Diagnosis and Treatment of Alzheimer’s Disease in Primary Care
Session 5: Diagnosis and Treatment of Alzheimer’s Disease in Primary Care

Learning Objectives

- Implement use of brief, practical, and office-based tools to enhance recognition of Alzheimer’s disease (AD) in primary care.
- Set realistic treatment expectations for patients and caregivers and provide counseling, education, and resource information to AD patients and their caregivers.

Faculty

Malaz Boustani, MD, MPH
Founder and Director of Research
Indianapolis Discovery Network for Dementia
Assistant Professor of Medicine
Indiana University School of Medicine
Indianapolis, Indiana
Scientist
Regenstrief Institute, Inc.
Indianapolis

Dr Boustani obtained his medical degree from Damascus University in Syria, finished the internal medicine residency program at Mt Sinai Medical Center, completed a geriatric research fellowship at the University of North Carolina, Chapel Hill, obtained a master’s of public health degree in healthcare and prevention, and completed a gero-informatics fellowship at Regenstrief Institute, Inc.

Dr Boustani’s research focuses on designing a system that accommodates the needs of older adults with acute and chronic cognitive disorders. As a Paul B. Beeson Physician Faculty Scholar in Aging Research, Dr Boustani is expanding his research to encompass the interface between information technology (IT) and healthcare delivery. He will help develop a dementia care system in which IT will translate clinical research discoveries into the daily delivery of care in ambulatory care, hospital care, long-term care, and community settings.

Dr Boustani has written multiple papers with significant policy implications (such as the United States Preventive Services Task Force guideline for dementia screening in the primary care setting), developed an innovative dementia care standard in long-term care, and successfully implemented a dementia management system in primary care.

David L. Sultzer, MD
Department of Psychiatry and Biobehavioral Sciences
David Geffen School of Medicine at the University of California, Los Angeles

Dr Sultzer received his medical degree from the University of North Carolina, Chapel Hill, and completed his residency training in psychiatry and fellowship training in neurobehavior at the University of California, Los Angeles (UCLA). He is a professor in the Department of Psychiatry and Biobehavioral Sciences at the David Geffen School of Medicine at UCLA. He directs the UCLA Geriatric Psychiatry Fellowship Training Program and the Gero/Neuropsychiatry Division at VA Greater Los Angeles Healthcare System.

Dr Sultzer is the principal investigator for several ongoing research projects with interests in AD and other cognitive disorders. He is recognized for his research to better understand the phenomenology, pathophysiology, and treatment of AD. Recently, he has used positron emission tomography (PET) imaging to elucidate the neurobiological mechanisms involved in medication treatment response in AD. He has completed clinical trials comparing the efficacy and adverse effects of medications for the treatment of psychosis and agitated behaviors in patients with dementia, and he is one of the few researchers to have examined the differential response of specific clinical symptoms to pharmacologic interventions.

Faculty Financial Disclosure Statements

The presenting faculty report the following:

Dr Boustani receives research support from Forest Pharmaceuticals, Inc. for being an investigator. He also receives research support from Pfizer Inc. for being an investigator and serves as a member of Pfizer’s speakers bureau.

Dr Sultzer receives research support from Forest Pharmaceuticals, Inc. and Pfizer Inc. for being an investigator. He also receives fees from Eli Lilly and Company and AstraZeneca Pharmaceuticals LP for being a consultant.
Educational Partner Financial Disclosure Statements
The content collaborators at Scienta Healthcare Education report the following:
Gabby Cruze, director of medical education, has nothing to disclose.
Jennifer Homan, program manager, has nothing to disclose.
Monique Johnson, MD, medical director, has nothing to disclose.
Sandra Manheimer, PhD, managing medical editor, has nothing to disclose.
Tracy Stewart, program director, has nothing to disclose.

