Alzheimer's Disease Update in Care

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Presenter

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- Disclosures
  - No relevant financial disclosures
  - No discussion of investigational or off-label medications

Objectives

- Discuss and differentiate between ‘mild cognitive impairment’ and the most common types of dementia encountered in practice
- Discuss evidence-based quality indicators that primary care physicians can incorporate into practice regarding dementia care
- Discuss the management of dementia and common associated problems

Overview of today's presentation

- Review of common conditions many people call "Alzheimers" or "Oldtimer's"
  - Mild Cognitive Impairment
  - Alzheimer's Disease
  - Other common dementias
- Brand new diagnostic guidelines for AD
- Diagnosis & management
- Quality indicators for improved outcomes

Quick Case Scenario #1

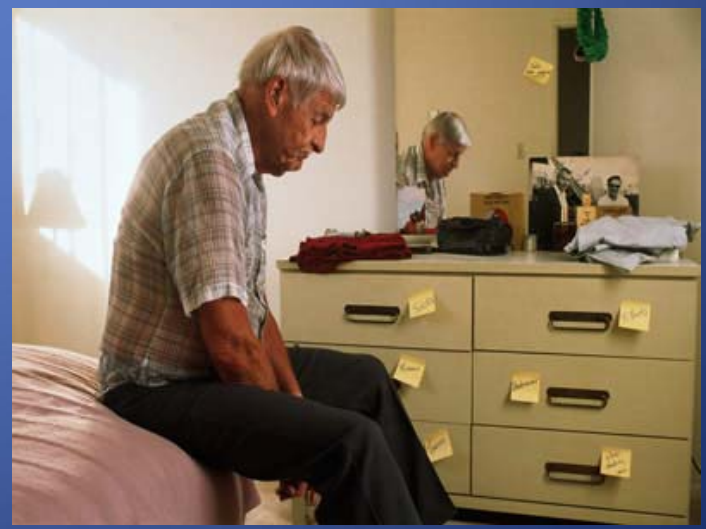
- 55 yo male comes to your office with the following concern during a general checkup
- He states that he notices that when he enters a room, he sometimes cannot remember why he went into the room
- How do you reassure him?

Quick Case Scenario #2

- 90 yo female presents for follow-up on her hypertension
- Your office staff hands you a note from her son just as you are about to enter the room
- He is concerned that she should not have her driver's license renewed, since she has become lost several times while driving lately
- How do you manage this?

Quick Case Scenario #3

- The daughter of one of your nursing home patients calls wanting to talk with you
- She is distressed by her father's behavior in the nursing home, but does not want him "drugged into submission"
- What do you say?



Scope of the issue

- 5.3 million Americans with AD
  - Expected to reach 15 million by 2030
- $172 billion in annual costs
- 6th leading cause of death in America
- 10.9 million unpaid caregivers
- AD mortality rate is on the rise
  - ↑ 46% from 2000 to 2006
- Lifetime risk
  - Men: 17%
  - Women: 20%

Alzheimer's Association (*www.alz.org*)

Other AD statistics

- 25% of hospitalized patients have dementia
- Dementia dx leads to 8 x higher risk of SNF placement
- 87% of dementia pts are cared for at home
- 66% of dementia pts die in LTCFs

Unwin BK. Care of the Vulnerable Elderly: Dementia Quality Indicators. **FPAudio.** 2010;9,4-6.

- Prevalence in >71 yo:
  - All dementias - 13.9% (3.4 million)
  - Alzheimer's only – 9.7% (2.4 million)

Plessman BL, et al. Prevalence of Dementia in the United States: The Aging, demographics, and Memory Study. **Neuroepidemiology.** 2007;29:125-132

