The University of Toledo
Center for Successful Aging,
Department of Public Health & Preventive Medicine,
Center for Continuing Medical Education as well as
the Ohio Geriatric Medicine Society, (OGS) and the
Alzheimer’s Association, Northwest Ohio Chapter

Present the:

18TH ANNUAL
GERIATRIC MEDICINE SYMPOSIUM:
Dementia:
Update on Evaluation & Treatment

Friday, March 7, 2014
8:00 a.m. - 4:15 p.m.

Hilton Garden Inn
Perrysburg, Ohio
ACKNOWLEDGEMENT
We gratefully acknowledge the following Organizations for their support:

Please be sure to visit the exhibitor booths.
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Franciscan Care Center
Franciscan Living Communities
HCR ManorCare – Heartland Healthcare Centers
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Walker Funeral Home
A *special thanks* to the members of our planning committee listed below who contributed their time and effort to ensure the success of this program:

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DISCLOSURE PAGE

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None of our planning committee members have any financial interest or other relationships with any manufacturer of commercial products or service to disclose that would pose a conflict of interest with regards to the content of this activity.

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The presenters and the planners of this activity have declared that there is no conflict of interest to disclose. All speakers/presenters have signed a statement that says she/he will present information fairly and without bias. This activity is sponsored by the Ohio Geriatric Society. Approved Provider status does not imply endorsement by the provider, ANCC, OBN or ONA of any products displayed in conjunction with an activity.
This activity has been planned and implemented in accordance with the Essential Areas and Policies of the Accreditation Council for Continuing Medical Education through the joint sponsorship of The University of Toledo and the Ohio Geriatrics Society. The University of Toledo is accredited by the Accreditation Council for Continuing Medical Education (ACCME) to provide continuing medical education for physicians.

The University of Toledo designates this live activity for a maximum of 6.5 AMA PRA Category 1 Credit(s)™. Physicians should claim only credit commensurate with the extent of their participation in the activity.

This Live activity, 2014 Geriatric Medicine Symposium: Dementia: Update on Evaluation and Treatment, with the beginning date of 03/07/2014, has been reviewed and is acceptable for up to 6.50 Prescribed credits by the American Academy of Family Physicians. Physicians should claim only the credit commensurate with the extent of their participation in the activity.

The University of Toledo Medical Center is an approved provider of continuing education for pharmacists by the Ohio State Board of Pharmacy. This program has been designated for 0.6 CEU’s with identification number 036-142-14-001-L01. Each pharmacist should claim only those hours of credit that he/she actually spent in the educational activity.

The State of Ohio Counselor, Social Worker and Marriage & Family Therapist Board have approved this activity for 6.5 clock hours of Continuing Professional Education (CPE) for Counselor and Social Workers. Approval Number: MCS031402

The University of Toledo, Psychiatry Department is approved by the Ohio Psychological Association - MCE Program to offer continuing professional education with Provider No. 00P0-340967014. This program has been approved for 6.5 credit hours.

The State of Ohio Board of Executives of Long Term Services & Supports (BELTSS) has approved this program for 6 course hours with BELTSS# 045-C-14.

This program has been approved by the Ohio Physical Therapy Association (OPTA) for 6.5 hours. Approval Number: 14S0030.

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The University of Toledo, College of Nursing (OH-026 2-1-17) is an approved provider of continuing nursing education by the Ohio Nurses Association (OBN-001-91), an accredited approver by the American Nurses Credentialing Center’s Commission on Accreditation. 5.3 Contact Hours of Continuing Nursing Education will be awarded for successful completion. Successful completion requires the learner to: Attend 80% of the session and completion and submission of an evaluation tool.

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For information regarding The University of Toledo, CME Upcoming Events, be sure to visit our website:

cme.utoledo.edu

The UT CME Office is pleased to announce that we have received the ACCME "Accreditation with Commendation" good through 2016.
TO OBTAIN YOUR CME CREDIT

Your CME Program Evaluation and Certificate will be available on Tuesday, March 11, 2014

1. Go to cme.utoledo.edu. (Omit the www/http://)
2. Click on DIRECT LINK TO LOGIN
3. Login:
   Username: lastnamefirstname (no commas, no spaces)
   Password: zip code
   (Your password is your zip code unless you specified another password in your profile)

4. An online forms inbox will appear with your program evaluation to complete.
5. Complete your online evaluation; be sure to answer all questions.
6. Click the submit tab.
7. You will be directed to print your certificate.
18th Annual Geriatric Medicine Symposium:

Dementia: Update on Evaluation and Treatment

Friday, March 7, 2014
Hilton Garden Inn
Perrysburg, OH

7:30 am Registration & Continental Breakfast - View Exhibits

8:00-8:15 Welcome
Salli Bollin, LSW, MSW
Executive Director of the NWO Chapter Alzheimer’s Association

Moderator: Victoria Steiner, PhD

8:15-9:00 Differential Diagnosis of Dementia:
The New Criteria for Alzheimer’s Disease
Bruno Giordani, PhD

9:00-9:45 Screening for Dementia
Bruno Giordani, PhD

9:45-10:05 Panel Discussion

10:05-10:20 Break/View Exhibits

Moderator: Michelle Masterson, PT, PhD

10:20-11:05 Dementia-Delirium-Depressions:
Are The Differences Between the 3D’s Still Relevant?
Barbara J. Messinger Rapport, MD, PhD, FACP, CMD

11:05-11:50 Dementia Pharmacotherapy Update
Gayle Kamm, PharmD, BCPS

11:50-12:10 Panel Discussion

12:10-1:15 Lunch

Continue →
18th Annual Geriatric Medicine Symposium:
Dementia: Update on Evaluation and Treatment
Friday, March 7, 2014
Hilton Garden Inn
Perrysburg, OH

Moderator: Traci Holland, BSG

1:15-2:00   Musculoskeletal Conditions in People with Dementia
            Michelle Masterson, PT, PhD

2:00-2:45   Programming for Persons with Memory Loss and their Families
            Cheryl J. Conley, MA, LSW

2:45-3:00   Break/View Exhibits

3:00-3:45   Legal Implications of Dementia
            A. John McSweeny, JD, PhD, ABPP (CN)

3:45-4:15   Panel Discussion

4:15pm      Adjournment
Objectives:

1. Discuss the different characteristics, basic prevalence/incidence, caregiver costs of the basic dementia types (AD, FTD, DLB, and VaD).

2. Identify how these basic conditions differentiate from MCI and normal aging.
Differential Diagnosis of Dementia: The New Criteria for Alzheimer’s Disease

Bruno Giordani, PhD
Professor, Departments of Psychiatry, Neurology, and Psychology
Chief Psychologist, Department of Psychiatry
University of Michigan
Associate Director, Michigan Alzheimer’s Disease Center
Board Member, Alzheimer’s Association, MGL Chapter

DISCLOSURE OF FINANCIAL RELATIONSHIPS
I do not have any relevant financial relationships with any commercial interests related to this talk

(besides, my children have all my money)

What’s on the Agenda?
To understand the new criteria, we need a little background
• Why do we need to worry about Alzheimer’s?
• Where have we come in our understanding about Alzheimer’s in the past 100 or so years?
• Where are we in identification?
• How does all this play into the new criteria and where will this take us?
Silver Tsunami and the AD Epidemic

• Age is the biggest risk factor for Alzheimer's Disease (up to 50% of persons over age 85 have AD)
• 5.5 million Americans have AD, now
• 13 million will have AD by 2025
• 16 million will have AD by 2050

Life Expectancy and Longevity

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There is now a 50% chance a person will live to be 100 years of age

Our Changing Demographics

(US Census, 1960-2040)

Watch the percentage of baby boomers rise as a percentage of the population

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Growing Caseload
Estimated number of new cases of Alzheimer’s per year in the US

Source: Alzheimer’s Association

Understanding

National Alzheimer’s Disease Burden

• Every 69 seconds someone in America develops AD
• Total estimated health care costs now and later:
  – 2011: $183 billion, including more than $123 billion for Medicare and Medicaid
  – 2050: Estimates top well over $1 trillion

Source: Alzheimer’s Association, 2011 AD Facts & Figures
The Major Primary Dementias

- AD -- by far the most common among primary dementias* (50-70%)
- Vascular dementia (10-15%)
- Dementia with Lewy bodies (DLB) (10-20%)
- Frontotemporal lobar degeneration (FTLD, multiple subtypes) (5-10%)
- Parkinson’s dementia (3-4%)

Each dementia has its characteristic neuropathology

*Alzheimer’s Association Facts and Figures, 2009

Characteristic psychopathology leads to distinct clinical signs

Dementia: A Focused Review; Psychiatric Times

www.psychiatrictimes.com
Examination of Auguste D, 1901

When objects are shown to her, she does not remember after a short time which objects have been shown...

Asked to write Auguste D, she tries to write Mrs and forgets the rest...

She seems not to understand what she reads...

During physical examination... she suddenly says, “Just now a child called, is he there?”

AD diagnosis recognized just over 100 years ago
Treatments really only developed over last 20 years

AD research: just now hitting full speed...

Case of Auguste D described by Dr. Alzheimer’s
Kraepelin declares AD “presenile” dementia
Basic biology on plaques and tangles
Causative AD genes found
First symptomatic drugs
Prevention trials
Initial diagnostic criteria published
New diagnostic criteria published

WHAT WE LEARNED IN THE 70’S AND 80’S
Neuropathology of AD

Plaques and Tangles

At the end of the process we have cells that can no longer function and die.

“Amyloid Cascade” and Treatment

- Increased brain amyloid
- Amyloid deposition
- Inflammation, oxidation
- Tangle formation
- Loss of nerve cells and neurochemicals

Behavioral Change is observed

Current Treatments

Neuropathology of AD

http://www.binderlab.northwestern.edu/neuronalpathology.html

http://www.ahaf.org/alzdis/about/AmyloidPlaques.htm
WHAT ARE WE LEARNING NOW?

Symptomatic Treatment to Disease Modifying?

How Do We Meet the Need?

- The current diagnosis of Alzheimer’s relies largely on documenting mental decline, though we now know that Alzheimer’s has already caused severe brain damage before that decline is evident.
- How early can you identify someone at risk?
  - Researchers hope to discover an easy and accurate way to detect Alzheimer’s before these devastating symptoms begin.
- BIOMARKERS
  - Biological markers are benchmarks in the body that can be reliably measured to indicate the presence or absence of a disease or the likelihood of later developing a disease.

Protecting a healthy brain makes more sense than trying to fix a broken one.

Protecting a healthy brain makes more sense than trying to fix a broken one.

Cognitive Decline

Normal Aging | AD Pathology? | MCI

Ideal Prevention/Treatment Zone

Mild AD

Moderate

Severe

Time (Years)

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The Hunt is On!

- Medicine has successful biomarkers for other diseases
  - Blood glucose levels for diabetes
  - Blood cholesterol levels for heart disease
- A definitive test for the earliest changes in AD would help direct treatment research
- Some possibilities on the horizon
  - Neuropsychological Testing
    - New computerized approaches for change
  - Biochemical markers
    - Protein markers for amyloid and tau in CSF
  - Brain imaging studies
    - Structural: Magnetic resonance imaging (MRI)
    - Functional: Positron emission tomography (PET)
    - Molecular: Radiotracers to detect beta-amyloid PIB / Flute / 18F-AV-45 / Bay 94-9172

ADNI Private Partner Scientific Board:
- 20 companies/2 non-profits
- PIB/PET Supplement: Alzheimer’s Association and GE Healthcare
- Cerebrospinal Fluid Extension: Alzheimer’s Association, AstraZeneca, Cure Alzheimer’s Fund, Merck, Pfizer and an anonymous foundation
- Genome-Wide Genotyping: Gene Network Sciences, Merck, Pfizer and an anonymous foundation
- Genome-Wide Genotyping Genetic Analysis: NIBIB, Merck, Pfizer and an anonymous foundation

Alzheimer’s Disease Neuroimaging Initiative (ADNI) Naturalistic study of AD progression
- 200 NORMAL 4 yrs
- 400 MCI 4 yrs
- 200 AD 2 yrs
- Visits every 6 mos.
- 57 sites
- Clinical, blood, LP
- Cognitive Tests
- 1.5T MRI
- Some also have
  - 3.0T MRI (25%)
  - FDG-PET (50%)
  - PiB-PET (approx 100)

All data in public database: UCLA/LONI/ADNI
Spinal Fluid & Blood Tests

<table>
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<tr>
<th>Test</th>
<th>Alzheimer’s disease (n = 102)</th>
<th>Mild cognitive impairment (n = 200)</th>
<th>Cognitively normal (n = 114)</th>
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<td>High-tau protein</td>
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<tr>
<td>Elevated phosphorylated tau</td>
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Biomarkers

- Low beta-amyloid 1-42
- High-tau protein
- Elevated phosphorylated tau

Genetic modifiers suggest routes to understanding and treating AD

Apolipoprotein E (ApoE) is by far the major genetic risk factor, but still only a risk factor

*Genes identified in recent GWAS studies (published in Nature Genetics, 2009)

http://www.alzgene.org/
Researchers have developed compounds (PIB) that bind to amyloid and allow plaques to be “seen” with brain imaging.
Biochemical Biomarkers of AD

Elevations of Aβ seem more specific than alterations in tau
• Type 1
  – Biomarkers of Aβ accumulation
    • Abnormal tracer retention on amyloid PET imaging
    • Low CSF Aβ42
  – Biomarkers of neuronal degeneration or injury
    • Elevated CSF tau (total and phosphorylated)
    • Decreased fluorodeoxyglucose uptake on PET in temporoparietal cortex
    • Atrophy on structural magnetic resonance involving medial, basal, and lateral temporal lobes and medial and lateral parietal cortices

"Big Data" Projects for AD

• Global Alzheimer's Association Interactive Network (GAAIN)
• Massive data network of genome sequencing data (estimated to be 200 terabytes)
• Represents the largest cohort of whole genome sequences of individuals related to a single disease with more than 800 ADNI participants
• By being open access, GAAIN will transform how neuroscience data is shared and accessed by scientists throughout the world and thereby accelerate investigation and discovery
New Biomarkers

- Abnormal
- Normal

Cognitively normal
MCI
Dementia

Clinical disease stage


Primary prevention
- Delay onset of AD pathology
- Decrease Aβ production
- Prevent tau tangle formation

Secondary prevention
- Delay onset of cognitive impairment in individuals with evidence of pathology
- Decrease accumulated Aβ burden
- Delay neurodegeneration with anti-Aβ or neuroprotective agents

Tertiary prevention and treatment
- Delay onset or progression of dementia
- Neuroprotection prevent neuronal loss
- Enhance function of remaining neurons
- Neuron replacement replication

An integrative model that accounts for biomarker changes.
(modified image courtesy of Clifford Jack and Lancet Neurology)

And finally, where is dementia research taking us?