Drug List

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<tr>
<td>donepezil</td>
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<td>galantamine</td>
<td>Razadyne</td>
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<td>galantamine ER</td>
<td>Razadyne ER</td>
<td>tacrine</td>
<td>Cognex</td>
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Note: Tacrine is approved by the US Food and Drug Administration for mild to moderate AD but is only mentioned for fair balance purposes. This drug is rarely used because of complex dosing regimens and hepatotoxicity.

Acronym List

AChEI: acetylcholinesterase inhibitor
AD: Alzheimer’s disease
ADL: activities of daily living
CDT: clock drawing test
ER: extended release
FAQ: functional activities questionnaire
MMSE: mini-mental status examination
ODT: oral disintegrating tablets
SIS: six-item screener

Suggested Reading List


Appendix A – AD Screening Tools

Six-Item Screener

- Measures 1- to 2-minute recall of 3 items
  - Year, month, day of week
- Takes 1 to 2 minutes to administer
- Can be administered face-to-face or via telephone
- Easily scored by a summation of errors
  - Range: 0 (lowest) to 6 (highest)
  - A score of 4 is similar to 25 or 26 on the MMSE

Mini-Cog

- Consists of 3-word recall and clock drawing test (CDT)
- Interpretation
  - Patient recalls 0 items → Patient is demented
  - Patient recalls 1 or 2 items and CDT is abnormal → Patient is demented
  - Patient recalls 1 or 2 items and CDT is normal → Patient is not demented
  - Patient recalls all 3 items → Patient is not demented

Clock-Drawing Test (CDT)

- Alzheimer’s Disease Cooperative Scoring System
  - 1 point for the clock circle
  - 1 point for all the numbers being in the correct order
  - 1 point for the numbers being in the proper spatial order
  - 1 point for the 2 hands of the clock
  - 1 point for the correct time
  - Normal score is 4 or 5 points

AD8

- Includes 8 questions
- Queries the informant about whether there has been a change in cognitive domains in the last several years
- Domains: judgment (handling finances, decision making), memory, (remembering appointments and repeats), temporal orientation, and function (use of appliances, reduction in interest in activity)
- Differentiates between demented and nondemented patients
- Is sensitive to early signs of cognitive change
- Correlates strongly with MMSE (inverse relationship)

Functional Activities Questionnaire

- This questionnaire asks the caregiver to rate the patient on level of performance with certain activities
- Each activity scored on a scale on which 0 = normal; 1 = has difficulty but does by self; 2 = requires assistance; 3 = dependent
• Tasks include writing checks/maintaining other financial records; assembling tax or business records; shopping alone; playing a game of skill; making coffee or tea and turning off stove; preparing a balanced meal; keeping track of current events; paying attention to and understanding a television program, book, or magazine; remembering appointments, family occasions, and medications; and traveling out of the neighborhood
• Higher scores indicate greater disability

Appendix B – RAPID-PC Cards

**RAPID-PC**

6 item screener for Cognitive Impairment *

I would like to ask you some questions that ask you to use your attention and concentration. I am going to name three objects. Please wait until I say all three words, then repeat them. Remember what they are because I am going to ask you to name them again in a few minutes. Please repeat these words for me:

APPLE — TABLE — PENNY

Did patient correctly repeat all three words? YES / NO

Incorrect / Correct

1. What year is this? 0 / 1
2. What month is this? 0 / 1
3. What is the day of the week? 0 / 1
4. What were the three objects I asked you to remember?

APPLE = 0 / 1
TABLE = 0 / 1
PENNY = 0 / 1

*If score is less than 6, further work up is recommended.*

*Ref: MedCare, 2002; 40:771-81.