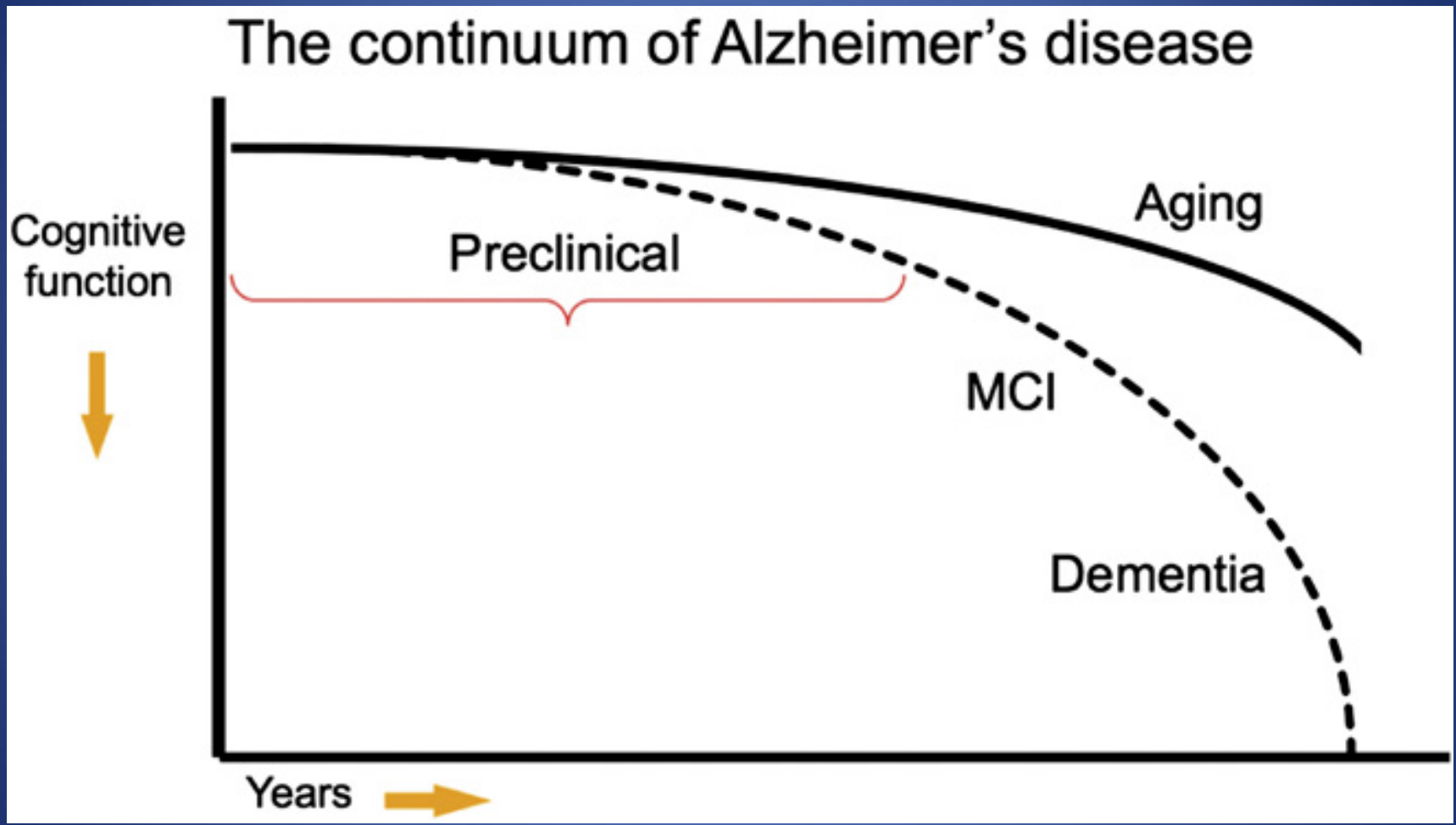
New diagnostic guidelines

- Formally announced 4/19/2011
  - Published in Journal Alzheimer's & Dementia available online – now in press
- National Institute on Aging and Alzheimer's Association
- First update on diagnostic criteria since 1984
  - Now we have MRIs, PET scans, biomarkers
  - Recognition of DLB and FTL dementia
  - Better understanding of pathogenesis of AD

New classification

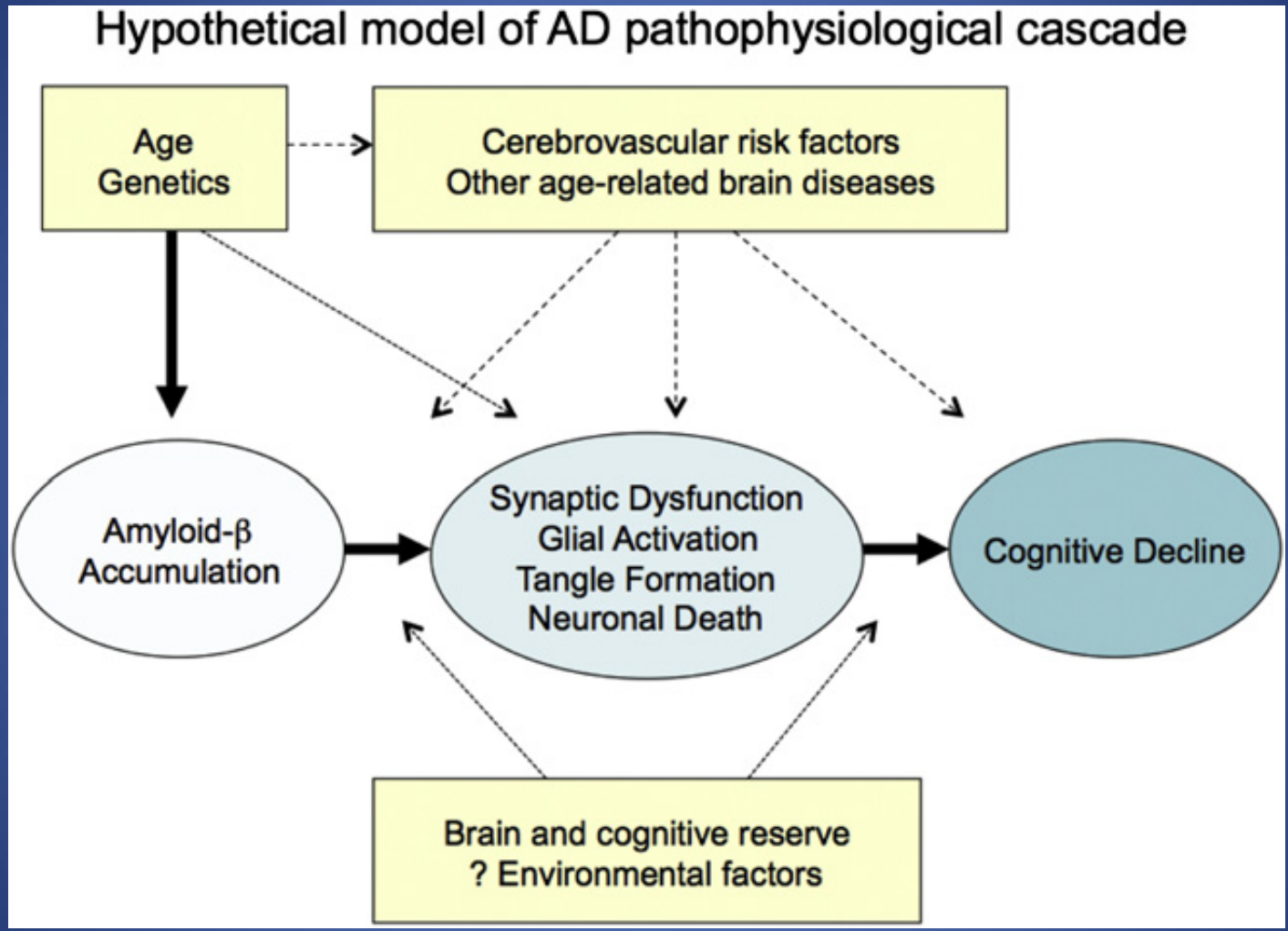
- Alzheimer's Disease is a spectrum of pathophysiological findings that, over years or decades, may manifest clinically
  - Analogy: hypercholesterolemia and CAD
- AD-P (pathophysiological or pre-clinical)
  - Disease present, pathophysiologically
  - Diagnosed by biomarkers – no clinical expression
  - Useful for *research* purposes
- AD-C (clinical)
  - MCI due to AD
  - Dementia due to AD

Another way of showing this



Sperling RA, et al. "Toward defining the preclinical stages of Alzheimer's disease: Recommendations from the National Institute on Aging and the Alzheimer's Association Workgroup." **Alzheimer's & Dementia**, doi:10.1016/j.jalz.2011.03.003

Temporal relationship: AD-P → AD-C



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AD-P

- Diagnosed by biomarkers associated with neurodegeneration
  - Accumulation of β-amyloid
  - Presence of neurofibrillary tangle formation & neuronal death associated with tau
  - Detected by tagged imaging and/or CSF analysis
- Individuals with such biomarkers have increased risk of developing AD-C, but a significant portion (~30%) do not progress
- Again – useful ***only*** for research purposes
  - Interventions after AD-P findings are present have been uniformly disappointing (if not harmful)
  - Emphasis now on preventing development of the pathophysiologic findings prior to the onset of clinical dz

New Criteria for MCI due to AD-C

- Cognitive concern reflecting a change in cognition reported by pt or informant or clinician
- Objective evidence of impairment in one or more cognitive domains, typically including memory
- Preservation of independence in functional abilities
- Not demented

Albert MS, et al. “The diagnosis of mild cognitive impairment due to Alzheimer's disease: Recommendations from the National Institute on Aging and Alzheimer's Association workgroup.” **Alzheimer's & Dementia**, doi:10.1016/j.jalz.2011.03.008

Screening for MCI?