New and Critical Understanding

Longitudinal Follow-Up: 15 Months
(given time all gets more fascinating)
**“Amyloid Cascade” in Early Onset AD**

- Increased brain amyloid
  - Amyloid deposition
  - Inflammation, oxidation
  - Tangle formation
  - Loss of nerve cells and neurochemicals

---

**Risk Factors**

- **Environment**
  - Head injury, depression, female, presence of APOE e4 allele, chronic illness
- **Genetic**
  - Amyloid plaques, NFTs
  - Neuronal and synaptic dysfunction

**Alzheimer's pathology**

**Cognitive Decline**

**Alzheimer's Disease Diagnosis**

---

**U.S. Adult Population - % Obese (BMI >30)**

- 2010
- CDC

- No Data
- <10%
- 10%-14%
- 15%-19%
- 20%-24%
- 25%-29%
- ≥30%

---
HOW DO THE NEW CRITERIA TAKE ADVANTAGE OF ALL THIS NEW INFORMATION AND LEAD US ON TO THE FUTURE OF DIAGNOSIS AND TREATMENT?

The Road to the New Criteria

- Initial diagnostic criteria for Alzheimer’s published in 1984
  - Alzheimer's Association and the National Institute of Neurological and Communicative Disorders and Stroke
- Time to take stock and move on
  - Two years ago, the Alzheimer’s Association and the National Institute on Aging (NIA) called together three expert workgroups to review diagnostic criteria
  - Panels made up of researchers and clinicians from around the globe
  - Primary goal was to link new research findings with the diagnostic criteria
  - Viewpoints have continued to be refined
What Are the Big Differences?

- Now 3 stages
  - First stage now defined as before symptoms such as memory loss occur
  - Whereas, the original criteria required memory loss and a decline in other abilities severe enough to affect daily life
- Biomarkers are now incorporated into the criteria, whereas the original criteria was based chiefly on clinical judgment
- The new criteria speak to directions in research

Redefinition of AD to Include 3 Stages

2011

Stage 1: Preclinical Asymptomatic Stage
  Staging hypothesis for further research related to the use of biomarkers
Stage 2: Mild Cognitive Impairment (MCI)
  Clinical criteria and guidelines of how to relate MCI to AD after further ongoing research and validation of biomarkers
Stage 3: Dementia
  Based on NINDS/ADRDA and revised NIA/AA clinical criteria
1. Preclinical Alzheimer’s disease

- Measurable changes in biomarkers indicate the earliest signs of disease, before symptoms such as memory loss and poor orientation are noticeable.
- Consistent with current thinking that Alzheimer’s begins creating measurable changes in the brain years and maybe even decades before symptoms occur.
- No clinical diagnostic criteria is yet established, as right now this is basically a call for additional biomarker research to develop the ability to confirm this diagnosis.

2. Mild Cognitive Impairment (MCI)

- Mild changes in memory and thinking abilities that are noticeable to the person and to family members and friends and can be measured, but do not affect one’s ability to carry out everyday activities.
- Formalizes the diagnosis as a “transitional” phase of high risk for Alzheimer’s progression.
- Four levels of diagnostic certainty established:
  - Recommended for widespread clinical use
    - MCI—Core clinical criteria
  - Research-based criteria needing further study
    - MCI due to AD—Intermediate likelihood
    - MCI due to AD—High likelihood
    - MCI—Unlikely due to AD

Increasing the Utility of the MCI Diagnosis

- How should we standardize the definition of MCI?
  - Early MCI / Late MCI
  - aMCI / aMCI+ / non-aMCI
- What are the best tests to detect the earliest changes in memory or other cognitive areas?
- Which individuals with MCI will progress to Alzheimer’s disease or another dementia?
- What biological changes are associated with MCI?
3. Dementia Due to Alzheimer’s Disease

- Impairments in memory, thinking, and behavior decrease a person’s ability to function independently in everyday life
- Critical criteria established to diagnose dementia from all causes and specifically from Alzheimer’s disease
- Probable AD dementia with core clinical features
  - Probable AD with increased level of certainty
  - Probably AD with documented decline
  - Probably AD in a carrier of a causative AD genetic mutation
- Possible AD: Atypical course or etiology mixed presentation
- Probable AD with evidence of AD pathophysiological process
- Possible AD with evidence of AD pathophysiological process
- Pathophysiologically proved AD dementia
- Dementia unlikely to be due to AD
- Expectation is that in the future, biomarker evidence may provide additional diagnostic certainty

Criteria for All-Cause Dementia

- Symptoms interfere with ability to function at work or at usual activities
- Symptoms represent a decline from previous levels of functioning and performing
- Symptoms not explained by delirium or major psychiatric disorder
- Cognitive Impairment detected with history-taking from patient and informant and objective cognitive assessment
- Cognitive and behavioral impairment involves minimum of two of the following
  1. Acquire & remember new info
  2. Impaired language
  3. Impaired reasoning/judgment
  4. Visuospatial impairments
  5. Changes in behavior/personality

Goals for Adoption of the New Criteria

- These criteria reinforce the consensus that treating the disease before symptoms occur is the best way to ensure that people will live long, healthy lives free of disability caused by Alzheimer’s
- No generally accepted way yet exists to identify Alzheimer’s at its presymptomatic – and potentially most treatable – stage
- These criteria emphasize the clear importance of increasing research participation
  - Visit www.alz.org/trialmatch
  - Call 1-800-272-3900

Alzheimer’s Association, 2012
**What Does All This Mean Today?**

- **Clinicians**
  - New criteria and guidelines are not a call for immediate preclinical diagnosis of Alzheimer’s disease.
  - Preclinical Alzheimer’s disease is intended for research purposes only.
  - The guidelines do emphasize that MCI due to Alzheimer’s disease can be distinguished from other causes.
  - The guidelines for dementia due to Alzheimer’s disease have been clarified and propose the biomarkers can be used to increase certainty of the diagnosis.

- **Researchers**
  - New guidelines are now offered to test experimental approaches for detecting disease.
  - Emphasis on biomarker research to develop the necessary techniques to identify individuals at increased risk of developing Alzheimer’s – those persons best suited for studies of new Alzheimer’s treatments.
  - These approaches can decrease length and cost of studies and speed research discoveries.

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Alzheimer’s Association, 2012

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**What Does This Mean for Treatment Strategies?**

<table>
<thead>
<tr>
<th>Ideal time for Intervention – Prevention</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal Aging</td>
</tr>
<tr>
<td>Cure</td>
</tr>
<tr>
<td>Arrest Progression</td>
</tr>
<tr>
<td>AD Natural Course</td>
</tr>
<tr>
<td>Symptomatic Therapy (NOW)</td>
</tr>
</tbody>
</table>

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**There Are Two Types of Alzheimer's Treatment Trials**

- **Treatments aimed at reducing symptoms**
  - Test new drugs and variations of existing drugs that aim to reduce the symptoms of Alzheimer’s disease.
  - Studies of existing drugs explore whether changing the dose, taking the medication on a different schedule (more or less often), or combining it with other medications might further reduce or delay symptoms.

- **Treatments aimed at slowing or stopping the disease**
  - Test new drugs designed to slow or stop Alzheimer’s disease.

- Now we can concentrate these disease altering trials.
Disrupt Amyloid formation: Secretase Inhibitors

Remove Amyloid: Soluble form and plaque

Disrupt Tau Hyperphosphorylation

New Approaches to Clinical Trials:
Presymptomatic Treatment Trials

- Anti-Amyloid Treatment of Asymptomatic Alzheimer's Disease (A4) trial of a monoclonal antibody in clinically normal older adults (over age 65) with PiB amyloid biomarker AD evidence
- Alzheimer's Prevention Initiative (API) with monoclonal antibody crenezumab in cognitively normal persons at highest risk for AD from kindred near Medellin, Columbia, affected by genetically-caused early onset AD
- Dominantly Inherited Alzheimer Network Therapeutic Trial Unit (DIAN-TTU) in persons with dominantly inherited risk using three different compounds in the first year
- TOMMORROW delay onset of MCI in healthy individuals at increased risk due to being older and being carriers of APOE4 and TOMM40 using low dose pioglitazone

Other Approaches/Combinations

- Tau protein
  - Chief component of tangles, the other hallmark brain abnormality
  - Researchers are investigating strategies to keep tau molecules from collapsing and twisting into tangles, a process that destroys a vital cell transport system
- Inflammation
  - Another key Alzheimer's brain abnormality
  - Scientists have learned a great deal about molecules involved in the body's overall inflammatory response and are working to better understand specific aspects of inflammation most active in the brain
- Insulin resistance
  - This and the way brain cells process insulin may be linked to AD
  - Researchers are exploring the role of insulin in the brain and how brain cells use sugar and produce energy
Stay Connected. Visit us!
http://alzheimers.med.umich.edu/

Alzheimer's Disease Center
Dementia Care - Research - Education

U-M Memory Connection Line: (734) 936-8803
www.med.umich.edu/alzheimers

www.alz.org/TrialMatch
The compassion to care, the leadership to conquer:
A World Without Alzheimer's
Screening for Dementia
Bruno Giordani, PhD

Objectives:

1. Discuss the differences in goals and techniques for assessment and screening in dementia care, special case of MCI and why this is now critical for new intervention/prevention models.

2. Describe the differences in knowledge base for assessment and screening techniques.

3. Identify basic explanations and pros/cons for different screening and assessment instruments in terms of validity/reliability and ease of use and appropriate settings.
Screening For Dementia

Bruno Giordani, PhD
Professor, Departments of Psychiatry, Neurology, and Psychology
Chief Psychologist, Department of Psychiatry
University of Michigan
Associate Director, Michigan Alzheimer’s Disease Center
Board Member, Alzheimer’s Association, MGL Chapter

What’s On the Agenda?

• To screen or not to screen………
• Types of clinic-based screening
• Issues in choosing screeners
• What to do after you screen
• Novel approaches to screening
• When is a duck not a duck – when is screening not sufficient

How Prevalent is AD in Clinical Practice?

• Sixth leading cause of death in the US
• Increasing age is greatest risk factor
• Alzheimer’s is the primary cause of dementia in persons over 65 years of age
  – 3% to 11% of persons older than 65
  – 25% to 47% of those older than 85
• Affects more than 5 million individuals in the US and more than 16 million worldwide
• By 2040, AD will affect 14 million in US, alone
Burden of AD

- Patients
  - Increased dependency
  - Complicates other comorbid conditions
- Families
  - Anxiety, depression
  - Increased, unpaid time spent in caring for a loved one
- Annual societal cost of dementia
  - Over $100 billion (healthcare and lost wages)

Comprehensive Evaluation Approaches

- Structural Neuroimaging
  - MTL atrophy & amyloid ligand PET imaging
- Functional Neuroimaging
  - fMRI, MRS, SPECT, PET
- Genomics
  - Presenilin-1, APP mutations, + genotyping
- Blood and CSF fluid assays
  - proteomics, transcriptomics, and metabolomics
- Neuropsychological Testing
  - Direct assessment & informant based testing
- These approaches can be expensive and not readily available in all areas; screening represents one way establishing the need for these approaches

To Screen or Not to Screen…..

That is the Question…………

“It is important to recognize the difference between a valuable research technique and a useful clinical study. A new technique can sometimes help us understand the pathophysiology of a disorder or see the relationship of one condition to another, yet fail to provide reliable, practical information that warrants widespread clinical application.” (Raoch, 2006)

“If there was treatment for AD, I'd recommend screening, but there is no disease-modifying therapy.”
Anonymous Alzheimer expert -2008
Myth: Most people don’t want to know if they have AD  

Fact: Most Americans want advanced notice  

National Surveys of Adults  

Terry R. Barclay, PhD, HealthPartners Neuropsychology  

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**Is Dementia Recognized?**  
- Clinicians using routine history and physical exams do not readily diagnose dementia during clinic visits  
- >50% of persons with dementia, including many with mild, but also moderate and severe dementia, have no documentation of dementia diagnosis  
- >90% of mildly impaired patients are unrecognized  
- Screening tests could identify persons with undiagnosed dementia and thereby permit patients and families to receive care at an earlier stage of disease progress

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**Screening for Cognitive Impairment**  
- No cognitive screening test is diagnostic  
- If normal, serious conditions are less likely  
- The “worried well” can be relieved that they were “tested” and they did fine, but there should be special attention to subjective memory complaints (SMC)  
- Serial screening should be considered over time  
- If abnormal, further evaluation may be considered
Why Don’t General Practitioners Screen?