**INDIANAPOLIS DISCOVERY NETWORK FOR DEMENTIA (IDND)**

Milaq Boustani, MD, MPH
cio Regenstrief Institute
Please do not copy without obtaining permission: mboustani@regenstrief.org

**RAPID-PC**

Recognizing and Assessing the Progression of Cognitive Impairment and Dementia in Primary Care

**Dementia Red Flags**

• Medication Adherence problems
• More than 7 prescribed medications
• Agitation
• Multiple falls in past year
• More than 2 hospitalizations/ER visits in past year
• Attending office visit with caregiver
• More than 2 missed appointments in past year
• DX of Diabetes + hypertension + CAD + hyperlipidemia
• History of CVA
• Taking more than 1 definite anticholinergic medication

Session 5
Appendix C – Algorithm: Approach to Evaluating a Patient With Cognitive Impairment

Appendix D – Algorithm: Approach to Screening for AD

Asymptomatic patient aged 65 or older based on patient’s, caregiver’s, or physician’s reports

Risk factor profiling:
- Age >75
- First-degree relative with dementia
- Head trauma
- Vascular risk factors: HTN, DM, hyperlipidemia, CVA/TIA

Reevaluate in 1 year

1 risk factor is present

Yes

At least 1 error on the Six-Item Screener

No

Yes

MMSE <24

Full diagnostic workup

Yes

Diagnosis and Treatment of Alzheimer Disease (AD) in Primary Care

Learning Objectives

At the conclusion of this CME activity, participants should be able to

- Implement use of brief, practical, and office-based tools to enhance recognition of AD in primary care
- Set realistic treatment expectations for patients and caregivers and provide counseling, education, and resource information to AD patients and their caregivers

Overview

- Diagnosing and Defining the Impact of AD
- Management Strategies

Diagnosing and Defining the Impact of AD

Malaz Boustani, MD, MPH
Founder and Director of Research
Indianapolis Discovery Network for Dementia
Assistant Professor of Medicine
Indiana University School of Medicine
Indianapolis, Indiana

Case: “My Wife Is Becoming More Forgetful”

- 76-year-old woman is brought into your office by her husband
  - She usually visits alone; today, her husband stops you to talk before you see her
- She became lost when separated while shopping downtown a few miles from their home
- Her husband is worried because she has been having memory problems
  - She has trouble learning new people’s names
  - She often forgets about meetings that she arranges herself
  - Her ability to speak well is declining, becoming vague and empty
- He is also worried because she already has 3 other chronic comorbid conditions and takes 7 different medications

Case: “My Wife Is Becoming More Forgetful”

- Initial inquiry reveals that her
  - Memory issues have been slowly progressing for >6 months
    - Husband has noticed that she has been forgetting names and repeating herself over the past 2 years
    - Husband has taken on many daily duties that she used to do, including handling the finances
    - Mother had a history of memory problems at an early age
    - Speech is not slurred
      - Answers are noticeably vague and circumlocutory
    - Overall physical health is stable
      - No known head injuries
      - No other obvious neurologic deficits
Is this patient showing signs of AD?
1. Yes, but AD is probably not the diagnosis. She has not been experiencing discrete symptoms for very long.
2. Possibly, based on her symptoms and her family history.
3. Very unlikely. This is part of normal aging.

Classification and Etiology of Various Dementias

- Reversible
  - No more than 1.5% of all dementia cases in memory clinics are fully reversed
- Irreversible
  - AD: 60% to 70%
    - Vascular or mixed: 20% to 30%
    - Other causes (eg, Lewy body dementia, frontotemporal dementia, etc)

Epidemiology of AD: Prevalence Is Increasing as Population Ages

- Prevalence
  - 1% to 2% at age 65
  - 35% or greater by age 85
  - Expected to quadruple in the next 50 years
- Most common form of dementia affecting the elderly in the US
- Median life expectancy after diagnosis
  - 6 to 12 years, with much variation
  - In 1 study, after adjustment for length bias: 3.3 to 9.3 years