- No definitive expert opinion on screening
- US Preventive Task Force does recommend assessment whenever cognitive impairment is suspected, based on
  - Pt report
  - Direct observation
  - Concerns raised by family members
- How common is MCI?
  - 5.4 million Americans older than 71 years
  - 22.2% of that total population
  - Greater than the number with Alzheimer's Disease

Plessman BL, et al. "Prevalence of Cognitive Impairment Without Dementia in the United States." **Ann Intern Med**. 2008;148:427-434.

Assessment tools for cognition

- Many are available
- Mini Mental State Exam (MMSE)
  - a.k.a. “The Folstein” (1975)
- CLOX2
- Mini-Cog
- Word list generation
  - Letter WLG – “FAS”
  - Category WLG – “animals”

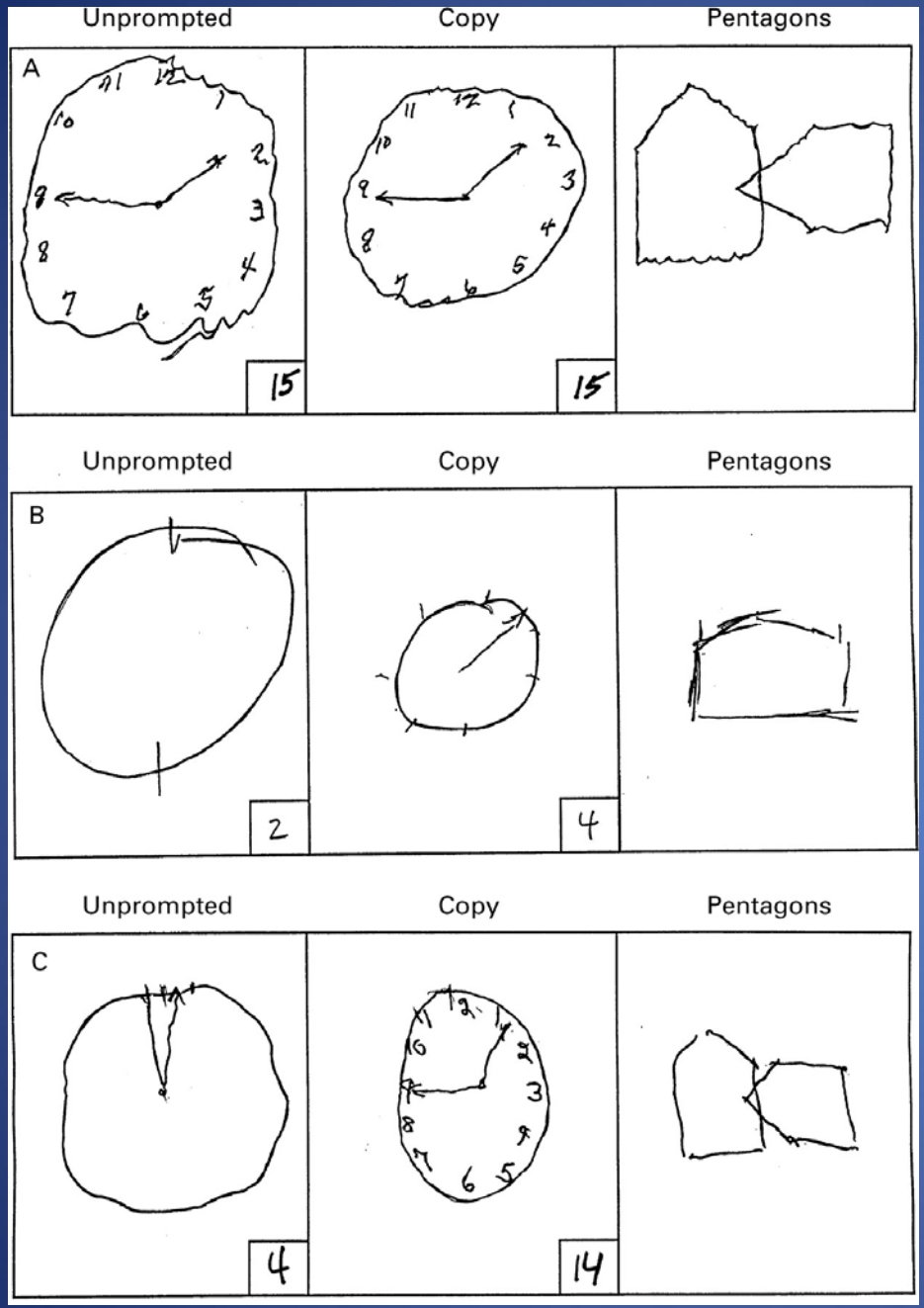
MMSE

- Standardized, copyrighted (!) test
- Divided into subscales
  - Temporal orientation index (0-5)
  - Physical orientation index (0-5)
  - Registration/Working Memory (0-3)
  - Language index (0-9)
  - Memory/Recall index (0-3)
  - Attention/Calculation index (0-5)
- Score <26/30 = cognitive impairment

CLOX2

- Prepare a paper with a clock drawn on one side
- Fold the paper, hand it to the subject blank side up and ask them to

  "draw the face of a clock, put in all the numbers & a time"
- Once complete, unfold the paper and ask them to copy the clock face they see
- Unable to draw clock = executive dysfunction
  - (EF is the ability to analyze, organize, decide, and execute)
- Unable to do either suggests dementia



A: 82-yo elderly control

B: 74-yo with Alzheimer's Dz

C: 74-yo with CAD, Htn, DM and falls
(i.e. Executive Dysfunction)

Royall, D. R et al. **J Neurol Neurosurg Psychiatry 1998;64:588-594**

Mini-Cog

- Combines parts of MMSE & clock drawing
- Do Registration part of MMSE
- Do clock-drawing
- Do Recall part of MMSE
- Detects deficits of
  - Executive dysfunction
  - Working memory
  - Memory

Borson S. The mini-cog: a cognitive “vitals signs” measure for dementia screening in multi-lingual elderly. **Int J Geriatr Psychiatry** 2000;15(11):1021.