- Only 24% - 39% of doctors routinely screen for dementia using any recognized method
- Most physicians are familiar with standard dementia screens
- Reasons given for not using screening tests:
  - Takes too much time
  - Too expensive
  - Too difficult to interpret
  - Not believed to be effective
  - Would be threatening to the patient
- 93% of physicians did say they would use a brief and simple instrument if effective

Bush et al., 1997

Barriers to Early Detection of AD

- Patients/caregivers often unaware, deny or minimize symptoms
- Evaluation may be time-consuming and not well reimbursed
- Belief that memory loss and cognitive decline are expected with normal aging
- Belief that treatments not really effective

Complications to Screening

- Diagnosis requires objective evidence of a memory impairment, but not quantitative evidence of a decline
  - Memory impairments in older people can be static and not related to any neurodegenerative disease process
  - Novelty of the testing situation can lower results
  - Mood disorder or other symptoms can interfere
  - Effects of education or premorbid intellectual levels
    - High functioning individuals may decline just to “normal” levels
    - Lower premorbid IQ persons may start out lower in accuracy/speed
  - Accuracy of screening techniques can be questioned
  - Instruments may not be sensitive to the earliest symptoms of AD or pre-AD conditions
If Instruments Exist, Why Not Use Them?

- Under-diagnosis is clearly evident
- Under-treatment is prevalent (< 25%), even if treatments are now only moderately effective
- Early diagnosis offers advantages
  - Timely education of caregivers and family members with correct prognosis
  - Early intervention through control of risk factors
  - Amelioration of behavioral problems and avoidance of “crisis healthcare”
  - Proper planning of care programs and financial issues with proactive strategies while patients are capable of participating results in more consistent and motivated participation
  - Accelerate translation of research advances into actual practice
  - Treatment of comorbidities or reversible conditions
  - Promote safety in driving, cooking, etc.
  - Availability of new clinical trials

Feedback for Screening Results

- Positive Results
  - Discuss need for further evaluations
  - Assure positive screen does not mean AD, simply need for more careful follow-up assessment
- Negative Results
  - Opportunity to reassure patient that although they may experience cognitive changes, these appear more consistent with normal changes with age
  - Discuss that this does not guarantee dementia is not present

Common Cognitive/Behavioral Screening Approaches in Primary Care

- Direct Screening
  - Clinician Administered Short Instruments
  - Reasonably short, but many with reasonable sensitivity and specificity if used judiciously
- Informant Screening
  - Questionnaires to Patient/Informant (ADLs, IADLs)
  - Can be as effective as direct screening, better in combination with direct screening
- Computer-based assessments
  - Many products are becoming available, but data still not available on validity and reliability when used alone
- Remote Screening
  - Telephone screening holds some promise
  - E-mail and mail approaches not generally successful
Criteria for Judging New Screening Tests

The ideal screening test will have high sensitivity and high specificity

- Be able to detect fundamental features of MCI
- Demonstrate validity through cases with later neuropathological confirmation
- At least 2 independent studies to determine sensitivity, specificity, and predictive values
- Sensitivity and specificity reach at least 80% and positive predictive value approaches 90%
- Precise (able to detect MCI early and distinguish it from other conditions)
- Reliable (including alternate form statistics)
- Noninvasive and short administration time
- Simple to perform
- Inexpensive and readily available on different platforms
- Clear separation between normal and abnormal

Informant-Completed Screening Instruments

<table>
<thead>
<tr>
<th>Instrument</th>
<th>Sensitivity</th>
<th>Specificity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Informant Questionnaire on Cognitive Decline (IQCODE)</td>
<td>80-90%</td>
<td>80-90%</td>
</tr>
<tr>
<td>AD Caregiver Questionnaire</td>
<td>80-90%</td>
<td>80-90%</td>
</tr>
<tr>
<td>Symptoms of Dementia Screen</td>
<td>80-90%</td>
<td>80-90%</td>
</tr>
<tr>
<td>AD 8</td>
<td>&gt; 84%</td>
<td>&gt; 80%</td>
</tr>
</tbody>
</table>

Sensitivity = Proportion of AD cases correctly identified
Specificity = Proportion of healthy correctly identified

Solomon & Murphy, 2005

Short Clinician-Administered AD Screeners

<table>
<thead>
<tr>
<th>Instrument</th>
<th>Time</th>
<th>Sensitivity</th>
<th>Specificity</th>
</tr>
</thead>
<tbody>
<tr>
<td>MMSE</td>
<td>5-10 min</td>
<td>78%</td>
<td>84%</td>
</tr>
<tr>
<td>7-Min Screen</td>
<td>5-10 min</td>
<td>92%</td>
<td>96%</td>
</tr>
<tr>
<td>Time &amp; Change</td>
<td>&lt; 5 min</td>
<td>&lt; 80%</td>
<td>80-90%</td>
</tr>
<tr>
<td>MIS</td>
<td>&lt; 5 min</td>
<td>&gt;90%</td>
<td>80-90%</td>
</tr>
<tr>
<td>Clock Drawing</td>
<td>3 min</td>
<td>83%</td>
<td>72%</td>
</tr>
<tr>
<td>Mini-Cog</td>
<td>&lt; 5 min</td>
<td>76%</td>
<td>89%</td>
</tr>
<tr>
<td>MoCA</td>
<td>10 min</td>
<td>100%</td>
<td>87%</td>
</tr>
<tr>
<td>ACE-R</td>
<td>15 - 20 min</td>
<td>94%</td>
<td>89%</td>
</tr>
</tbody>
</table>

Solomon & Murphy, 2005; Mioshi et al., 2006
7 Minute Screen

SCORING SUMMARY

<table>
<thead>
<tr>
<th>TEST</th>
<th>RANGE</th>
<th>SCORE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Orientation</td>
<td>113-0*</td>
<td></td>
</tr>
<tr>
<td>Memory Test</td>
<td>0-16*</td>
<td></td>
</tr>
<tr>
<td>Visuospatial (Clock Drawing)</td>
<td>0-7</td>
<td></td>
</tr>
<tr>
<td>Verbal Fluency (Animals)</td>
<td>0-45*</td>
<td></td>
</tr>
</tbody>
</table>

* = Perfect Score
Please enter these scores in the calculator to find your patient's probability rating.

MMSE

MoCA
Special Case:
Self-Administered
SAGE

Sensitivity: 95%
Specificity: 79%
10 – 15 mins.

Scharre et al. Alzheimer Dis Assoc Disord 2009

Natural History of AD

Importance of Early MCI Diagnosis

- Decreases hospital admissions or emergency room visits
- Improves quality of life of patient and caregiver
- Reduces burden and chronic stress effects on caregivers
- Current AD meds work better if started earlier
- Disease modifying agents are coming
- Preventing or delaying AD with both pharmacological and non-pharmacological treatment approaches could save billions of dollars
### MCI Screener Comparison

<table>
<thead>
<tr>
<th>Test</th>
<th>Cut-Offs</th>
<th>Sensitivity</th>
<th>Specificity</th>
</tr>
</thead>
<tbody>
<tr>
<td>MMSE</td>
<td>&lt; 29</td>
<td>77%</td>
<td>81%</td>
</tr>
<tr>
<td>ACE-R</td>
<td>&lt; 94</td>
<td>83%</td>
<td>73%</td>
</tr>
<tr>
<td>MoCA</td>
<td>&lt; 25</td>
<td>77%</td>
<td>83%</td>
</tr>
</tbody>
</table>

Results not as clear as for dementia, but are important in knowing when to refer for a more comprehensive neuropsychological examination.

Pendlebury et al., 2011

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### Screening: Clinical vs. Clinical Trials

<table>
<thead>
<tr>
<th>Original Criteria (AAMI)</th>
<th>Revised Original Criteria (MCI)</th>
<th>Current Criteria (MCI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Immediate recall impairment on two verbal paragraphs and a word list task OR impairment in immediate visual learning</td>
<td>• Delayed recall impairment in a single paragraph OR a word list task</td>
<td>• Delayed recall impairment in a single paragraph</td>
</tr>
<tr>
<td>• No specific age or education adjustment</td>
<td>• Age adjusted</td>
<td>• Education adjusted</td>
</tr>
<tr>
<td>• 10 minutes</td>
<td>• 6 minutes</td>
<td>• 2 minutes</td>
</tr>
</tbody>
</table>

Trade-offs: What Is Success?

Comparison to the “gold standard” consensus conference

<table>
<thead>
<tr>
<th>Criteria</th>
<th>Chi-Square</th>
<th>Sensitivity</th>
<th>Specificity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Original</td>
<td>$\chi^2 = 40.80, \ p &lt; .0001$, Table 1</td>
<td>96%</td>
<td>40%</td>
</tr>
<tr>
<td>Revised Original</td>
<td>$\chi^2 = 46.80, \ p &lt; .0001$, Table 2</td>
<td>45%</td>
<td>100%</td>
</tr>
<tr>
<td>Current</td>
<td>$\chi^2 = 9.02, \ p = .003$, Table 3</td>
<td>29%</td>
<td>89%</td>
</tr>
</tbody>
</table>
**By the Numbers: Criteria Make a Difference and So Does Your Goal**

In an MCI trial, do you want to identify MCI or healthy controls at a high success rate?

<table>
<thead>
<tr>
<th>Table 1. Original Criteria Chi-Square Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Consensus Diagnosis</td>
</tr>
<tr>
<td>Control</td>
</tr>
<tr>
<td>Original Criteria</td>
</tr>
<tr>
<td>Control</td>
</tr>
<tr>
<td>MCI</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Table 2. Revised Original Criteria Chi-Square Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Consensus Diagnosis</td>
</tr>
<tr>
<td>Control</td>
</tr>
<tr>
<td>Revised</td>
</tr>
<tr>
<td>Original Criteria</td>
</tr>
<tr>
<td>MCI</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Table 3. Current Criteria Chi-Square Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Consensus Diagnosis</td>
</tr>
<tr>
<td>Control</td>
</tr>
<tr>
<td>Current Criteria</td>
</tr>
<tr>
<td>Control</td>
</tr>
<tr>
<td>MCI</td>
</tr>
</tbody>
</table>

**Annual Wellness Visit: Medicare**

- Took effect January 1, 2011
- Affordable Care Act
  - Medicare will cover an annual wellness visit which will include the creation of a personalized prevention plan
  - For first time, “detection of cognitive impairment” is core feature of the exam
- However, no clear guidance regarding:
  - What screening tools to use
  - What to do if patient fails screening
- Also, there may be no time to screen everyone

**Age-Based Screening Recommendations**

<table>
<thead>
<tr>
<th>Age Range</th>
<th>Prevalence</th>
<th>Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>65 – 74</td>
<td>3%</td>
<td>Discretionary, based on risk factors (e.g., family history, complaint)</td>
</tr>
<tr>
<td>75 – 84</td>
<td>19%</td>
<td>Every 2 years or earlier if complaints appear</td>
</tr>
<tr>
<td>&gt; 85</td>
<td>47%</td>
<td>Annually</td>
</tr>
</tbody>
</table>

*Solomon & Murphy, 2005*
**2 M’s & 2 T’s to Trigger a Screen**

- IADL concerns from patient or family member that call for a more careful screening in everyday practice with older individuals
  - Medication management
  - Money/financial management
  - Telephone management
  - Transportation management

**Staged Screening Approach for Cognitive Impairment**

- One single test or score should not be the only criteria to embark on an expensive dementia evaluation
- Doing a screening process in stages may provide better evidence for diagnosis of MCI or dementia
- A staged screening process is recommended

**Staged Screening Approach**

1. Age over 65?
   - Yes
     - Schedule appointment with patient and informant
     - AD8 < 2
       - Re-screen yearly
     - MOCA > 25
       - Re-screen in 2 years
   - No
     - Screen if concerns
     - SAGE Test
       - < 17
         - Yes
           - Consider dementia evaluation
         - No
           - Re-screen yearly
       - 17-22
         - Yes
           - Re-screen in one year or consider neuropsychological testing
You Can ACT Now to Improve Care

We all need to understand the components of quality care for people with Alzheimer’s disease and other related dementias. This includes:

- Early disease detection
- Use of recommended practice tools
- Continuity education about the disease

www.actonalzheimers.org

Provider Practice Tools

• Medicare Annual Wellness Visit Algorithm for Assessment of Cognition
• Cognitive assessment examples
• Family/observer rating forms examples

ALZHEIMER’S ASSOCIATION
Medicare Annual Wellness Visit Algorithm for Assessment of Cognition

A. Review WA, clinical observation, self-reported concerns, responses to queries

B. Conduct brief structured assessment
- Patient assessment: MMSE or shortened MMSE
- Informal assessment of patient: short-10 or AD8 or PSCS

C. Rule of thumb: Conduct full dementia evaluation
Empirical Model: Dementia Risk Calculator

- In primary care settings help clinicians determine which older patients should be further screened
- Based on four large cohort studies (CHS, FHS, HRS, SALSA)
- Scores ≥ 22 identified 65-79 year-olds whose 6-year dementia risk comparable to 80-84 year-olds

HRS 6-Year Dementia Incidence by Age and Dementia Risk Group

Innovations in MCI Screening

- Multiple & longitudinal assessments
- Attention to statistical modeling
- Multiple cognitive assessment areas
- Multiple domains and techniques of assessment
- Use of computerized and web-based cognitive/behavioral assessments
Issues with Traditional Single Time Point Screening

- Memory impairments can be static, rather than progressive in elderly
- Unfamiliarity with the testing situation may lead to lowered performance
- Mood disturbance (e.g., depression, anxiety) may increase during testing and/or confound test results
- Other symptoms may interfere with testing
- Large variability in memory test performance is seen in healthy older persons across assessments
- High functioning persons may decline just to normal
- Test-retest reliability may outweigh task-specific impairments

Why Consider Rate of Decline?