Current Profile of AD Patients in the US

- Average comorbidity
  - Has 2.4 chronic medical conditions
    - Hypertension (HTN): 82%
    - Diabetes mellitus: 29%
    - Coronary artery disease (CAD): 21%
    - Chronic heart failure: 14%
    - Stroke: 10%
    - Is prescribed 5.1 medications
- Exposure to at least 1 medication with anticholinergic properties
  - Definite central activity: 22%
  - Possible central activity: 40%
  - Definite or possible general activity: 50%
- Exposure to at least 1 psychotropic medication
  - Antidepressant: 11%
  - Anxiolytic: 7%
  - Antipsychotic: 4%

AD in the Primary Care Office Setting

- Approximately 6% of people over age 65 have AD
- Most patients with AD live at home
- More than 60% of individuals with AD go undiagnosed in the primary care setting
  - Refers to the proportion of patients who did not receive a diagnosis of AD from the first physician seen

AD in the Nursing Home Setting

- Nursing home placement is a common, major event in the natural history of AD
- AD-type dementia is 1 of the primary indications for nursing home placement
  - As many as 75% to 90% of patients with AD-type dementia reportedly reside in long-term nursing homes before death

References:
Cognitive Decline

Dementia, Multiple Cognitive Deficits

Required Impairment

Gradual and continuing Decline from previous higher function, impaired occupational or social function

Memory impairment and at least 1 of the following:

- Aphasia
- Apraxia
- Agnosia
- Disturbed executive functioning

DSM-IV-TR Criteria

Criteria for Diagnosing AD


What Isn’t AD

- Other dementias due to:
  - Vascular disease (multiple types)
  - Parkinson’s disease
  - Space-occupying lesions (eg, tumor, hematoma)
  - Alcoholism or other substance abuse
  - Frontotemporal degeneration, eg Pick’s
  - Normal pressure hydrocephalus
  - Medication effects
  - Hypothyroidism
  - B12 deficiency
  - Creutzfeldt-Jakob disease
  - HIV infection
  - Neurosyphilis
  - Lewy body disease

- Usually easily distinguished from AD
  - History
  - Imaging
  - Blood tests

Classification of AD: 3 Stages

<table>
<thead>
<tr>
<th>Mild</th>
<th>Moderate</th>
<th>Severe</th>
</tr>
</thead>
<tbody>
<tr>
<td>May need reminders</td>
<td>Marked memory loss; some wandering</td>
<td>Severe confusion; little language</td>
</tr>
<tr>
<td>Daily routines difficult</td>
<td>Requires significant help with activities of daily living (ADL)</td>
<td>Loss of fundamental ADL; needs personal hands-on care</td>
</tr>
<tr>
<td>Difficulty with complex task (eg, managing finances)</td>
<td>Insomnia and delusions</td>
<td>May not recognize self or family; agitation, incontinence</td>
</tr>
</tbody>
</table>

Dementia: Differential Diagnosis

- Delirium
  - Often with abrupt onset
  - Symptoms fluctuate
  - Impaired attention
- Depression
- Mild cognitive impairment
- Psychotic disorders
- Medication-induced cognitive problems
- Sensory impairment
- Developmental disability/mental retardation
- Low literacy or education

Mild Cognitive Impairment—Amnestic Type (MCI-A)

- Presence of 1 or more subjective cognitive complaints
- Presence of objective deficit in 1 or more cognitive domain
- Preserved ADL
- Absence of dementia (ie, not meeting dementia criteria)
- Absence of delirium


Mini-Mental Status Exam (MMSE) Is a Useful Tool for Measuring Cognitive Function

- Brief, quantitative measure of global cognitive function
- Requires approximately 10 minutes to administer
- Tests for orientation, memory, language, and visual perception
- Maximum score of 30 points


Quick Tools for Clarifying Cognitive and Functional Deficits in the Busy Office

- Cognitive screening tools
  - Six-Item Screener (SIS) 1
  - Mini-Cog 2
  - Clock-Drawing Test (CDT) 3, 4

- Functional screening tools
  - AD 5
  - Functional Activities Questionnaire (FAQ) 6

Please see Appendix A for more information on these screening tools.