Word List Generation

- Letter WLG “FAS”
  - Name as many words as possible that start with the letter
    - “F”, then “A”, then “S” in 60 seconds each
    - Sum the responses
  - Normal is ≥ 40
  - Abnormal suggests AD type dementia
- Category WLG
  - Names as many words as possible that are “animals”
  - Normal is ≥ 20
  - Abnormal suggests non-AD dementia

Barr A, Brandt J. **Word-list generation deficits in dementia.** J Clin Exp Neuropsychol. 1996 Dec;18(6):810-22.

Importance of MCI

- It is a physical change
  - Family/friends/others – need to be made aware this is not intentionally done
- It may be a precursor to something else
- May be a warning signal to seek treatment
- Let pt/family know not serious enough such that:
  - Does ***not*** limit decision-making
  - Does ***not*** limit IADL's
  - Does ***not*** require alternative living arrangements for this reason

Treatment

- No FDA approved treatments
- Donepezil for individuals with MCI
  - Reduced risk of 'progression' in first year
  - No difference in risk after three years
  - Vitamin E also studied – no benefit

    Petersen RC et al. "Vitamin E and Donepezil for the Treatment of Mild Cognitive Impairment." *NEJM June 9, 2005.*
- Galantamine studied in two trials
  - No benefit
  - Increased death rates compared to controls

    Unpublished studies

Treatment (cont)

- Other drugs inadequately studied
- Cognitive interventions
  - Performance gains noted, but not significantly more than actively treated controls
  - No adverse effects
  - Studies too short to determine prolonged effects

Martin M, et al. "Cognition-based interventions for healthy older people and people with mild cognitive impairment." **Cochrane Review**. 2011.

- Bottom line
  - No drugs / Consider cognitive interventions / monitor

New Dementia Core Clinical Criteria

Cognitive or neuropsychiatric symptoms that:

1. Interfere with the ability to function at work or at usual activities; and
2. Represent a decline from previous function
3. Are not explained by delirium or psychiatric disorder;
4. Cognitive impairment detected/diagnosed by history and cognitive assessment;

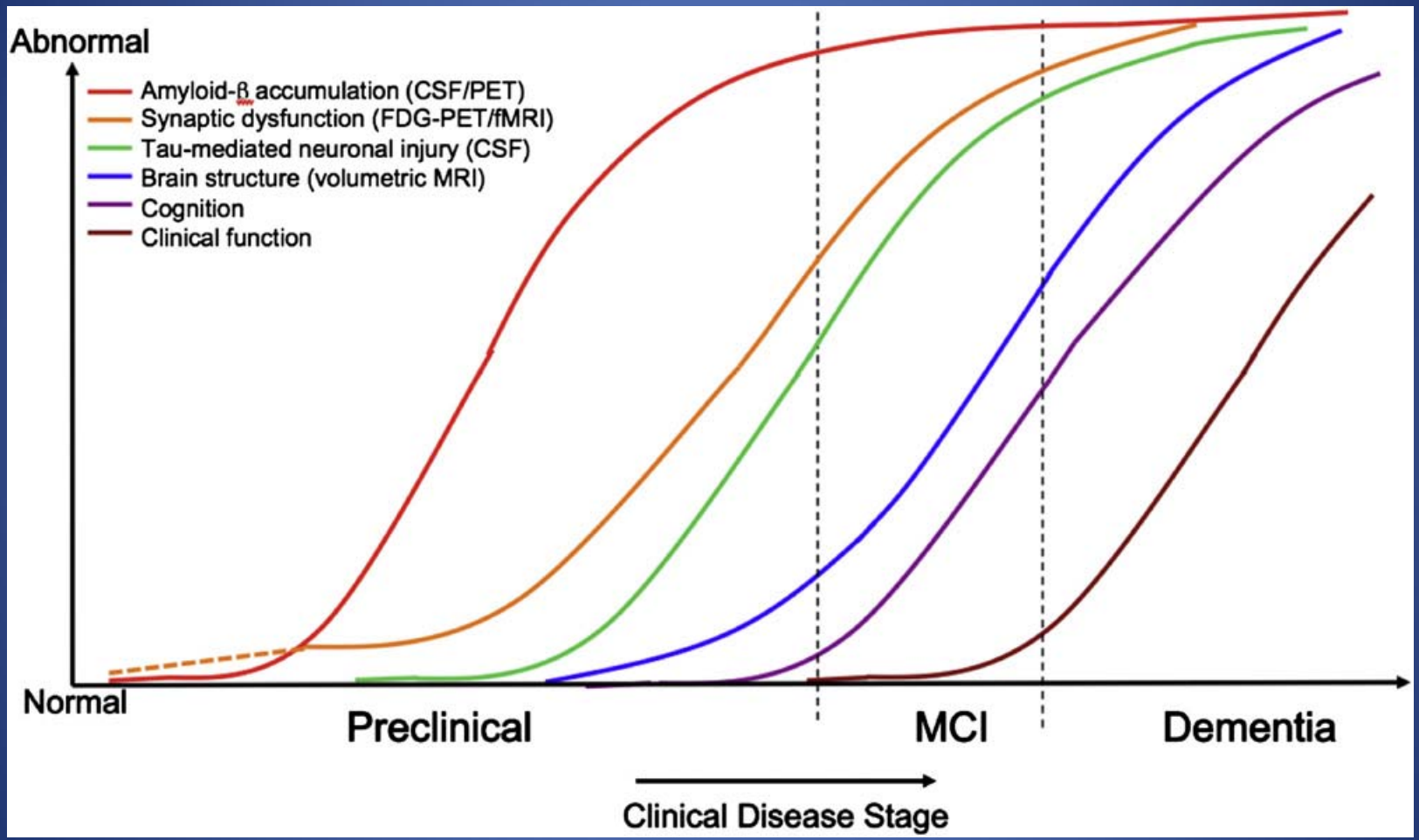
McKahnn GM, et al. “The diagnosis of dementia due to Alzheimer's disease: Recommendations from the National Institute on Aging and the Alzheimer's Association workgroup.” **Alzheimer's & Dementia**, doi:10.1016/j.jalz.2011.03.005

Dementia Core Clinical Criteria (cont.)