- Progressive cognitive decline is the hallmark of AD
- Decline model consistent with common clinical practice
- Improved sensitivity for detecting change from normal
  - Using a person as their own control avoids issues with comparisons to variable, hard to match normative data to register impairment
  - Reduces reliance on artificial single time point cut-scores that can be affected by mood, fatigue, or other factors
  - Can usually be done with fewer measures to avoid burden and increase motivation
  - Rate of decline can be calculated over time even if overall scores remain within healthy population limits
  - Can help account for practice effects and missing data
  - Allows for use of sophisticated slope fitting and other longitudinal statistics to assess true change

Verbal Meaning Test and Age

Ken Wilson, University of Liverpool
Differentiation of MCI and controls was not possible on the first assessment, but became significant at the third and fourth testing times (Collie et al., 2001)
Attention to Multiple Cognitive Assessment Areas

• Refining episodic memory assessment
  – Tests sensitive to semantic knowledge
  • e.g., story recall, semantic cueding, category fluency

• Recognition of differential patterns of cognitive decline
  – Importance of tests targeting varied hippocampal functioning
  – Importance of tests targeting executive dysfunction
  – Importance of throughput (accuracy/speed trade-off)

• Careful consideration of age, education, and premorbid functioning

• Developing appropriate IADL measurements

Clinical Outcome in IMI patients

Paragraph delayed recall, hippocampal volume, and “time to walk 30 feet” contributed independently to prediction of time to onset of questionable dementia (Marquis et al., 2002)
Can Come to a Community Near You

High-performance, fully automated ERP systems are now available

• Advanced Active Electrodes
  – Can be used in a clinical setting
  – Shielding issues no longer a drawback
  – Self-enclosed, water-soluble gel electrodes

• Wireless and Battery-powered
  – Extreme portability

• Internet-enabled with Online Database
  – Centralized storage of all patient and test data

• Standardized Protocols for data acquisition/analysis
  – Allows comparisons to normalize results

• Automated Analysis
  Allows repeat evaluation of test results

COGNITION™ System

Benefits of MCI Screening with Computers

• Easy to use and validated for use with older individuals and error-free scoring
• Game-like presentation reduces anxiety and increases motivation
• Allow for longitudinal assessments to characterize change
• Allow consideration of demographic factors
• Appear effective in distinguishing those patients who would benefit from further neuropsychological or imaging testing
• Automated administration, scoring, and report generation make systems ideal for “field” work
• Response accuracy and latency simultaneously measured
• Most systems are available in multiple languages
• Costs can be low for an assessment ($30 - $495)
• Objective data and large normative samples will aid in diagnosis and establishment of appropriate cut points
• Provide the opportunity of tracking treatment effectiveness

CogState: Computer Testing & Playing Card Stimuli
(culturally neutral, minimal language, game-like)

Is it there? Detection (simple RT)
Is it red? Identification (choice)
Same as the one before? Working Memory
Seen it already? Learning/Memory

• Measures the speed, accuracy and consistency of responses
• Little practice effect
• Sensitivity but not specificity
• Good scientific validation
CogState Battery

Simple Reaction Time 1
Choice Reaction Time
Complex Reaction Time
Dynamic Monitoring
Working Memory
Divided Attention
Simple Reaction Time 2
Matching
Memory
Simple Reaction Time 3

CANTAB Battery

Paired Associate Learning (PAL) appears particularly sensitive pre-clinical change in cognition and conversion to AD

In comparison to other measures, QD patients with performance similar to AD patients at six month follow-up all met NINCDS-ADRDA criteria for probable AD at 2 years

CANTAB PAL Test Performance

QD diagnosis
CDR of 0.5, but all NP testing WNL

Two Year Outcome
All QD-deteriorating diagnosed with AD (also one QD-Stable and one Control)
NeuroTrax Mindstreams™ Cognitive Health Assessment

Tests in the battery include:
- Verbal Memory
- Non-Verbal Memory
- Go-NoGo Test
- Problem Solving
- Stroop Test
- Verbal Function
- Visual Spatial Imagery
- Staged Information Processing
- Finger Tapping
- Hand-eye coordination

The test appears to effectively distinguish MCI from AD and NC, though longitudinal studies need to be completed.

CANS-MCI

Assessment areas include
- Memory
- Language Fluency
- Spatial Relations
- Executive Functions

Consideration of context factors
- Age
- Education
- Depression
- Alcohol/drug use

Preliminary data has been presented related to MCI vs NC.

Other Computerized Batteries

- Cogtest
- MicroCog
- Neurological Chronometric Assessment
- MEMTRAX
Cautions with Computerized Testing

- Validity and reliability issues
- Problems with human-computer interface
- Limitations in expressive and receptive language ability
- Adaptation of existing tasks may not be valid
- Equipment failures or problems with operating systems
- Reliance on unfamiliar interactive manipulanda or touch-screen
- Costs can be relatively high
- Lack of skilled examiner
- Frequent reliance on ratio scoring
- Ecological validity of tasks
- Need for long warm-up and practice periods
- Significant visuoperceptual demands

Australian TREAD Database

- Large community screening for progressive memory decline using remote internet-based computerized screening (CGS) in volunteers 50 years or age and older (aim is 10,000 Ss)
- Monthly email reminders and tracking whether testing completed
- Once decline is established
  - Evaluate for identifiable causes
  - If no identifiable cause, enroll participant in biomarker studies (e.g., CSF, PiB) and benchmark studies for later trials (e.g., neuropsych, MRI, PET)
- Enroll rapidly into clinical trials where trajectories can be worked out in advance to shorten trials

AAN Task Force Guidelines

- Patients with mild cognitive impairment should be recognized and monitored for cognitive and functional decline due to their increased risk for subsequent dementia.
- General cognitive screening instruments (e.g., MMSE) should be considered for the detection of dementia in individuals with suspected cognitive impairment
- Neuropsychological batteries should be considered useful in identifying patients with dementia or better understanding the type of dementia, particularly when administered to a population at increased risk of cognitive impairment (e.g., memory complaint)
Is it always a duck?  
When is screening not enough?

<table>
<thead>
<tr>
<th>Dementia</th>
<th>Neuropsychological Features</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alzheimer’s</td>
<td>Rapid forgetting</td>
</tr>
<tr>
<td></td>
<td>Impaired visuospatial skills</td>
</tr>
<tr>
<td></td>
<td>Impaired naming</td>
</tr>
<tr>
<td></td>
<td>No benefit from recognition memory trials</td>
</tr>
<tr>
<td>Vascular</td>
<td>Executive function compromised</td>
</tr>
<tr>
<td></td>
<td>Executive-based memory impairment</td>
</tr>
<tr>
<td></td>
<td>Attention/concentration impaired</td>
</tr>
<tr>
<td>Fronto-temporal</td>
<td>Executive function compromised</td>
</tr>
<tr>
<td></td>
<td>Perseveration</td>
</tr>
<tr>
<td></td>
<td>Impaired sequencing</td>
</tr>
<tr>
<td>Lewy Body</td>
<td>Impaired attention</td>
</tr>
<tr>
<td></td>
<td>Impaired visuospatial skills</td>
</tr>
<tr>
<td></td>
<td>Impaired frontal-subcortical tasks</td>
</tr>
<tr>
<td>Parkinson’s</td>
<td>Impaired frontal-subcortical tasks</td>
</tr>
<tr>
<td></td>
<td>Executive function compromised</td>
</tr>
<tr>
<td></td>
<td>Slowed performance</td>
</tr>
<tr>
<td></td>
<td>Retrieval memory deficit (recognition unimpaired)</td>
</tr>
<tr>
<td>Huntington’s</td>
<td>Impaired verbal fluency</td>
</tr>
<tr>
<td></td>
<td>Executive function compromised</td>
</tr>
<tr>
<td></td>
<td>Slowed performance</td>
</tr>
<tr>
<td></td>
<td>Retrieval memory deficit</td>
</tr>
</tbody>
</table>

**Conclusions**

- Methods currently exist that can likely improve recognition of dementia in elderly primary care patients
- These methods will be most effective if positive results lead to more careful monitoring and diagnostic testing
- Because of the high prevalence and social costs of dementias in late life and the emergence of useful therapies, a growing consensus favors cognitive screening as a part of routine primary care of the elderly
- Proof of the value of widespread screening must be established by health services intervention trials in primary care practices
Dementia-Delirium-Depressions: Are The Differences Between the 3D’s Still Relevant?

Barbara J. Messinger Rapport, MD, PhD, FACP, CMD

Objectives:

1. Distinguish between dementia, delirium, and depression in older adults.

2. Anticipate an alteration in cognitive trajectory after delirium.

3. Anticipate new patient needs after discharge of a delirious patient.
Are the differences between the 3D's still relevant?

BJ Messinger-Rapport, MD
Director, Center for Geriatric Medicine,
Cleveland Clinic Medicine Institute
March 7, 2014

After this presentation, learners will be able to

1. Distinguish between dementia, delirium, and depression in older adults
2. Anticipate an alteration in cognitive trajectory after delirium
3. Anticipate new patient needs after discharge of a delirious patient

Speaker Disclosures

Dr. Messinger-Rapport has disclosed that she has no relevant financial relationship(s).
Mental State Change - Differential Diagnosis

<table>
<thead>
<tr>
<th>Mental State Change - Differential Diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Delirium</td>
</tr>
<tr>
<td>Onset</td>
</tr>
<tr>
<td>Course</td>
</tr>
<tr>
<td>Consciousness/ orientation</td>
</tr>
<tr>
<td>Attention, memory</td>
</tr>
<tr>
<td>Psychosis</td>
</tr>
<tr>
<td>EEG</td>
</tr>
</tbody>
</table>

Clinical Case
Mrs. Smith

- 78 years old widow
- PMH: hypertension, cholesterol
- Lives alone, drives
- Trouble paying bills, taking meds, keeping appointments
- Given up bowling, knitting
- Symptoms at least 6 months

Physical Exam

- Wgt 162# VS: 160/78, 82
- Pleasant, well groomed, smiling
- Affect: good eye contact, interactive
- No delusions, hallucinations
- Exam normal, GDS 0/15
- MOCA 17/30 (recall 0/5; HS ed)
- Labs, CT brain normal
Geriatric Depression Scale

1. Are you basically satisfied with your life?  
2. Have you dropped many of your activities and interests?  
3. Do you feel tired that your life is empty?  
4. Do you often get bored?  
5. Are you in good spirits most of the time?  
6. Do you think that something will happen to you?  
7. Do you feel happy most of the time?  
8. Do you often feel helpless?  
9. Do you prefer to stay at home, rather than going out and doing new things?  
10. Do you feel you have more problems with memory than usual?  
11. Do you think it is wonderful to be alive now?  
12. Do you feel guilty because the way you are now?  
13. Do you feel full of energy?  
14. Do you feel that your situation is hopeless?  
15. Do you think that people are better off that you are?  

Summing up: 0-15: normal; 16-19: mild depression; 20-27: severe depression

---

PHQ-9

1. Litter interest or pleasure in doing things.  
2. Feeling down, depressed, or hopeless  
3. Trouble falling or staying asleep, or sleeping too much  
4. Feeling tired or having little energy  
5. Poor appetite or overeating  
6. Feeling bad about yourself—or that you are a failure or have let yourself or your family down  
7. Trouble concentrating or things, such as reading the newspaper or watching television  
8. Moving or speaking so slowly that other people could have noticed. Or the opposite—being so hyper or restless that you have been moving around a lot more than usual  
9. Thoughts that you would be better off dead, or of hurting yourself in some way  

Scoring—add up all checked boxes on PHQ-9  

For every ‘?’ Not at all = 0; Several days = 1; More than half the days = 2; Nearly every day = 3  

Interpretation of Total Score  

<table>
<thead>
<tr>
<th>Total Score</th>
<th>Depression Severity</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-4</td>
<td>Minimal depression</td>
</tr>
<tr>
<td>5-9</td>
<td>Mild depression</td>
</tr>
<tr>
<td>10-14</td>
<td>Moderate depression</td>
</tr>
<tr>
<td>15-19</td>
<td>Moderately severe depression</td>
</tr>
<tr>
<td>20-27</td>
<td>Severe depression</td>
</tr>
</tbody>
</table>

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Montreal Cognitive Assessment

---
Daughter says:

- Mom is isolated, misses husband
- Loves to bowl, knit, exercise
- Not doing now
- Must be depressed
  - Isn’t depression subtle?
  - Isn’t depression reversible?
- Fix it with a pill!

Patient states

- I feel fine
- I am sleeping and eating well
- I do not feel guilty or worthless
- I do not dwell on death
  - But my time has to be soon!
- I do miss my husband
- Some friends died, still have friends
- Enjoys family, good food

The patient continues:

- I don’t need to bowl any more, I’m 78
- I might knit today, just didn’t occur to me
- I exercise every day, my daughter just doesn’t know*

*The exercise machine is dusty and clearly has not been used!
What is her diagnosis

- Dementia?
- Depression?
- Delirium?
- Combination?