RAPID-PC Cards for Dementia Screening and Detection

RAPID-PC cards are available at the registration desk. A copy of this image appears in Appendix B.

Stepwise Approach to Evaluating a Patient With Cognitive Impairment


A copy of this image appears in Appendix C.

MDS-Cog: Items for Nursing Home Residents

<p>| | |</p>
<table>
<thead>
<tr>
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<tbody>
<tr>
<td>B2</td>
<td>Memory</td>
</tr>
<tr>
<td>B3</td>
<td>Memory/Recall Ability</td>
</tr>
<tr>
<td>B4</td>
<td>Cognitive Skills for Daily Decision Making</td>
</tr>
<tr>
<td>B5</td>
<td>Indicators of Delirium—Periodic Disordered Thinking/Awareness</td>
</tr>
<tr>
<td>C4</td>
<td>Making Self Understood</td>
</tr>
<tr>
<td>C6</td>
<td>Ability to Understand Others</td>
</tr>
</tbody>
</table>


Approach to Screening for AD


A copy of this image appears in Appendix D.

Medications With Central Anticholinergic Properties

- Use of agents with central anticholinergic properties in patients on an acetylcholinesterase inhibitor (AChEI) can result in pharmacologic antagonism
- Some agents that you don’t suspect to have anticholinergic effect can or do
  - Captopril
  - Codeine
  - Coumadin
  - Digoxin
  - Ipratropium bromide
  - Prednisone

Brain Imaging in AD

- MRI or CT
  - Absence of focal lesions
  - Absence of severe cerebrovascular disease
  - Atrophy, particularly temporal or parietal

Case: Patient Is Becoming More Forgetful

- Problems appear to be gradual and continuing, according to her husband
- Cognitive Decline: Has impaired functioning; impaired social functioning, not mentioned, but likely
- Required Impairment: Has impaired functioning; impaired social functioning, not mentioned, but likely
- Cognitive Decline: Gradual and continuing
- Problems appear to be gradual and continuing, according to her husband

Specific DSM-IV-TR Criteria

<table>
<thead>
<tr>
<th>Dementia, Multiple Cognitive Deficits</th>
<th>Patient</th>
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<tr>
<td>Memory impairment and at least one of the following: aphasia, agnosia, apraxia, or disturbed executive functioning</td>
<td>Has memory impairment, aphasia, no clear agnosia, no clear apraxia, has disturbed executive functioning</td>
</tr>
<tr>
<td>Required Impairment: Gradual from previous higher function, impaired occupational or social function; Has impaired functioning; impaired social functioning, not mentioned, but likely</td>
<td></td>
</tr>
<tr>
<td>Cognitive Decline: Gradual and continuing; Problems appear to be gradual and continuing, according to her husband</td>
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</tr>
</tbody>
</table>

Case: Confirmation and Staging of Dementia

- Cognition: MMSE score was 22
- Function: FAQ score was 12
- Behavior: Verbally abusive towards husband when corrected
- Imaging: MRI scan indicates generalized atrophy but no other conditions

What next step(s) would you take to care for this patient?

1. Consider pharmacologic therapy
2. Suggest regular exercise and nonpharmacologic interventions
3. Refer her husband to a support group
4. All of the above
5. None of the above
Patient and Family Expectations of Healthcare Providers in AD

- Recognition of the problem
- Clear diagnosis
- Compassionate communication
- Explicit plan of care
- Anticipatory guidance

ACP and AAFP Guidelines for Current Pharmacologic Treatment of AD

- Recommendation 1
  - Clinicians should base the decision of whether to initiate a trial of therapy with an AChEI or memantine on individualized assessment
- Recommendation 2
  - Clinicians should base the choice of pharmacologic agents on tolerability, adverse effect profile, ease of use, and cost
- Recommendation 3
  - There is an urgent need for further research on the clinical effectiveness of pharmacologic management of dementia

ACP and AAFP Guidelines: What Do They Mean?