5. Impairment involves at least 2 of following
   - Impaired ability to acquire/remember new info
   - Impaired reasoning & handling of complex tasks
   - Impaired visuospatial abilities
   - Impaired language functions
   - Changes in personality, behavior, comportment
- ***Should not*** be applied if evidence of concomitant cerebrovascular disease or core features of another type of dementia

McKahnn GM, et al. "The diagnosis of dementia due to Alzheimer's disease: Recommendations from the National Institute on Aging and the Alzheimer's Association workgroup." **Alzheimer's & Dementia**, doi:10.1016/j.jalz.2011.03.005

Dynamic findings in progression of AD



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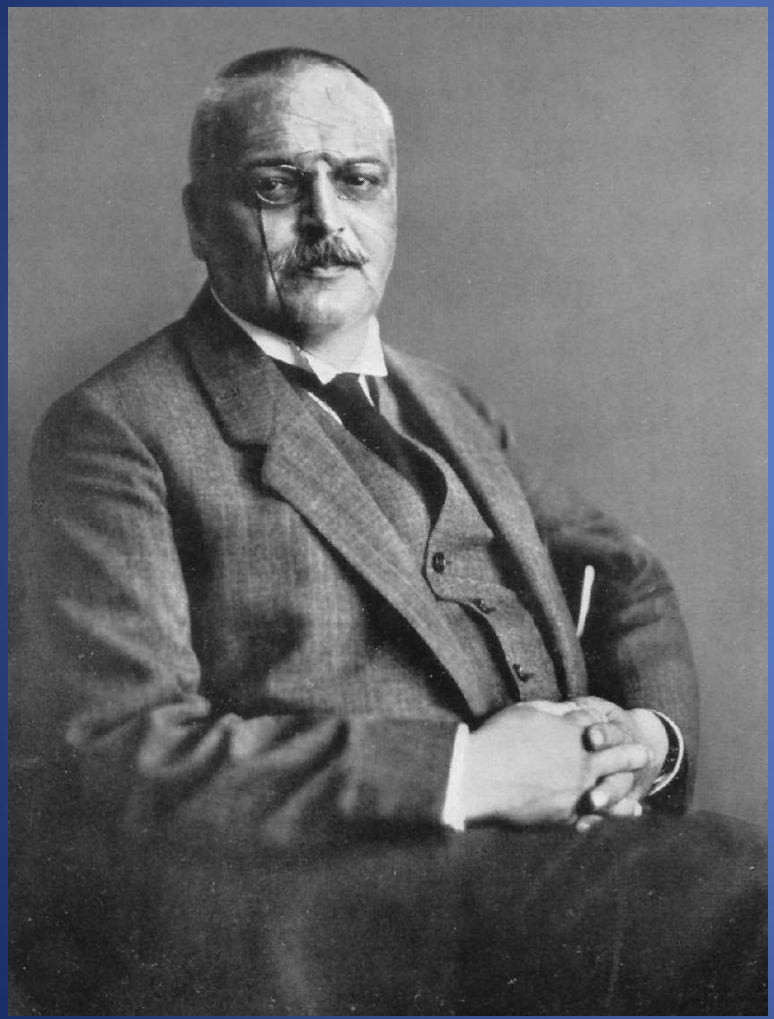
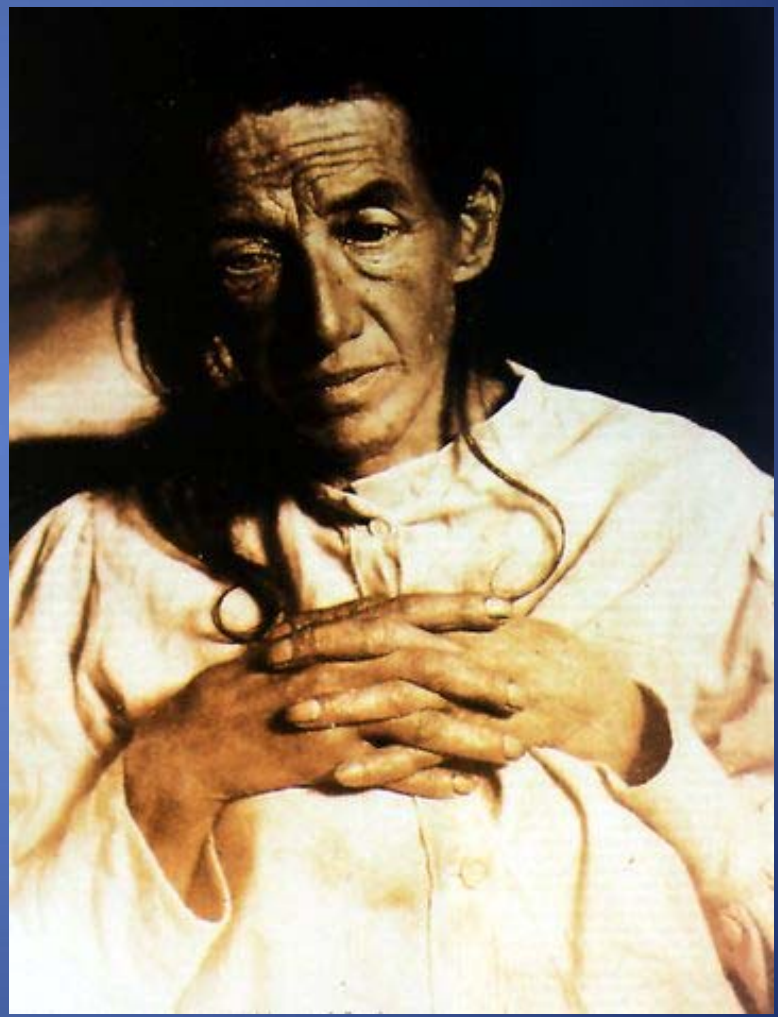
Noteworthy persons