Dementia

- Decline in at least 2 brain functions,
- AND: interferes with social or occupational functioning
- AND: clear consciousness
- Multiple conditions can cause dementia
  - Stroke, parkinson's disease, huntington's disease, ALS, Alzheimer’s disease, etc.
- Fewer than 1.5% cases are “reversible”
Alzheimer's Disease

- Memory- and Cognitive loss in ≥ 1 domains
  - Aphasia (Language disturbance)
  - Apraxia (motor activities)
  - Agnosia (visual / spatial processing)
  - Impaired executive function (planning, organization, sequencing, abstraction)

- Progressive, gradual. Clear consciousness. Absence of systemic d/o or other brain disease affecting cognition. Decline previous level function

Prevalence Alzheimer Disease

2000: 4.5 million
2030: 7.7 million
2050: 13.2 million

PREDICTORS OF AD

Risks:
- Age
- APO E-4
- Diabetes
- Vascular risks
- Amnestic MCI
- Head Trauma
- Depressive Symptoms

Protection:
- Higher education
- Life-style factors
  - Exercise
  - Socialization
- Hypertension Tx
Alzheimer's Disease
Pharmacological Interventions

<table>
<thead>
<tr>
<th>Mild Cognitive Impairment</th>
<th>Dementia – Mild</th>
<th>Dementia – Moderate</th>
<th>Dementia – Severe</th>
</tr>
</thead>
<tbody>
<tr>
<td>No FDA-approved drug therapies currently available</td>
<td>Cholinesterase inhibitors</td>
<td>Cholinesterase inhibitors, Memantine</td>
<td>Cholinesterase inhibitors, Memantine</td>
</tr>
</tbody>
</table>

Medication Side effects

- Acetylcholinesterase inhibitors:
  - Donepezil (Aricept)
  - Rivastigmine (Exelon)
  - Galantamine
  
  - Diarrhea
  - Loss of appetite/weight loss
  - Nausea
  - Syncope
  - Bradycardia
  - Confusion
  - Dizziness
  - Insomnia or Hypersomnolence
  - Fatigue
  - Headache

- Memantine (Namenda)
  
  - Syncope
  - Confusion
  - Dizziness
  - Headache
  - Diarrhea or Constipation
  - Vomiting
  - Hypertension

Diagnosis of Depression
DSM-IV

- Depressed mood or anhedonia

- Abnormality in 4 of the following:
  - Weight/appetite
  - Sleep
  - Activity
  - Energy
  - Self-reproach
  - Concentration
  - Fixation on death
Depression diagnosis also requires

- Symptom persistence most of the time
- Duration > 2 weeks
- A decline in function as a result of the depressive symptoms

Prevalence of Major Depression

- Elders in the community: < 5%
- Homebound: 13.5%
- Elderly hospital patients: 11.5 % and above

Effects of depression on medical conditions

- ↑ functional disability
- ↓ ability to rehabilitation from stroke, treat Parkinson disease, heart disease, pulmonary disease, and recover from fractures
- ↑ risk adverse weight loss
- ↑ mortality (in some studies x3-4)
Why so important?

- Risk of suicide
- Burden to the families and institutions
- Increased use of health care resources
- Patient and/or provider may not recognize signs of depression

What makes depression in the elderly difficult to diagnose?

- Multiple physical problems
- Depressed mood may be less prominent than
  - ↓ appetite
  - Sleeplessness
  - ↓ interest
  - ↓ enjoyment of activity

Heterogeneity of depression in late life

- Early onset
  - Starts early in life
  - Recurrent course throughout older years
- Late onset
  - More chronic course
  - Variety of structural brain abnormalities (white matter hyperintensities, ventriculomegaly)
  - Often cognitive impairment
Subtypes of depression in later life

<table>
<thead>
<tr>
<th>Bipolar disorder</th>
<th>Major depression, single episode or recurrent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Psychotic disorder</td>
<td></td>
</tr>
<tr>
<td>Dysthymic disorder</td>
<td>Minor or subsyndromal depression</td>
</tr>
<tr>
<td>Bereavement</td>
<td>Adjustment disorder with depressed mood</td>
</tr>
<tr>
<td></td>
<td>Depression associated with medical illness</td>
</tr>
<tr>
<td></td>
<td>Vascular Depression</td>
</tr>
</tbody>
</table>

“Vascular depression” Subtype of late-onset depression

- Depression in patients with cerebrovascular disease
- Prominant motor retardation, lack of insight, impairment of executive function
- Dysfunction of frontal brain systems is a possible contributing factor in depression in late life
- Less response to antidepressants

Vascular depression

Risk factors:
- Age
- Hypertension
- Hyperlipidemia
- Cigarettes
- Diabetes mellitus

Atherosclerosis

Deep white matter lesions (vulnerability to LOID)

Negative life events

Lack of social support

Vascular depression with executive dysfunction

Sneed at al, 2011. LOD – late onset depression
Holocaust survivor treatment resistant depression; vascular findings

Behavioral symptoms of dementia

Mega, Neurology, 1996
Apathy: Will it...

- Respond to antidepressant?
  - If part of depression, probably yes
  - If part of dementia, probably not
  - ↑ doses SSRI may worsen apathy

- Respond to cholinesterase inhibitors?
  - If part of dementia, may respond

Apathy is common to depression and dementia

- Apathy symptoms in both depression & dementia:
  - Lack of interest
  - Psychomotor retardation
  - Hypersomnia

- Dysphoria, guilt, and/or suicidal ideation
  - NOT part of dementia
  - Likely require drug treatment
Mrs. Smith:
Which criteria does she meet?

**Depression?**
- Depressed mood or anhedonia +
- Abnormality in 4 of the following:
  - Weight/appetite
  - Sleep, Activity
  - Energy
  - Self-reproach, Concentration
  - Fixation on death
- Lasted > 2 weeks, decline in function

**Dementia?**
- Decline in 2 cognitive domains
- Progressive
- Decline in function
- Preserved consciousness

---

**Outcome: clinical case**

- Diagnosis, treatment of dementia
- Mild Alzheimer's Dementia
- Donepezil
- Daughter supervises all meds
- Adult day care
  - Exercise
  - Socialization
  - Therapeutic cognitive activities
- Referral Alzheimer Association
  - Advance planning re: living situation
  - Caregiver Education- maintain as much independence with sensitivity to ability

---

**Mrs. Smith feels badly**

- Doing well 6 months, then
- Adult day care notes
  - Social withdrawal, poor intake & hygiene
  - Weight loss, tearful
- Tearful, anxious in office
  - Lost 5# over past 3 months
  - Feels guilty, burden, sad
  - Not sleeping well
- MOCA 17/30, GDS 9/15
Evidence for medications for older adults w/ depression

- 11 Trials TCA v. Placebo
  - OR 0.32 (CI .21 - .47) NNT = 4
- 2 trials SSRI v. placebo
  - OR 0.51 (.36 - .72) NNT 8.5
- 2 trials MAO inhibitors v. placebo
  - OR .17 (CI .07 - .39) NNT = 3
- Atypicals: OR .52 (.29 - .93) NNT = 6.6
- Higher dropout rate TCA


Drug not more effective than placebo EXCEPT with severe depression

Hamilton Depression Severity Score
Mild: 8-13; Moderate: 14-18; Severe 19-22; Very severe: 23+
Fournier. JAMA. 2010

Possible adverse effects SSRI

- Sexual dysfunction
- Bleeding (PLT dysfunction)
- Hyponatremia
- Weight loss (early)
- Tremor (paroxetine)
- Sedation
- Apathy (higher doses)
- Diarrhea (sertraline)
- Urinary incontinence (not duloxetine)
- Falls, bone loss
FDA Safety Communication
Citalopram 8-24-2011

- No dose > 40 mg any age
- MAX 20 mg/d if:
  - Hepatic impairment
  - Age 60+ years
  - Poor metabolizor of CYP 2C19
  - Taking drugs that inhibit CYP 2C19
    • Cimetidine (multiple CYP enzymes)
    • PPI (e.g. omeprazole)

SSRI metabolized at CYP 2C19

- Citalopram
- Escitalopram
- Sertraline

Depression In Dementia

- Depressive Sx: 30-50%
- VaD > AD
- Female > Male
Diagnostic Challenges

- May be different than Depression in cognitively intact adults
  - Higher rates of psychomotor agitation/retardation.
  - More fear and suspiciousness
- 50% Dx based on caregiver report
  - Do caregivers over-estimate depression?
- Depression versus hypoactive delirium.
- Apathy v. depression in AD

Pharmacological Treatment: Depression in Dementia

- Antidepressants? Very few studies
- 9 randomized trials
  - 5 Selective Serotonin Reuptake Inhibitors (SSRI)
  - 3 Tricyclic antidepressants (TCA)
  - 1 moclobemide monoamine oxidase inhibitor
  - Not approved for use in the US
- SSRI, TCA comparable efficacy
  - Tolerability issues
- 2 Meta-analyses: variable- strong support

Antidepressant Therapy for Depression in AD

<table>
<thead>
<tr>
<th>Study</th>
<th>Zucman 2001</th>
<th>Beck 2001</th>
<th>Rucci 2001</th>
<th>Weighted Hedges' g (SMD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>SSRI</td>
<td>0.05</td>
<td>0.05</td>
<td>0.05</td>
<td>0.05</td>
</tr>
<tr>
<td>TCA</td>
<td>0.05</td>
<td>0.05</td>
<td>0.05</td>
<td>0.05</td>
</tr>
<tr>
<td></td>
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</tr>
</tbody>
</table>

Sources: Barts, The Cochrane Collaboration, 2007
Updated trial of anti-depressives in dementia

• 326 elders recruited from England psych clinics
  - Alzheimer's disease, +
  - Depression ≥ 4 wks, Cornell (CSDD) scale ≥ 8
• Randomized to mirtazapine (max dose 45 mg), sertraline (max dose 150 mg), PL
• Results:
  - Higher withdrawal rate in drug groups
  - No change in CSDD at 13 weeks
  - More adverse effects in drug groups
  - Mortality same in all groups by week 39

Banerjee. Lancet. 2011

Mrs. Smith is treated

• Placed on citalopram 10 mg/d
  - Increased in 2 weeks to 20 mg/d
• In 4 weeks, ADC reports
  - Better appetite
  - Less tearfulness & anxiety
  - More social

6 months later
Mrs. Smith gets sick

• Fever, cough, poor intake
• Hospitalized with
  - dehydration, acute kidney injury, Pneumonia.
• Several new medications, bladder catheter
• Sits in room, stares out window
• Duration: 5 days
  - Poor intake, mobility. Seen by PT: not interested
• Supposed to be dc tomorrow
Daughter calls you

• Mom is not herself
• Mom’s sister had depression
• Mom must be depressed
• Treat it with a pill

Delirium Prevalence

• Medical pts: 11-42% hospitalized pts
  - Undiagnosed in 30-60%
• Surgical pts: up to 53% elderly on floor, 80% elderly in ICU
• Post-cabg patients: about half
• Immediate post-acute: About ¼
• Overall long-term by MDS 3.0: 7%

Marcantonio, JAGS, 2003
Demeure. JACS. 2006 (surgical)
Siddiqi. Age Ageing. 2006 (medical)
Rudolph. Circulation. 2009 (cabg)

Delirium (DSM IV)

1. Disturbed consciousness
2. Change in cognition or perception (not dementia)
3. Acute onset; fluctuation
4. Physiological consequence of medical condition
Cardinal Features of Delirium

- Recent onset fluctuating awareness
  - Beginning 2-7d after insult (illness, drug, surgery, etc)
- Impairment of memory & attention
- Disorganized thinking
- Also may have
  - Hallucinations
  - Disturbance of sleep-wake cycle

Inouye SK. NEJM 2006; 354:1157

Delirium Subtypes

Hyperactive type: Risk falls, injury, interruptions in care

Hypoactive type: Risk decub, deconditioning

Liptzin. BJP. 1992

Delirium: Precipitating factors - Hospital

Medical: Severity illness; restraints; psychotropic drug(s);
> 3 medications; bladder catheter; iatrogenic event
Surgical: Type surgery; Intra-operative blood loss; post-op anemia

Predisposing Factors

Old
- Sensory impaired
- Cognitive impaired
- Malnourished
- Dehydration
- Depression
- Prior delirium

Protective Factors

Young
- Healthy
- High functional status

Adverse Outcomes of Delirium

Delirium Mortality over 12 months

- ↑ Risk of
  - Mortality
  - Prolonged LOS
  - Readmission (if dc to SNF with delirium)
  - Cognitive Decline
  - Functional Decline
  - Nursing Home Placement
- ↑ Hospital Cost
- ↑ Psychological distress

Leslie. Arch IM 2005

Delirium: Precipitating factors - Hospital

Medical: Severity illness; restraints; psychotropic drug(s);
> 3 medications; bladder catheter; iatrogenic event
Surgical: Type surgery; intra-operative blood loss; post-op anemia

Protective Factors
- Young
- Healthy
- High functional status

Predisposing Factors
- Old
- Sensory impaired
- Cognitive impaired
- Malnourished
- Dehydration
- Depression
- Prior delirium

No delirium
Delirium

Rate of decline

- (assuming no rehospitalizations)
- BIMC score decline by
  - Delirium: 3.5 IMC points per year
  - No delirium: 1.5 IMC points per year

(BIMC = Blessed Information Memory Concentration)

Delirium superimposed on depressive symptoms & adverse outcomes

Givens. JAGS. 2009

Delirium duration and return to pre-hospital cognition

Saczynski. NEJM. 2012
Outcomes of post-acute delirium

- 25% Delirium (HR=4.9, 1.7-13.5)
- 18.3% Subsyndromal (HR=3.4, 1.2-9.4)
- 5.7% No Delirium (HR=1.9)

Kiely. J of Gerontology. 2006

Delirium duration & % ADL performing on PAC discharge c/w pre-hospital

Delirium resolves < 2 weeks
Delirium resolves > 2 weeks
Recurrent delirium
Delirium never resolves

Kiely. J of Gerontology. 2006

Kiely. J of Gerontology. 2007
Challenges

- Reducing the risk of delirium
- Detecting delirium as early as possible
- Altering course of delirium once started
  - Finding the inciting medical/surgical condition
  - Identifying/qualifying pain if involved
- (Terminal Delirium)

Reducing the risk of delirium in medical hospitalization: **ELDER LIFE PROGRAM**

Matching controlled trial—Intervention:
- Optimize cognitive function
- Prevent sleep deprivation
- Avoid immobility
- Improve vision, hearing
- Treat dehydration

Inouye SK et al. NEJM 1999
ELDER LIFE PROGRAM RESULTS

Pharmacological risk reduction
Small studies

- **Risperidone** for subsyndromal delirium:
  - ↓ 60% incidence delirium c/w PL. Hakim. Anesth. 2012
- **Prophylactic haloperidol**: ↓ severity, duration delirium periop hip surgery. Devlin. Crit Care Med. 2010
- **Risperidone, 1 mg SL s/p CABG**:
  - ↓ 67% Incidence delirium c/w PL. Prakanrattana. Anesth IC 2007
- **Olanzapine 5 mg prior, 5 mg post elective ortho surgery**
  - ↓ 64% Incidence delirium c/w PL. Larsen. Psychosomatics. 2010

What pharmaceuticals have not reduced risk of post-op delirium

- **Rivastigmine** prior to elective cardiac surgery:
  - No reduction in incidence delirium
- **Donepezil** prior to hip fracture repair
  - No reduction in incidence, severity delirium
  - Marcantonio. JAGS. 2011
What pharmaceuticals have not reduced risk of ICU delirium?