- Recommendation 1
  - Not all patients with AD should be given pharmacologic therapy as treatment
  - Pharmacologic treatment may have a modest effect on stabilizing or slowing decline, which may not be useful for patients with advanced disease
- Recommendation 2
  - The ACP and AAFP do not mention efficacy as a criterion to use in choosing a pharmacotherapy
  - If used, the choice of therapy should depend on tolerability, side effect profile, ease of use, and cost

Clinically Important Improvements Versus Statistical Significance

- The ACP and AAFP Guideline Panel differentiated clinically important effects of therapy from statistical significance of results
  - ADAS-Cog scale: a change of 4 points or more defines a clinically important improvement for mild to moderate dementia
  - MMSE: a change of 3 points or more is considered clinically important
  - CIBIC-plus scale: any change in score is considered clinical improvement
  - Results depend on an individual physician’s perception
- These guidelines emphasize the importance of the statistical significance of data in the context of their clinical significance

Management Guidelines for Early AD

- Nonpharmacologic
  - Connect caregiver with support groups and resources
- Pharmacologic
  - Treatment with an AChEI—only medication approved for mild AD stage
- Reassess every 3 to 6 months
  - Cognitive ability, daily function, behavior
  - Comorbid medical conditions, depression, anxiety
  - Caregiver status

Case: 3-Month Follow-up

- Nonpharmacologic
  - Her husband has joined his local Alzheimer Association group
- Pharmacologic
  - Patient is taking an AChEI and is tolerating it well
- Assessment
  - No significant change in cognition or function is evident
    - Abusive verbal behavior towards husband has improved
  - No new medical updates
  - Husband reports that he is healthy and coping


If Pharmacotherapy Is Used, Long-term Treatment May Provide Better Outcomes

- Treatment may preserve patient’s abilities and delay adverse outcomes
  - Initiated early
  - Maintained long-term
- Treatment guidelines should be reviewed to
  - Address newer medications
  - Consider more recent outcomes of treatment

Comparison of FDA-Approved Agents for the Treatment of AD (conventional oral tablets)

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Donepezil</th>
<th>Galantamine</th>
<th>Rivastigmine</th>
<th>Memantine</th>
<th>Rivastigmine Transdermal</th>
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<td>Stage</td>
<td>Mild to moderate</td>
<td>Mild to moderate</td>
<td>Moderate</td>
<td>Mild to moderate</td>
<td>Mild to moderate</td>
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<tr>
<td>MOA(s)</td>
<td>AChe</td>
<td>AChe</td>
<td>NMDA receptor antagonist</td>
<td>AChe</td>
<td>AChe/BChe</td>
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<tr>
<td>Dose/Duration</td>
<td>2 to 4 steps</td>
<td>2 to 4 steps</td>
<td>4 steps</td>
<td>3 to 4 steps</td>
<td>2 steps</td>
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<td>Starting Dose</td>
<td>5 mg 1x daily</td>
<td>6 mg 1x daily</td>
<td>6 mg 1x daily</td>
<td>2 mg 1x daily</td>
<td>1.5 mg 2x daily</td>
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<tr>
<td>Max Dose</td>
<td>10 mg 2x daily</td>
<td>12 mg 1x daily</td>
<td>14 mg 1x daily</td>
<td>4 mg 2x daily</td>
<td>4.5 mg every 24 hrs</td>
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</table>

Tacrine is an FDA-approved therapy, but is rarely used because of QID dosing and hepatotoxicity. BuChEI = butyrylcholinesterase inhibitor.