Dr. Alois Alzheimer

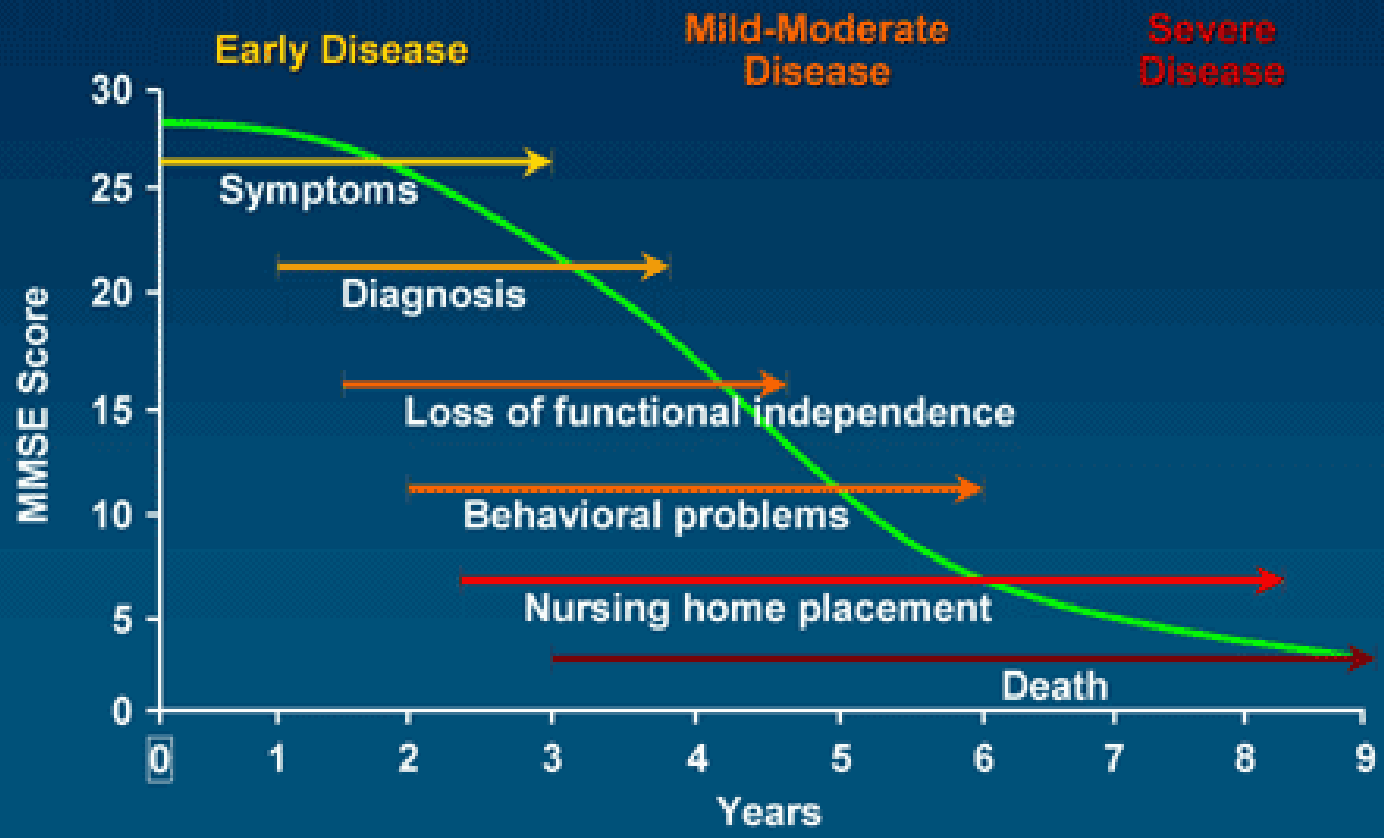


Auguste

Natural course of AD

- Average survival after dx
  - ~ 4-10 years (wide variation among studies)
  - Similar in all neurodegenerative dementias
  - Depends on stage at diagnosis
- Average survival for late stages of disease
  - Up to 2-3 years
- Death doesn't occur as a result of neurodegeneration
- Death occurs as a consequence of complications
- AD is an ultimately terminal diagnosis

Alzheimer's Disease: Natural History



Adapted from Feldman H, Gracon S. Alzheimer's disease: symptomatic drugs under development. In: Gauthier S (ed). Clinical Diagnosis and Management of Alzheimer's Disease. Martin Dunitz: London, 1996:239_259.

Treatment

- Cholinesterase Inhibitors
  - Tacrine (Cognex®)
  - Donepezil (Aricept®)
  - Rivastigmine (Exelon®)
  - Galantamine (Razadyne®)
- Mode of action
  - Increase acetylcholine levels in the brain

Treatment (cont)

- NMDA antagonist
  - Memantine (Namenda®)
- What does it do?
  - NMDA receptors over-stimulated by glutamate
  - Slows Ca++ influx
  - Slows (prevents?) neuronal damage

How well do these work?

- Cholinesterase inhibitors
  - Clinical efficacy debatable
  - Donepezil (mild/moderate/severe)
    - Benefits cognitive function, ADLs, behavior
    - Lowest side effects
  - Rivastigmine (mild/moderate)
    - Benefits rate of decline, ADLs
    - Side effects somewhat mitigated by patch
  - Galantamine (mild/moderate)
    - Similar benefits
- NMDA Antagonist
  - Memantine (mild/moderate)
    - Best tolerated
    - Similar benefits
    - Can be used combined with one of the above

Cochrane Reviews (*www.cochrane.org*)

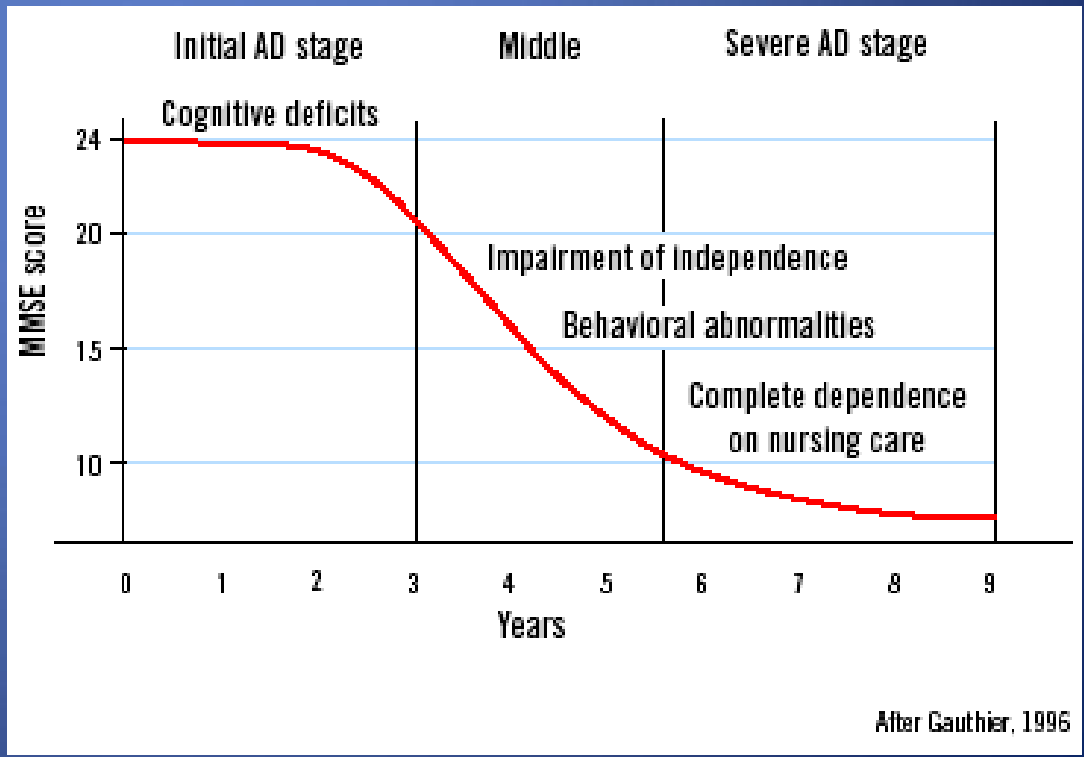
Meds to avoid or use with caution

- Anticholinergic medicines
  - Tolterodine (Detrol®)
  - Oxybutynin (Ditropan®)
  - Hyoscyamine (Levsin®, others)
  - Many others
- Medicines w/ anticholinergic side effects
  - Diphenhydramine (Benadryl®,Tylenol PM®)
  - Meclizine
  - Tricyclic antidepressants
  - Others