- **Rivastigmine** for delirium in ICU:
  - ↑Duration of delirium, mortality c/w PL
  - Van Eijk. Lancet. 2010
- **Haldol 2.5 mg** to prevent or treat delirium
  - No difference in
    - LOS, days alive, days w/o delirium, days w/o COMA
    - Page. Lancet. 2013

Identifying delirium

- **Classic**: Confusion Assessment Method
  - Hospitalized patients 1988-1990
- **Modifications**:
  - CAM-ICU Critical Care Medicine. 2001
  - Short CAM (United Kingdom)
  - MDS 3.0 CAM (Saliba)

Back to Mrs. Smith

- Diagnoses with hypoactive delirium
- Removed bladder catheter
- Streamlined medications
- Discharged to subacute care
  - Delirium persisted > 2 weeks
  - Subacute discharge MOCA: 10 / 30
  - Unable to reliably perform self-care
- She was discharged to an assisted living
Summary

- Substantial overlap between
  - Dementia
  - Depression (or, depressive symptoms)
  - Delirium
- Pharmacological options to prevent, treat
  - Modest benefit, substantial adverse effects
- Prolonged delirium may prevent attainment of pre-morbid function
- Future treatment targets
  - Early diagnosis; biomarkers;
  - More efficacious drugs, fewer adverse effects
  - Prevention

THE END!
Dementia Pharmacotherapy Update
Gayle Kamm, PharmD, BCPS

Objectives:

1. Review the most common medications that should be avoided in older adults with dementia.

2. Evaluate the risk associated with the use of antipsychotics in the elderly.

3. Discuss alternative treatment options for treating behavioral problems in the geriatric population.

4. Investigate newer medications for the treatment of dementia and dementia related behaviors.
Dementia Pharmacotherapy Update

Gayle Kamm, PharmD, BCPS
March 7, 2014

Objectives

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Adverse Drug Events (ADEs)

- 27% of ADEs in primary care and 42% of ADEs in long term care are potentially preventable\(^1\)
- elderly dementia patients
- reduce ADEs:
  - Avoid PIMs
  - Reduce drug interactions and therapeutic duplications

Potentially Inappropriate Medications (PIMs)

• Limited effectiveness
• Serious side effects
  – Confusion
  – Delirium
  – Falls
  – GI bleeding
• Integral part of policies in CMS and part D
• Quality measures used by National Committee for Quality Assurance (NCQA), Pharmacy Quality Alliance (PQA)

Beers Criteria

• Updated 2012 with American Geriatrics Society
• Evidence based systematic review
• 3 broad groups
  – meds to avoid in older adults
  – meds considered inappropriate in older adults with certain diseases
  – meds that should be used with caution (need to do a risk/benefit analysis)

Medications to avoid

• **anticholinergics:**
  – Confusion, sedation, orthostasis, constipation

  *1st generation antihistamines* (diphenhydramine, chlorpheniramine, brompheniramine, doxylamine, hydroxyzine, promethazine, meclizine)

  *tertiary TCAs* (amitriptyline, doxepin >6mg/d, imipramine)

  *Suggested alternatives:*
  Non-sedating antihistamines (Allegra, Claritin, Zyrtec?)

  SSRI (except fluoxetine), bupropion, mirtazapine

  benzotropine, trihexyphenidyl
Medications to avoid

**anticholinergics:**

- Antispasmodics (Librax, belladonna, hyoscyamine, scopolamine, dicyclomine)
- Muscle relaxants (carisoprodol, cyclobenzaprine, chlorzoxasone, metaxalone, orphenadrine)
- Bladder anticholinergics - oxybutynin

**Suggested alternatives:**

No specific antispasmodics – treat diarrhea or constipation

Behavioral therapy; more selective agents (tolf candles (Detrol), trospium (Sanctura), derifenacin (Enablex), solifenacin (Vesicare), trospium (Sanctura), fesoterodine (Toviaz))

---

Medications to avoid

- Alpha blockers (doxazosin, prazosin, terazosin)
  - Orthostasis
  - “avoid use as antihypertensive”
  - OK for behaviors?
- Digoxin > 0.125mg
- With comorbid syncope: AChEIs

---

Medications to avoid

- Barbiturates (Pb, butalbital)
- Benzodiazepines (alprazolam, lorazepam, clonazepam, chlordiazepoxide)
  - May be approp. for seizures, RBD, severe GAD
- Hypnotics (zolpidem, eszopiclone, zaleplon)
  - Avoid for > 90 days
- Meperidine
- H2-receptor antagonists (**cimetidine, ranitidine?, famotidine?, nizatidine?)

**Suggested alternatives:**

- Buspirone, SNRIs, SSRIs
- Non-pharmacologic
- Dependent on indication
- ??? PPIs
Medications to avoid

- Antipsychotics
  - 1st generation: chlorpromazine, fluphenazine, haloperidol, thioridazine, trifluoperazine, perphenazine)
  - 2nd generation: aripiprazole, asenapine, clozapine, iloperidone, lurasidone, olanzapine, paliperidone, quetiapine, risperidone, ziprasidone
- Limited efficacy? Serious SE?

Antipsychotic efficacy and safety in older adults with dementia related psychosis or behavioral disturbances

- Efficacy: mixed results; olanzapine and risperidone have most evidence for atypicals; not superior to typicals in efficacy, but better tolerated
- April 2005 FDA warning:
  - 17 RCTs: 1.7 times increased risk of all-cause mortality associated with atypical AP use in elderly with dementia (olanzapine, aripiprazole, risperidone, quetiapine)
- June 2008 FDA warning extended to typical AP

Antipsychotic efficacy and safety in older adults with dementia related psychosis or behavioral disturbances

- Cerebrovascular adverse events (CVAEs)
  - 22 studies (2 placebo controlled trials): risk of events increased by 1.3 to 2 times
  - Risk factors: higher doses, older age, vascular dementia, A-fib
- Deaths
  - 14 studies (3 placebo): risk 1.2 to 1.6 times higher with AP use
  - Risk factors: older age, male, severe dementia, functional impairment
  - Most deaths thought to be CV in nature; some infectious
    - QT prolongation?, thrombosis?

Am J Alzheimers Dis Other Demen 2011;26(1):10
Some Guidelines for AP use

- Try non-pharmacologic approaches first
  - Identify triggers / sources of behaviors
- Only use when patient is a danger to him/herself or to someone else
- Evaluate CV risk factors; metabolic risk factors
- Need to continually reevaluate need for AP

Alternatives to APs & Benzos for Dementia Related Psychosis/Behaviors

- citalopram
- prazosin
- carbamazepine
- propranolol
- Nuedexta (specific indication)
- AChEIs / memantine

### Citalopram

<table>
<thead>
<tr>
<th>Study</th>
<th>patients</th>
<th>Intervention</th>
<th>results</th>
<th>comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pollock et al (1997)</td>
<td>DAT w/ sev. Behavioral or psychotic sx. NRS 4+ on any agitation or psychosis item Excl.: NRS 4+ on depression item MMSE 8.7</td>
<td>Open-label, inpatient, 17 day trial Citalopram 10mg x 3 days, 20mg x 14 days</td>
<td>16 patients: 2-3 point reductions on NBRs items for disinhibition, agitation, hostility, suspicion (p&lt; 0.05); total NBRs: 114.84 to 88.31 (p=0.0005)</td>
<td>small, short, inpatient</td>
</tr>
<tr>
<td>Scherr et al (2003)</td>
<td>Probable AD: Severe aberrant motor behaviors (clinical judgment) Excl.: MDD MMSE = 13.4</td>
<td>Open-label, outpatient, 12 week Citalopram 10mg/day (max 40mg/day)</td>
<td>19 patients NPI-total decreased at 12 weeks 27.2 to 16.8 (p=0.0003) (out of 120)</td>
<td>Low impairment at baseline Clinically sig?</td>
</tr>
</tbody>
</table>
Citalopram

<table>
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<th>Intervention</th>
<th>Results</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pollock et al. (2002)</td>
<td>DAT, ID, mixed dementia, NOS without delirium, schizophrenia, bipolar, or MDD; NRS 3+ on any agitation or psychosis item</td>
<td>Citalopram: 10mg/d x 5d, 20mg/d x 14 days or OR perphenazine 0.25mg/kg/day x 3 days, 0.1mg/kg/day x 14 days OR placebo (3:3:2)</td>
<td>Cit: NRS abridged total 53.5 to 43.5</td>
<td>Overviewed fed effect seen? Cital MMSE higher at baseline</td>
</tr>
</tbody>
</table>

<table>
<thead>
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<th>Study</th>
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<th>Results</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pollock et al. (2007)</td>
<td>DAT, ID, mixed dementia, LBD</td>
<td>Citalopram: 10mg/d x 3d, 20mg/d x 14d, then up to 40mg/d OR risperidone 0.5mg/d x 3d, 1mg/d x 14d, then up to 2mg/d</td>
<td>Cit: NRS agitation: Citalopram 10.18 to 8.81 (p=0.05), Risperidone 8.94 to 8.20 (p=0.30)</td>
<td>No placebo allowed – No subanalysis</td>
</tr>
</tbody>
</table>

Citalopram

- Conclusion
  - modest efficacy for agitation, aggression, psychosis
  - Strength of evidence?
  - Unanswered questions
    - benefit in patients with and without depression?
    - clinically significant?
    - change in caregiver stress?
    - duration of effect?
    - synergy with AChE inhibitors?

- Concerns:
  - Dosage limitations
    - Max 20mg/d in age > 60
    - QT prolongation
      - increased risk with drug interactions (omeprazole) or baseline CV disease
  - Time to effect?

Prazosin (Beers list: avoid in HTN)

- Theoretical MOA: enhanced responsiveness to NE at alpha-1 adrenoreceptor in AD has been thought to contribute to behaviors; prazosin is a central alpha-1 blocker
- Wang et al. 2009
- DBPC parallel group study
- 22 NH & outpt., probable or possible AD;
  - baseline MMSE 9.3(praz) vs. 14(placebo)
  - NPI: 49 vs. 43
  - BPRS 45 vs. 44
- prazosin 1mg/d, inc. up to 6mg/d (mean 5.7mg)
  - vs. placebo

<table>
<thead>
<tr>
<th>NPI</th>
<th>BPRS</th>
<th>CGI-C</th>
<th>Side effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>prazosin</td>
<td>49</td>
<td>7.6</td>
<td>No sig diff</td>
</tr>
<tr>
<td>placebo</td>
<td>2</td>
<td>4.5</td>
<td></td>
</tr>
<tr>
<td>P=0.012</td>
<td>P=0.036</td>
<td>P=0.011</td>
<td></td>
</tr>
</tbody>
</table>

- Concerns: orthostasis / hypotension; give at bedtime

Arq J Geriatr Psychiatry 2009;17(9): 744
carbamazepine

- Tariot, et al. 1998
- 6 wk randomized, parallel-group study
- 51 NH patients; probable or possible AD, vascular dementia, or mixed dementia; agitation for 22wks; BPRS≥3 on tension, hostility, uncooperativeness, or excitement item
  - MMSE 3.9 (CBZ), 8.3 (placebo)
  - BPRS 55.1 (CBZ), 53.3 (placebo)
  - behaviors: verbal disruption(47), physical disruption(36), social inappropriateness(16), aggression(47)
- Carbamazepine 100mg/d increased by 50mg Q2-4 days based on SE and serum levels (5-8 mcg/ml)
  - Mean 304mg/d

<table>
<thead>
<tr>
<th></th>
<th>CBZ</th>
<th>placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td>BPRS</td>
<td>-7.7</td>
<td>-0.9</td>
</tr>
<tr>
<td>Overt</td>
<td>6.7</td>
<td>-1.9</td>
</tr>
<tr>
<td>Aggression</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Scale</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CGI</td>
<td>77% at least min. improved</td>
<td>21% at least min. improved</td>
</tr>
<tr>
<td></td>
<td>50% much improved</td>
<td>17% much improved</td>
</tr>
<tr>
<td></td>
<td>23% unchanged or worse</td>
<td>79% unchanged or worse</td>
</tr>
<tr>
<td>SE &amp; dropouts</td>
<td>59% (Ataxia &amp; disorientation &gt; but diff. not SS)</td>
<td>29%</td>
</tr>
</tbody>
</table>

| difference    | 6.8 (CI 3.3-10.2) | 4.8 (p=0.008) |
| p-value       | p=0.001           |             |

carbamazepine

- Olin 2001
- 6wk RDBPC parallel group outpatient setting
- 21 patients, probable or possible AD, unresponsive to AP, BPRS≥4 on 2 of 4 items: tension, hostility, uncooperativeness, excitement
  - MMSE = 6
  - Most pts had mod-sev agitation sx., minimal psychosis/hallucinations
- CBZ 100mg QAM x 7 days, then 100mg QID x 5wks