Comparison of FDA-Approved Agents for the Treatment of AD (alternate dosing forms)

- Donepezil
  - Orally disintegrating tablet
- Galantamine
  - Extended-release capsules
  - Oral solution
- Rivastigmine
  - Transdermal patch
  - Oral solution

Safety and Tolerability: AChEIs

- GI complaints are the most frequent adverse events (AEs)
  - In 1 study of all AChEIs, 5.2% of patients discontinued treatment because of an adverse drug reaction over 9 months
- Use with caution in patients
  - With sinus bradycardia
  - With a recent GI bleed
  - Who are severely underweight

Response to AChEi Therapy: Cognition

- AChEi-treated (donepezil) patients were more likely than untreated patients to be stable
- Average period of improvement or no decline was 6 to 12 months
- The average change in cognitive score with donepezil was statistically significant but not clinically important
- Pooled data from AChEi-treated (galantamine) patients showed statistically significant cognitive improvement; however, these improvements did not reach the level of clinical importance
  - 3 studies suggested a subgroup of patients had some clinically important benefit from treatment

Safety and Tolerability: AChEIs

- Direct comparison studies
  - Fewer patients experience GI effects on donepezil than on oral rivastigmine
  - Slower dose titration is associated with fewer adverse effects
  - Donepezil
  - Rivastigmine
    - Rivastigmine transdermal has near-placebo levels of reported GI side effects

Response to AChEi Therapy: Cognition

- AChEi-treated (donepezil) patients were more likely than untreated patients to be stable
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  - 3 studies suggested a subgroup of patients had some clinically important benefit from treatment

References:

Response to AChEI Therapy:

**Cognition**
- ADAS-Cog data (shown) was statistically significant but did not show improvement in cognition clinically.
- Clinically important improvements were seen using CIBIC-plus data (not shown).

Rivastigmine (observed cases, ADAS-Cog)


Clinically important improvements were seen using CIBIC-plus data (not shown).

Response to AChEI Therapy:

**Daily Functioning**
- On average, treated patients maintained daily function for at least 1 year.
- A greater proportion of patients maintained function when treated (compared with those taking placebo).

Rivastigmine (observed cases, progressive deterioration scale)


Greater Proportion of Patients Maintain ADL Over 1 Year

Criteria-based definition of ADL preservation; intent-to-treat population.

Response to AChEI Therapy:

**Behavior**
- AChEIs may delay emergence of adverse behaviors.
- Meta-analysis showed modest beneficial impact of AChEIs on behavioral symptoms.
- Trials of AChEIs have had consistent—but small—positive effects on behavioral symptoms.


Managing Behavioral Symptoms in AD
- Behavioral interventions in all cases.
  - Patient: redirection, reassurance
  - Caregiver: education, support
  - Environment: safety, level of stimulation
- Consider pharmacotherapy: depression, anxiety, psychosis.
  - Evidence for modest efficacy
  - Off-label in all cases
  - Black-box warning for atypical antipsychotics.
Behavioral Responses in Mild-to-Moderate AD: Delayed Adverse Behaviors With Galantamine

<table>
<thead>
<tr>
<th>Dose Increments</th>
<th>Improvement</th>
<th>Deterioration</th>
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<tbody>
<tr>
<td>Placebo</td>
<td>Galantamine 12 mg/d</td>
<td>Galantamine 24 mg/d</td>
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<tr>
<td>* P &lt; .05 versus placebo (both doses).</td>
<td>* P &lt; .05 versus baseline.</td>
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NPI = neuropsychiatric inventory.

Adapted with permission from Tariot PN, Solomon PR, Morris JC, Kershaw P, Lilienfeld S, Ding C; and Galantamine USA-10 Study Group. A 5-month, randomized, placebo-controlled trial of galantamine in AD. Neurology. 2000;54(12):2269-2276.