Role of meds in “end-stage” AD

- Generally have been tried and failed
- Concerns about “withdrawal deterioration”
  - The myth of “you don’t get back to where you were if stopped and restarted”

- Meds on hospice
  - CI’s
  - Memantine



Dementia types

- Alzheimer's disease
  - Memory deficit + another cognitive deficit
- Vascular dementia
  - Memory + another cognitive change d/t stroke(s)
- Mixed dementia
  - Combination of the above two etiologies
- Dementia with Lewy bodies
  - Social/occupational cognitive dysfunction
  - Visual hallucinations / fluctuating cognition (early) / Parkinson-like features (at least 2 of 3)
  - Parkinson's dementia
- Frontotemporal dementia
  - Behavioral / Affective / Speech disorders
- Others

Vascular dementia (VaD)

- Progressive worsening of memory and deficits in least one other area of cognition
  - Deficits of cognition, not just motor disability
- No disturbance of consciousness
- Cerebrovascular disease (CVD) evidence
- Relationship determined between cognitive changes and CVD

Roman GC, Tatemichi TK, Erkinjuntti T, et al. Vascular dementia: diagnostic criteria for research studies. Report of the NINDS-AIREN International Workshop. **Neurology**. 1993;43:250-260.

VaD treatment

- Stroke prevention
  - Aspirin or other similar agent
  - Hypertension control
  - Heart rhythm control
- Specific meds
  - Small benefit with donepezil
  - Minimal or no benefit with others
  - Data is very limited

Cochrane Reviews (*www.cochrane.org*)

- VaD is not automatically terminal

Dementia with Lewy bodies (DLB)

- Progressive cognitive decline interfering with social/occupational function
- Memory ↓ may not be apparent until late
- Two of the following are essential
  - Fluctuating cognition with variations in attention/alertness
  - Recurrent visual hallucinations
  - Spontaneous motor features of parkinsonism

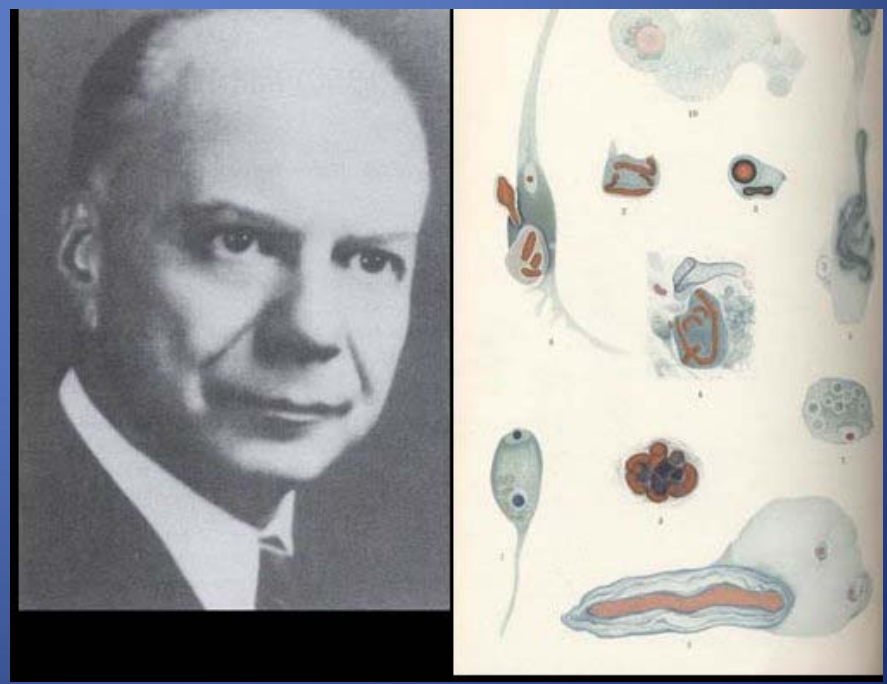
McKeith IG, Galasko D, Kosaka K, et al. Consensus guidelines for the clinical and pathologic diagnosis of dementia with Lewy bodies (DLB): report of the consortium on DLB international workshop. **Neurol**. 1996;47:1113-1124.

- Also includes Parkinson's dementia

Lewy Body Dementia Association (*www.lbda.org)*

DLB treatment

- Insufficient evidence to recommend
- Of prime importance
  - Avoid antipsychotics (especially “typicals”)



Dr. Friederich H Lewy and his first illustration of Lewy bodies

Contrasting AD vs. DLB

- Alzheimer's
  - Aphasia
  - Recall impaired
  - Recognition impaired
  - V/S deficits
  - Executive deficits = other impairments
  - Processing normal
  - No insight
- Lewy Body
  - Language preserved
  - Recall impaired
  - Recognition okay
  - V/S deficits – Early!
  - Executive deficits > other impairments
  - Slow processing
  - Mood & motor sx's

Course of DLB

- Similar progressively deteriorating trajectory
- May be more rapid than AD
  - Typical antipsychotics may greatly *speed* deterioration
- Loss of cognitive abilities is different than AD
- Think “late onset” Parkinson’s

Frontotemporal dementia
(a.k.a. Pick's disease)


Dr. Arnold Pick

- Behavioral disorder
- Affective symptoms
- Speech disorder
- Spatial orientation & praxis preserved
  - Intact abilities to negotiate environment
- Supportive features
  - Onset < 65
  - Positive family history

Clinical and neuropathological criteria for frontotemporal dementia. The Lund and Manchester Groups. **Jour Neurolog Neurosurg Psychiat.** 1994;57:416-418.

Other issues

- Agitation / Behavioral dyscontrol
- Nursing home placement
- End-stage dementia management
- So what does work?

