approved medications for the treatment of MCI / Minor neurocognitive disorder

PHARMACOLOGICAL MANAGEMENT

FDA Approved Medications for Alzheimer’s Dementia:

1. Cholinesterase Inhibitors:
   a) Donepezil/Aricept: Mild to Moderate and Moderate to Severe AD
   b) Galantamine/Razadyne: Mild to Moderate AD
   c) Rivastigmine/Exelon: Mild to Moderate AD

2. NMDA Receptor Antagonist:
   a) Memantine/Namenda: Moderate to Severe AD

3. Combination:
   a) Memantine/Donepezil: Moderate to Severe AD

PHARMACOLOGICAL MANAGEMENT

- Memantine (Namenda) XR (FDA approved 6/2010)
  - Dose: 28 mg PO Daily
  - Cost: $330/month

- Donepezil (Aricept) XL (FDA approved 7/2010)
  - Dose: 23 mg PO Daily
  - Cost: $110

- Memantine XR/Donepezil (Namzaric) (FDA approved 12/2014)
  - Dose: 28 mg/10 mg PO QHS
  - Cost: $360/month
**Generic Name and Dose** | **Brand Name** | **Frequency of Use per Day** | **Average Monthly Cost** |
---|---|---|---|
Donepezil 5mg | Aricept | One | $12 - $260 |
Donepezil 10mg | Aricept | One | $208 - $407 |
Donepezil 23mg | Aricept | One | $123 - $443 |
Memantine 10mg | Namenda | Two | $320 - $400 |
Galantamine 12mg | Razadyne | Two | $94 - $238 |
Galantamine ER 24mg | Razadyne | One | $42 - $300 |
Rivastigmine 9.5mg/24hr patch | Exelon | One | $94 - $370 |

**SIDE EFFECTS**

- Cholinesterase Inhibitors
  - Nausea
  - Diarrhea
  - Insomnia
  - Vomiting
  - Muscle cramps
  - Fatigue
  - Anorexia

- NMRA Receptor Antagonist
  - Dizziness
  - Headache
  - Confusion
  - Constipation

20-25% of people stop taking an Alzheimer’s drug due to side effects!

**SIDE EFFECTS**

- AV block
- Bradycardia
- Syncope
- Seizures
- GI bleeding
- Hemolytic anemia

**AAFP and ACP CLINICAL PRACTICE GUIDELINES**

- Recommendation 1:
  Clinicians should base the decision to initiate a trial of therapy with a cholinesterase inhibitor or memantine on individual assessment.
**SUPPLEMENTS**

- Vitamin E
- Caprylic acid
- Coconut Oil
- Ginkgo Biloba

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**VITAMIN E**

Take Home Point: We are not routinely prescribing Vitamin E for patients.

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**CAPRYLIC ACID**

- Caprylic Acid= Axona (Brand Name)
  - “Medical Food”
  - Prescription dietary supplement
- Medium-chain triglyceride produced from coconut or palm kernel oil thought to act as alternative energy source for brain
- NO phase III studies to confirm effectiveness
- Adverse Effects: Diarrhea, nausea, flatulence
- Cost = $100 a month

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**COCONUT OIL**

- Coconut oil is broken down into a medium-chain triglyceride that is thought to act as alternative energy source for brain
- USF Health Byrd Alzheimer’s Institute has ongoing clinical trial on the use of Coconut Oil in mild to moderate AD = more info to come!
- No Phase III Trials to confirm effectiveness
- Adverse effects: Unknown, ? Increased cholesterol levels
- Cost = $4 a month

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**GINKO BILOBA**

- Plant extract thought to have antioxidant and anti-inflammatory properties
- Large National Institute of Health trial showed Ginko is NO better than placebo at preventing or delaying AD
- Adverse Effects: Increased bleeding risk, nausea, headache, constipation, allergic reaction, interaction with medications (Aspirin, Plavix, Warfarin, Fluoxetine...)
- Cost = $9 a month
FDA EXPANDS ADVISE ON STATIN RISKS

- “The post-marketing adverse event reports generally described individuals over the age of 50 years who experienced notable, but ill defined memory loss or impairment that was reversible upon discontinuation of statin therapy. Time to onset of the event was highly variable, ranging from one day to years after statin exposure. The cases did not appear to be associated with fixed or progressive dementia.”
- www.fda.gov/drugs/drugsafety/ucm293101.htm
- U.S. Department of Health and Human Services

NEUROPSYCIATRIC SYMPTOMS OF DEMENTIA

- BMJ 2012 Article: Differential risk of death in older residents in nursing homes prescribed specific antipsychotic drugs: population based cohort study
  - “The data suggested the risk of mortality with these drugs is generally increased with higher doses and seems to be the highest for haloperidol and least for quetiapine.”
- Clinical Pearls:
  - Document your risk/benefit discussion with the patient/HCPOA
  - Start low and go slow
  - Closely monitor for side effects and efficacy
  - Be mindful to discontinue the medication if no benefit

FITNESS TO DRIVE THORNY ISSUES FOR GPs

- Multiple states including WI (encourage or allow physician reporting, but do not make it mandatory.)
- In early dementia when sufficient skills are retained and progression is slow, a licence may be issued subject to annual review
- A formal driving assessment may be necessary

ENDANGERED PERSON

- These persons are not “missing” They are “endangered”
- Time is of the essence
- Won’t knock on doors. Won’t flag you down
- They won’t answer if you call their name
- They don’t think they are lost
- They may not stand out in a crowd
- Will be drawn to water, ditches, culverts
- Will walk in the snow shoeless & coatless
- They wander on foot, by car, and by boat
- Do they have an ID bracelet?
- Are they registered in the Alzheimer’s associations safe return program?

ENDANGERED PERSON

Survival Rates

- 50% chance to find them alive in the first 16 hours
- That percentage drops by 10% each hour they are lost
- 46% of those found dead died of hypothermia or dehydration
SAFE RETURN PROGRAM

• SRP provides identification products
  – ID bracelets/necklace /key chains
• 24 hour hotline
• Registration in National data base
• Access to law enforcement agencies
• Direct connect to nationwide Alzheimer’s Association offices

RESEARCH OPPORTUNITIES

Patient Engagement:

Reasearch Participation:

• Alzheimer’s Association Trial Match
  – Free, easy-to-use clinical studies matching service that connects individuals with Alzheimer’s, caregivers, healthy volunteers and physicians with current studies.
  – http://www.alz.org/research/clinical_trials/find_clinical_trials_trialmatch.asp
• National Institute of Health (NIH)
  – http://clinicaltrials.gov

References

• ACP 2013 Dementia Guidelines: http://smartmedicine.acponline.org/content.aspx?gbosId=164&resultClick=3&ClientActionType=SOLR%20Direct%20to%20Content&ClientActionData=Module%20link%20Click
• Budson, Andrew E., M.D. - Memory Loss: A Practical Guide for Clinicians, 71-78 © 2011
• Geriatric Review Syllabus, 8th Edition

Resources

• Attorney for will, conservatorship, estate planning
• Community: neighbors & friends, aging & mental health networks, adult day care, respite care, home-health agency
• Organizations: Alzheimer’s Association, Area Agencies on Aging, Councils on Aging
• Services: Meals-on-Wheels, senior citizen centers

References