<table>
<thead>
<tr>
<th></th>
<th>CBZ</th>
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<tbody>
<tr>
<td>BPRS</td>
<td>-4.0</td>
<td>-4.2</td>
</tr>
<tr>
<td>CGI</td>
<td>-5.0</td>
<td>-4.5</td>
</tr>
<tr>
<td>IADL</td>
<td>0.7</td>
<td>0.3</td>
</tr>
<tr>
<td>PSMS</td>
<td>0.5</td>
<td>0.6</td>
</tr>
<tr>
<td>side effects</td>
<td>3 dropout - cog. Worse</td>
<td>3 dropout - 3 agit, 1 CVA 44% SE</td>
</tr>
<tr>
<td></td>
<td>44% SE, halluc. worse, diarrhea</td>
<td></td>
</tr>
<tr>
<td></td>
<td>66% SE</td>
<td></td>
</tr>
</tbody>
</table>

| p-value       | p=0.519 | p=0.015 | p=0.408 | p=1 |

Am J Psychiatry 2001; 155(1):54

Am J Geriatr Psychiatry 2001; 9(4):400
carbamazepine

- Considerations:
  - Side effects: hyponatremia (SIADH), CNS, leukopenia, decreased bone mineral density/vitD
    - Beers list: "use w/ caution" in all & "avoid" if h/o falls
  - Enzyme inducer: many DI's and induces its own metabolism
    - Requires monitoring to assure therapeutic levels
  - Oxcarbazepine & Depakote not effective in trials

propranolol

- Peskind 2005
- RDBPC x 6wks
- 31 pts in NH; probable or possible AD; treatment resistant disruptive behaviors; AP allowed;
- Propranolol mean dose 106mg/d
- Improvement on NPI: agitation/aggression & anxiety
- For responders: after 6 months of open label, improvement diminished

Nuedexta

- dextromethorphan and quinidine
- FDA approved for pseudobulbar affect
  - Studies done in MS and ALS patients
- NMDA antagonist; efficacy possibly related to binding to sigma-1 brain receptors
- Cautions:
  - QT prolongation, contraindicated in heart failure
  - Many drug interactions
  - Serotonin syndrome (esp. with fluoxetine & paroxetine)
- SE: diarrhea, dizziness, peripheral edema
- AWP for 30day supply = $774
Alternatives to APs & Benzos for Dementia Related Psychosis/Behaviors

- citalopram
- prazosin
- carbamazepine
- propranolol
- Nuedexta (specific indication)
- AChEIs / memantine

New Dementia Treatments

- Axona: FDA approved “medical food”
- Targets improving neuronal metabolism
- Brain glucose metabolism may be reduced in early AD
- medium chain triglycerides – metabolized by liver to ketone bodies – alternative energy source
- 2 trials; one 2-dose trial, one 90 day trial
- Benefit seen in ADAS-Cog in APOE4(+) only
  - Benefit disappeared 2 wks after Axona DC’d
- GI SE common

Investigational treatments

- Vitamin E
  - 4 controlled trials, at least 3 observational trials
  - Mixed results; benefit & harm
  - Dysken et al. 2014
    - 14VA medical ctrs; MMSE=20.8-21.3; ADAS-cog=18-19.5
    - 561 pts: all on AChEi; memantine vs. vit E 2000iu/day vs. combo vs. placebo
    - Mean follow up 2.27 yrs
    - ADCS-ADL Inventory scores declined by 3.15 units more in vit E group than placebo  \( p = .03 \); (19% per year delay in progression)
    - No sig benefit seen in memantine group or combo group
    - 2° MMSE and ADAS-cog ; no sig change in any group
    - Efficacy dependent on APOE status? Other meds? stage of disease?
Investigational treatments

- ACEIs: 4 yr cohort; continuous ACEIs vs intermittent ACEIs vs other antihypertensives vs no antihypertensives
- Patients who had ever used ACEIs had a slower MMSE decline than those who had never used ACEIs (7.5 vs 9.7, p=0.03)


Pipeline

- Antiamyloid therapies: bapineuzumab & solanezumab – disappointing results in phase 3
  -- prevention?
- BACE inhibitors – blocks beta secretase
  -- At least 1 moving on to phase 3

Pipeline

- Lu AE58054: 5-HT6 antagonist - in phase III trials
  -- Stimulate dopamine & norepi release in frontal cortex
- EVP-6124: partial alpha-7 nicotinic agonist – successful in phase2b
Clinical Pearls

- Mirtazapine – depression, appetite, and sleep
  – Lower doses more sedating
- Lewy Body Dementia: APs may actually worsen psychosis; treat with AChEIs
- Seizures & Alzheimers1: levetiracetam and lamotrigine > efficacy/better tolerated than PHT

1. Vossel KA JAMA Neurol 2013;70:1158
Objectives:

1. Discuss strategies for managing the cognitive deficits of a client with dementia while providing treatment for musculoskeletal disorders.
INTRODUCTION

What were you thinking?

OBJECTIVE

Discuss strategies for managing the cognitive deficits of a client with dementia while providing treatment for musculoskeletal disorders...

But, must first try to differentiate extrinsic sources of pain (discomfort) from intrinsic sources of pain.
DISCOMFORT

- Source of Discomfort Scale (SODS)
  - A few simple questions (how are you, are you comfortable), but mostly observational items.
- Mini Mental State Examination (MMSE)
- Pain Assessment in Noncommunicative Elderly Persons (PAINE)
  - Given to patient’s direct nursing caregiver
- All administered by trained researchers
  - 179 NH residents in 10 different facilities
    - Mean age = 86 y.o.; mean MMSE = 8.79
  

SOURCES OF DISCOMFORT

- Average of 3 sources/person
  - Sleepy/tired = 61.5%
  - Sitting in same place for >2 hrs = 49.7%
  - Resident is restrained = 28.5%
  - Insufficient light = 27.4%
  - Resident is fidgeting/seating = 25.7%
  - Cold or hot to the touch = 15.1% / 6.7%
  - Scratching a body part = 9.5%
  - Excessively touching clothing = 8.4%
- Correlation b/w pain and discomfort; r = .287

DISCOMFORT

- Consider environmental modifications, such as:
- Consider daily activities to improve quality of care/life, such as:
PAIN

- 45-83% of NH patients experience acute or chronic pain, especially those with moderate to severe dementia
  - Most common is of musculoskeletal system
  - 40% experience pain in internal organs, skin and other systems
    - pressure ulcers, SBO, peptic ulcers, catheter associated UTIs, orofacial/dental pain


MUSCULOSKELETAL PAIN

- Vicious cycle of:
  - Pain → Immobility → Decreased Function → Pain
- Treatment can be painful:
  - Weight bearing
  - ROM and Stretching

ASSESSMENT OF PAIN

- The self-report is the gold standard of pain assessment:
  - May be used with early/mild cognitive changes
  - Must comprehend pain scale
    - Comprehension = the ability to explain the scale and correctly indicate positions for no pain and extreme pain on two separate occasions

ASSESSMENT OF PAIN

- If moderate/severe cognitive impairment:
  - Attempt self-report
  - Identify potential causes of pain
    - Known acute and persistent painful conditions
    - Consider recent diagnoses and/or procedures
  - Use observational pain behavior scales
    - Formal and informal caregivers, family members
  - If pain suspected, determine patient’s response to analgesic trial

OBSERVABLE PAIN SCALES

- Facial expressions, vocalizations, and body movements at rest and during ADLs:
  - Presence/absence
  - Frequency
  - Intensity
- Scoring and interpretation not clearly established, especially for intensity

- PADE
- Pain Assessment for the Dementing Elderly
- PAINE
- DS-DAT
- Discomfort Scale for Dementia of Alzheimer Type
- CNPI
- Checklist of Nonverbal Pain Indicators
- PAINAD
- Pain Assessment in Advanced Dementia

INTERVENTIONS

- Regardless of M-S diagnosis, must address pain:
  - Determine how you will assess it (monitor)
  - Modalities to reduce it
    - Sensory stimulation such as touch, temperature
  - Ways to "work around it"...
    - Make treatment meaningful and purposeful
**INTERVENTIONS**

- Must incorporate creative treatment approaches with the more traditional interventions.
- So, consider whatever plan of care is most appropriate for the given M-S condition and incorporate:
  - Communication Strategies
  - Approach Strategies
  - Other strategies


**COMMUNICATION STRATEGIES**

- Non-verbal cues
  - Smile!!!
- Sensory cues
- Slow, simple phrases
- Time for processing
- Minimize distractions
- "Visit" with patient before starting treatment
  - Use their “Life Stories”

**APPROACH STRATEGIES**

- Use of familiar, function-oriented tasks
- Ask patient to “help you”
  - Requests vs. commands
- Exhibit patience in an unhurried manner
- Exhibit respect
  - Mr. or Mrs.
  - Thank you
  - Age-appropriate tasks
OTHER STRATEGIES

- Sensory Stimulation
  - Help connect to environment
  - Smell, movement, touch, vision, hearing, taste
- Montessori Approach
  - Go with the flow
  - Initiate with Autonomy
    - Offer a choice
- Strength-based Activities
  - Gardner’s Theory of Multiple Intelligences

IN SUMMARY

- Consider sources of discomfort
  - Make modifications if necessary
- Assess pain
  - Severity and sources
- Treatment of pain from M-S sources
  - Modify environment
  - Decrease pain (determine how to monitor)
  - Make treatment meaningful

Thank you!
Objectives:

1. List at least three types of supportive programs for people who have memory lost and their families.
The Alzheimer's Association: Your Partner in Care

ALZHEIMER’S DISEASE AND DEMENTIA

- Alzheimer’s disease is no longer viewed as a crisis in the making - it is now seen as a major public health problem that is seriously affecting millions of Americans and their families today

- Every 68 seconds another individual is diagnosed with Alzheimer’s disease or a related dementia

FROM 2000-2010, ALZHEIMER’S DISEASE DEATHS INCREASED 68% WHILE ...
WHEN SOMEONE IS SHOWING SIGNS OF DEMENTIA

- Assessment and diagnosis is critical
- Early diagnosis can be helpful
- Medications that may be modestly helpful are available
- Refer person or family to Alzheimer’s Association for supportive programs and services

ENCOURAGE THE CAREGIVER TO ACCEPT HELP

- Honor the caregiver’s role
  - Recognize she/he is the expert who knows the person best
  - Recognize she/he feels responsible for providing the care
- Consider emphasizing benefit to the person with dementia (PWD), rather than the caregiver’s needs
- Encourage the caregiver to see self as transitioning to becoming a member of a care team
  - Help caregiver in dealing with PWD concerns and resistance because these can interfere with caregiver’s willingness to accept help
- Be an advocate - contact the Alzheimer’s Association on behalf of the caregiver or patient (with permission)

MALE VS. FEMALE CAREGIVERS

- Are there male/female differences in caregiving?
  - Male caregivers tend to focus on home repairs and managing finances
  - Women usually take on household duties and personal care (bathing, dressing, feeding)
  - Men do give full care if it’s their wives who need the help
  - Women caregivers are more often more personally involved and distressed than male caregivers
THE PERSON WITH DEMENTIA

What does it feel like to have Alzheimer’s disease?

- “I feel that people would rather disable me than enable me to be all that I can be. I feel lonely, less attached to my family. Is it me or is it them?” - Richard Taylor, *Alzheimer’s from the Inside Out*

- “It is much easier to stay in the safety of my home, than to expose myself to people who don’t understand, people who raise their eyebrows when I have trouble making the right change at the cash register, or when I’m unable to think of the right words when asked a question.” - Larry Rose, *Show Me the Way to Go Home*

MORE REFLECTIONS

- “I think one of the worst things about Alzheimer’s disease is that you are so alone with it. Nobody around you really knows what’s going on. And half the time, or most of the time, we don’t know what’s going on ourselves.” - Cary Henderson, *A Partial View: An Alzheimer’s Journal*
MORE REFLECTIONS

- How it feels to have AD
  - “I think one of the worst things about Alzheimer’s disease is that you are so alone with it. Nobody around you really knows what’s going on. And half the time, or most of the time, we don’t know what’s going on ourselves.” – Cary Henderson, A Partial View: An Alzheimer’s Journal
  
  - “I am still the same person, but I just can’t do my work anymore. I am still here and I need your friendship and acceptance.” – Robert Davis, My Journey into Alzheimer’s Disease

ALZHEIMER’S ASSOCIATION

- The major organization that provides information and supportive services to families, individuals who have dementia, professionals, and other interested persons
  
  - Chapters throughout the U.S.
    - The Helpline number 1-800-272-3900 connects to the nearest Chapter during business hours and to the National office on evenings and weekends

ALZHEIMER’S ASSOCIATION, NORTHWEST OHIO CHAPTER

- Serves 24 counties - Allen, Ashland, Auglaize, Crawford, Defiance, Erie, Fulton, Hancock, Hardin, Henry, Huron, Know, Lucas, Mercer, Ottawa, Paulding, Putnam, Richland, Sandusky, Seneca, Van Wert, Williams, Wood, Wyandot

- Offices in Toledo, Findlay, Lima, and Ontario (Mansfield area)
PROGRAMS AND SERVICES

- Helpline
  - Information, education, and support 24/7
- Care Consultations/Counseling
  - Face-to-face meetings with staff of the Association to receive education, emotional support, and resource information
  - PASSPORT provider
  - Caregiver Support Program provider
- Caregiver support groups
  - Monthly support groups for family caregivers
  - Special groups for male caregivers and caregivers of persons with FTD

ADULT DAY SERVICES

- Adult day centers
  - Two locations in the greater Toledo area
  - Provide social interaction, cognitive stimulation, support
  - Offer families respite from caregiving responsibilities or to maintain employment
- PASSPORT provider, including Choices
- VA provider

REDUCING DISEASE IN ALZHEIMER'S DISEASE (RDAD)

An exercise and caregiver education program
- in the home
- in groups
EARLY STAGE PROGRAMS
- Transitions support and education groups
  - Groups in Toledo, Lima, Defiance, Findlay, Sandusky, Ontario
  - Social engagement groups in Toledo, Findlay, Sandusky
- Early Stage workshops
- SHARE - research study that helps plan for future
- Meet Me at TMA (Toledo Museum of Art)
- Meet Me at the Zoo
- Mind Works
- Art Café and Brush with Art
- Theater Groups
- Volunteer Groups

EDUCATIONAL PROGRAMS
- Speakers Bureau
- Family Education
- Training for Professionals
- Topics tailored to the group, including the disease process, current research, family caregiving, and care techniques

BUILDING A DEMENTIA-FRIENDLY COMMUNITY
- Supporting the Hancock County Dementia Coalition
  - Public awareness
    - Speakers Bureau
    - Reaching out to schools, businesses, faith communities
  - Caregiver support
    - Resource guide
  - Professional education
PROGRAMS AND SERVICES

- Website  www.alz.org/nwohio
  - Numerous topical pages for caregivers, persons with dementia, and other audiences
  - Professional support (practice recommendations, online certification, and information)
  - More than 70 downloadable, free publications
  - AlzConnect - Social networking and message boards for professionals, caregivers, persons with memory loss
  - Links to local Chapter events and educational programs
  - AlzNavigator - an online, self-directed assessment and care planning tool

- Advocacy
  - At state and federal levels for research, effective programs and services, quality of life

- Medic Alert+Alzheimer’s Association Safe Return
  - Nationwide program to aid in the recovery of a lost elder
  - Enrollment forms available online or through the Chapter
  - Financial assistance to help pay for enrollment

- Comfort Zone
  - Program that uses the Internet and a variety of devices to track the location of a person

- Respite financial assistance
  - Reimbursement program to help families pay for in-home care

- TrialMatch
  - Personalized linkage to clinical studies

- ISTAART - International Society to Advance Alzheimer’s Research and Treatment
  - Opportunity to join or create a Professional Interest Area (PIA)
  - Subscription to Alzheimer’s and Dementia: The Journal of the Alzheimer’s Association
  - Monthly e-newsletter with latest research updates
  - Early notification of grant opportunities through the Alzheimer’s Association
Caring Companions - Trained volunteers provide a break for family caregivers within their homes. Serves Ashland, Crawford, Huron, Knox, Richland, Seneca, and Wyandot counties.