Memantine

Cognition

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<tr>
<td>Placebo</td>
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ADL

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<td>Memantine 24 mg/d</td>
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<td>137</td>
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<tr>
<td>Placebo</td>
<td>136</td>
<td>136</td>
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Treatment Responses With an NMDA Receptor Antagonist: Moderate-to-Severe AD

Memantine


Memantine + donepezil


ACP and AAFP Guidelines:

Conclusions

- Interventions with FDA-approved drugs for dementia have provided statistically significant data
- Interpretation of the clinical importance of these data is challenging
- Evidence of improvement in cognition was, on average, not clinically significant
- Evidence of improvement on global assessment was modest on average
- No convincing evidence demonstrates that one therapeutic treatment is more effective than another
- The duration of trials in most cases was less than 1 year
- Limited, but inconclusive, evidence suggests that a subgroup of patients may achieve clinically important improvements
  - There is no current way to predict which patients may have a clinically important response


Future Treatments for AD

- Target specific pathophysiologic events
- Medications on the horizon
  - Prevent amyloid production
  - Foster amyloid clearance
  - Immunotherapy
  - Anti-inflammatory
  - Neuroprotection
  - Neuroregeneration

Nonpharmacologic Management Strategies

- Provide a predictable and prompted routine
- Maintain familiar possessions and clothes
- Simplify tasks
- Reduce stimulation and crowds
- Register in the Alzheimer’s Association Safe Return Program
  - http://www.alz.org/we_can_help_medicalert_safereturn.asp

Case: 1-Year Follow-up

- Her husband feels that she has been having more severe verbal and memory problems within the last few months
- She scored 20 on the MMSE and 14 on the FAQ
- She has no new health problems

To what might you attribute this drop in her abilities?
1. Stroke
2. Dementia progression
3. Parkinson disease
4. Depression
5. Old age

Role of the Caregiver in the Treatment of AD

- Caregivers help AD patients receive persistent therapy
- PCPs, NPs, and PAs can help forge a therapeutic alliance with caregiver and patient
- The health of an elderly caregiver, both physical and psychological, should be of concern to the treating healthcare professional
- Pharmacologic therapy may reduce caregiver burden, making caregivers more effective in helping patients

Coping Tips for Caregivers

- Educate themselves about AD
- Find sources of help for caregiver tasks
- Protect personal time for something they enjoy
- Try to find time to exercise, eat well, and sleep enough
- Use personal network of family and friends for support
- Seek respite care and services such as adult day care

A Team Approach

- Medical diagnosis or treatment plan consultation
  - Geriatric psychiatrist
  - Neuropsychologist
  - Geneticist
  - Neurologist
- Patient and caregiver assistance
  - Alzheimer’s Association: www.alz.org (800.272.3900)
  - Social work professional
  - Support groups, respite care
  - Legal/financial consultant
  - Educational materials
Summary

• Prevalence of AD is increasing
• Primary care providers need to be aware of presenting signs and symptoms of AD
• Several screening tests for AD exist that are quick and user-friendly
• It is important to use a team approach when caring for patients with AD

To Do List for Treating Patients With AD in Primary Care

• Talk with caregiver about support groups, counseling, respite care (refer to the local Alzheimer Association)
• Detect and modify vascular risk factors
• Decrease anticholinergic burden
• Enhance medication adherence
• Discuss driving and safety issues
• Start AChEIs, and/or memantine in patients for whom slowing of decline is an acceptable goal
• Consider aspirin therapy in patients with high vascular risk
• Detect and treat depression
• Detect and treat psychosis
• Detect and treat aggression

Summary

• Individually assess patients to ensure they receive proper therapy
• If pharmacotherapy is used for patients for whom slowing decline is an acceptable goal
  – Begin treatment with an AChEi for mild-to-moderate AD
  – Begin treatment as early in the course of the disease as possible
  – Add on therapy with memantine for moderate-to-severe AD
• Recognize that nonpharmacologic therapy is an important component of care
• Set realistic goals
• Recognize the crucial role of the caregiver and the importance of caregiver health

Faculty Members

• A special thanks to our faculty members for their help in creating this presentation
  – Dr David A. Smith
  – Dr Malaz Boustani
  – Dr Howard Fillit
  – Dr George Grossberg
  – Dr David Sultzer