Agitation

- Antipsychotics are commonly used
- There is evidence that antipsychotics will reduce aggression
  - Should not be used routinely for other manifestations of agitation

    Cochrane Reviews (*www.cochrane.org*)
- FDA Black Box Warning
  - Elderly patients with dementia-related psychosis treated with antipsychotic drugs are at an increased risk of death
- There is no high-quality evidence that any other therapy (pharmacologic or non-pharmacologic) is effective for agitation related to dementia

Medications for agitation

- **NOTHING** is approved for this
- **ALL** antipsychotics increase the risk of death when used for this
- If used:
  - Document informed consent
  - Attempt monotherapy
  - Take advantage of side-effect profile
  - Start low, go slow, but go!

Nursing home placement

- Dementia is the most common diagnosis resulting in LTCF placement
  - 66% of dementia pts die in LTCFs
- Decision for placement is very hard for caregivers
  - When pt's care requirements exceed the caregiver's ability to safely manage the pt
  - Early counseling about "promises"

End-stage dementia

- Neurocognitive
  - Meds don’t work any more
- Functional
  - Very limited
- Nutritional
  - Impaired
- Complications
  - So-called “secondary conditions”
  - Usual “cause” of death

This is the terminal stage

- Alzheimer's dz is 6th leading cause of death in the US
- Dysphagia
  - Malnutrition
  - Aspiration
- Actual *cause* of death
  - Pneumonia (aspiration)
  - Urosepsis
  - Failure to thrive
  - Decubiti-associated sepsis

Guidelines for hospice admission of end-stage Alzheimer's disease

- End-stage dementia
  - Non-verbal / Non-ambulatory / Dependent for all ADLs

AND

- A significant secondary condition or comorbidity
- With these criteria, average life-expectancy is < 6 months

So what does work?

ACOVE Quality Indicators

- Assessing Care Of Vulnerable Elders
  - A RAND Corporation project
    www.rand.org/health/projects/acove.html
- Validated indicators that when accomplished, improve:
  - Overall quality of life
  - Counseling of patient and family
  - Links to community agencies
  - Behavioral and cognitive symptoms

ACOVE QI for Dementia (1)

- Cognitive & functional screening whenever
  - Someone >75 yo is hospitalized
  - Someone >75 yo is new to a physician's practice
- Medication review
  - New dementia symptoms $\Rightarrow$ review meds for possible causes of cognitive decline & discontinue offenders, if at all possible
  - Avoid anticholinergic medications
- Laboratory testing
  - New dementia symptoms $\Rightarrow$ obtain B_{12} and TSH levels

ACOVE QI for Dementia (2)

- Neuroimaging
  - New dementia symptoms **and** focal neurologic findings ⇒ offer neuroimaging
- Cholinesterase inhibitors
  - Mild-moderate Alzheimer's disease ⇒ discuss CI's with patient and primary caregiver
- Caregiver support and patient safety
  - Caregivers of patients with dementia should be referred for discussion of: patient safety, how to deal with conflicts at home, and community resources (e.g. Alzheimer's Association)**

** QI most strongly associated with improved outcomes

ACOVE QI for Dementia (3)

- Screen for depression
  - For all dementia patients
  - Institute treatment if found
- Driving privileges
  - Evaluate (or refer for evaluation) to determine safety while driving
  - Recommend discontinuation if not safe (state laws vary)
- Memory loss
  - If someone fails a memory screen, then physician must document: memory assessment, or diagnose dementia, or explain memory loss, or refer the patient

ACOVE QI for Dementia (4)

- Restraints
  - If an agitated dementia patient is to be restrained in a hospital setting, informed consent must be obtained from patient's responsible party with discussion of risks and appropriate documentation of discussions
  - If restrained, attempt to identify and directly address cause of agitation that is causing need for restraint
  - If restrained, close in-person monitoring is required with attention to safety and patient's ADLs

ACOVE QI for Dementia (5)

- End-of-life care
  - All persons should have treatment preferences documented, preferably in the form of advance directives
  - If a patient with dementia is hospitalized, identify any advance directives and/or surrogate decision makers within 48 hours of admission and document in chart
  - Utilize any advance directives in determining treatment decisions affecting patients with moderate to severe dementia

Quick Case Scenario #1

- 55 yo male comes to your office with the following concern during a general checkup
- He states that he notices that when he enters a room, he sometimes cannot remember why he went into the room
- How do you reassure him?

ARS Question: Do you . . .

1. Tell him, “Nothing is wrong – don’t worry”
2. Diagnose him with Alzheimer’s disease
3. Order an MRI
4. Perform word generation list and Mini-Cog screens

Quick Case Scenario #2

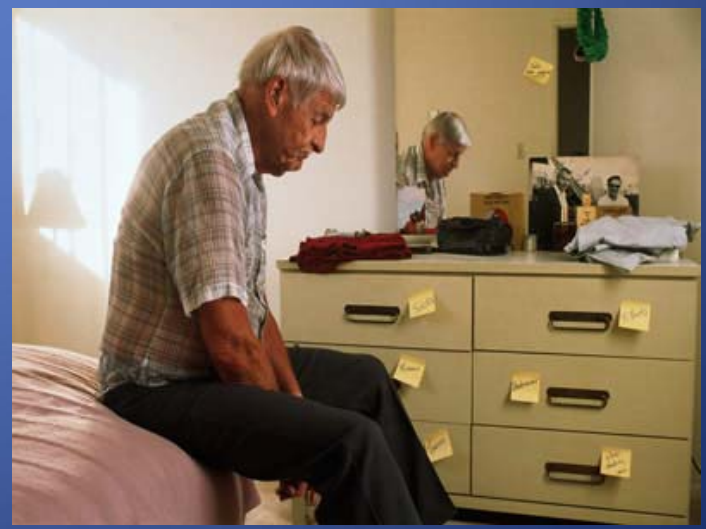
- 90 yo female presents for follow-up on her hypertension
- Your office staff hands you a note from her son just as you are about to enter the room
- He is concerned that she should not have her driver's license renewed, since she has become lost several times while driving lately
- How do you manage this?

ARS Question: Do you . . .

1. Cancel your next three appts so you can do a full neurologic evaluation
2. Explain to the pt that you automatically refer someone her age for a driving evaluation
3. Perform screening tests, explaining that you do this for anyone her age and presentation
4. Ignore the son's note & just treat her hypertension

Quick Case Scenario #3

- The daughter of one of your nursing home patients calls wanting to talk with you
- She is distressed by her father's behavior in the nursing home, but does not want him "drugged into submission"
- What do you say?



ARS Question: Do you . . .

1. Call the NH to determine pt's current status
2. Make a patient visit before calling her back
3. Inform her that medications are often needed to manage this
4. Have your office nurse call her to say "stop worrying so much"

Questions

Answers