- Refer patients/clients to the Helpline or adult day services
- Refer patients/clients to TrialMatch
- Form a team or participate as an individual in the Walk to End Alzheimer’s
- Join ISTAART
- Become a member of the Alzheimer’s Association

ALZHEIMER’S ASSOCIATION, NORTHWEST OHIO CHAPTER

- 1-800-272-3900
- alz.org/nwohio
Legal Implications of Dementia
A. John McSweeny, JD, PhD, ABPP (CN)

Objectives:

1. Explain how capacity is evaluated.

2. Discuss ethical implications of a legal consultation with a client who has diminished capacity due to dementia.
Legal Implications of Dementia
A. John McSweeney, J.D., Ph.D.
Professor and Interim Chair of Psychology
Professor Emeritus of Psychiatry and Neurology

Definition of “Emeritus”
- Two parts
  - “E” = “out”
  - “Meritus” = “Deserves to be”

Disclaimer
Although I am an attorney licensed in Ohio, this presentation is not legal advice and you should not rely on it for legal purposes. If you require legal advice you should contact an attorney licensed in Ohio or the jurisdiction in which you practice.
Legal topics relevant to Dementia

- Capacity – The ability to make legal decisions*
- Advance Directives – Life, Death and Care Instructions*
- Financial Support I – Private monies that provide for support and care
  - Special Needs Trusts
  - Pooled Trusts
* To discuss today

Legal topics relevant to Dementia

- Financial Support II - Government Benefits
  - Medicare and Medicaid
  - Veterans Benefits
- Guardianships and Conservatorships*
- Financial Exploitation and Scams
- Personal Care Agreements and Nursing Home Contracts
*To discuss today

Capacity: Outline

- Basic Concepts of Capacity and Competence
- Examples of Legal Capacities
- Basic Issues in the Clinical Assessment of Capacity
- Clinicians who perform assessments of capacity.
- Problems in the Assessment of Clinical Capacity
- Models in the Clinical Assessment of Capacity
Basic Concepts in Capacity: Historical View

Competence vs. Capacity

- Competence
  - The legal right to make self-directed decisions or perform self-directed legal acts.

- Capacity
  - Clinical status assessed by a health-care professional in response to questions raised a person’s ability to make decisions or perform acts.
  - Capacity information was provided to a probate court judge who made legal decisions regarding competence.

Basic Concepts in Capacity: Historical View

Competence vs. Capacity

- Competence and capacity have been used inconsistently as legal or clinical terms.

- Examples:
  - “Physician judgments of competency.”
  - Testamentary Capacity

- No universal agreement on terminology

Basic Concepts in Capacity: Current View

Legal Capacity vs. Clinical Capacity

- “Capacity” is used to cover both legal and clinical judgments of a person’s abilities.

- Legal Capacity – A legal judgment is at issue.

- Clinical Capacity – A clinical judgment, usually in the service of a probate court’s judgment of legal capacity.
Basic Concepts in Capacity: Legal Capacity

- Legal capacity is assumed for adults but can be challenged in probate court.

- Court may exercise the state’s protective powers - *parens patriae* – and appoint a substitute decision-maker: a guardian or conservator.

- Clinical capacity evidence is persuasive but not dispositive.

- Other considerations
  - Individual’s Life Situation
  - Legal standards
  - General principles of justice and equity

Basic Concepts in Capacity: Legal Capacity

- General vs. Specific Legal Capacity
  - General legal capacity - General legal right to make decisions about one’s legal affairs.
    - Example: Guardianship hearings.
  - Specific legal capacity - Right to make decisions about specific legal affairs.
    - Examples: Contractual Capacity, Sexual Consent Capacity, testamentary capacity.
    - Not recognized in all states

Basic Concepts in Capacity: Legal Capacity

- Limited Legal Capacity
  - A person has the authority to make certain decisions but not others within a general or specific legal capacity.
  - Defined by a limiting order issued by a probate judge.
  - Example – A person is declared to lack financial capacity with regard to financial transactions of over $500.
Basic Concepts in Capacity: Legal Capacity

- Intermittent Legal capacity
  - Legal incapacity can be temporary or intermittent in individuals whose cognitive abilities fluctuate or improve due to treatment or natural course of events.
  - A judge may restore legal capacity at a hearing subsequent to removing it.

Basic Concepts in Capacity: Examples of Legal Capacities

- Consent to Medical Treatment
- Contractual Capacity
- Donative Capacity
- Capacity to Convey Real Property
- Capacity to Consent to Sexual Relations
- Driving Capacity
- Financial Capacity
- Testamentary Capacity

Basic Concepts in Capacity: Consent to Medical Treatment

- Right to refuse Treatment
  - Common-law battery rationale
    - "Every human being of adult years and sound mind has a right to determine what shall be done with his own body" – Justice Benjamin Cardozo (Schloendoff v. The Society of the New York Hospital, N.Y., 1914).
    - "A harmful or offensive intentional touching . . ."
Basic Concepts in Capacity: Consent to Medical Treatment

• Right to refuse Treatment
  • Liberty Interest under Due Process Clause of the 14th Amendment (Cruzan v. Mo. Dept. of Health, U.S., 1990)
  • Constitutional Privacy Right (Gray v. Romeo, D.R.I, 1988)

Basic Concepts in Capacity: Consent to Medical Treatment

• Right to Choose preferred treatment and informed consent
  • Consent to choose is voluntary and knowing, i.e., capacity is implied.
  • "True consent to what happens to one's self is the informed exercise of a choice, and that entails an opportunity to evaluate knowledgably the options available and the risks attendant upon each." (Canterbury v. Spence, D.C. Cir., 1972).
  • Knowledge includes
    • Risks and benefits of alternative treatments
    • Relative competence of different practitioners in applying the treatments to specific conditions.

Basic Concepts in Capacity: Consent to Medical Treatment

• Defined by state statute, typically in relation to advance directives for healthcare decision making.
• Uniform Health Care Decisions Act
  • A "model" act - Provides guidance to state legislatures.
  • Definition of medical consent capacity "... an individual's ability to understand the significant benefits, risks, and alternatives to proposed health care and to make and communicate a health-care decision."
  • Includes knowing, decisional and executional aspects of capacity.
Basic Concepts in Capacity:

Testamentary Capacity

- Testamentary capacity is presumed in Ohio if a person is
  - 18 years or over
  - Not under any legal restraints and
  - Is of “sound mind and memory.”
- Basic elements - The testator has sufficient mind and memory to
  - Understand the nature or what he or she is doing, i.e., executing a will;
  - Generally understand the nature and extent of his or her property;
  - Know those who would have “natural claims” on his or her estate via inheritance via intestacy, i.e., spouse, children and other relatives.
  - Understand his or her relationship to close relatives.

* O.R.C. § 2107.02  ** Niemes v. Niemes, 119 N.E. 503, (Ohio 1917)

Basic Concepts in Capacity:

Financial Capacity

- An “umbrella” capacity: It encompasses more specific forms of capacity including contractual capacity, donative capacity and testamentary capacity.
- Includes
  - The ability to manage one’s financial affairs in a fashion consistent with personal self interest and values.
  - The ability to manage one’s estate.
- Often at issue when probate courts consider appointing a guardian or conservator for all or part of one’s estate.
Basic Concepts in Capacity: 
Capacity to Consent to Sexual Relations

• Relatively complex and contentious legal area.
• Wide variation from state to state in standards.
• Three criteria (Most states include two or all three)
  1. Knowledge of the risks, benefits, and other information relevant to the decision to engage in sexual relations.
  2. Ability to understand information and/or engage in rational reasoning such that the decision is consistent with his or her known values.
  3. The decision is voluntary and not the result of coercion.
• Fourth Criterion: Morality Standard (New York)
  4. The person is capable of understanding the social mores involved in sexual behavior including stigmatization and ostracism.

Basic Concepts in Capacity: 
Clinical Capacity

• Concerns clinical status as assessed by a healthcare professional, usually a physician or psychologist.

• The extensiveness of clinical capacity exams and the expertise of the examiner vary considerably.

• Extensive and detailed examinations conducted by specialists are atypical.

• Often based on a subjective judgment of a generalist physician.
Basic Concepts in Capacity: Assessing Clinical Capacity

- Multiple Clinical Capacities
  - Ask "capacity for what?"
  - Focus on relevant clinical capacities.

- Decisional vs. Executional Capacities
  - Decisional - Involve making a decision
  - Executional - Involve the ability to implement a decision.

Basic Concepts in Capacity: Clinical Capacity

- Clinical Capacity as Continuous vs. Dichotomous
  - Dichotomous view - Lawyers, judges, some clinicians.
  - Continuous view - Psychologists and other clinicians.

Basic Concepts in Capacity: Clinical Capacity

- Clinical Capacity and the Diagnosis of Dementia
  - Dementia ≠ Loss of Clinical Capacity
  - Relevant but insufficient evidence of lack of capacity.
  - A functional analysis of the abilities inherent in the transactions in a legal capacity is necessary.
• Permanent vs. Temporary Incapacity: Relationship to three categories of dementia.
  • Progressive Dementia
  • Arrestable Dementia with persisting deficits.
  • Reversible Dementia without persisting deficits.

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Some Representative Causes of the Dementia Syndrome

<table>
<thead>
<tr>
<th>Reversible Dementia</th>
<th>Arrestable Dementia with Persisting Deficits</th>
<th>Progressive Deficit</th>
</tr>
</thead>
<tbody>
<tr>
<td>Depression</td>
<td>Vascular dementia</td>
<td>Alzheimer’s Disease</td>
</tr>
<tr>
<td>Hypoxia (e.g., from anemia, decreased cardiac output, lung disease)</td>
<td>Alcoholic dementia</td>
<td>Frontotemporal Dementia</td>
</tr>
<tr>
<td>Electrolyte imbalance (e.g., hyponatremia)</td>
<td>Trauma (e.g., dementia pugilistica)</td>
<td>Huntington’s disease</td>
</tr>
<tr>
<td>Hepatic insufficiency</td>
<td>Syphilis (i.e., general paresis)</td>
<td>Parkinson’s disease</td>
</tr>
<tr>
<td>Endocrine disease (e.g., hypothyroidism, Addison’s disease, Cushing’s disease)</td>
<td>B12 deficiency (e.g., long-standing)</td>
<td>Diffuse Lewy Body Disease</td>
</tr>
<tr>
<td>Some intoxications (e.g., therapeutic drugs)</td>
<td>Normal pressure hydrocephalus (e.g., long-standing)</td>
<td>Multiple sclerosis</td>
</tr>
<tr>
<td>B12 deficiency (e.g. of short duration)</td>
<td>Postencephalitic dementia</td>
<td>Creutzfeldt-Jakob disease</td>
</tr>
<tr>
<td>Normal pressure hydrocephalus</td>
<td>Anoxic dementia</td>
<td>Human Immunodeficiency virus dementia</td>
</tr>
<tr>
<td>Diffuse Lewy Body Disease</td>
<td>Progressive Supranuclear palsy</td>
<td>Amyotrophic lateral</td>
</tr>
</tbody>
</table>
Clinicians who may Evaluate Capacity

- May be determined by statute or probate court rules
  - Example 1 - ORC §2111.033
    - Refers to expert opinion for the determination of guardianship
    - General in scope – “Licensed physicians and other persons.”
  - Example 2 - Ohio Rule of Superintendence 66 for probate courts
    - Specifies two classes of experts who may provide opinions on the need for guardianship
      - Physicians
      - Clinical Psychologists

Clinicians Who Evaluate Capacity

- Example 3 - ORC §2111.49(A)(1)(i) – Specifies five classes of experts who may provide opinions on the need for continuation of a guardianship
  1. Licensed Physician
  2. Licensed Clinical Psychologist
  3. Licensed Independent Social Worker
  4. Licensed Professional Clinical Counselor
  5. Mental Retardation Team

Clinicians Who Typically Evaluate Capacity

- Physicians
  - Primary Care or Generalist Physicians
    - Often an individual’s personal physician
  - Specialist physicians - Board Certified Specialties*
    - Psychiatrists
    - Neurologists
    - Geriatricians

- Professional Psychologists – Board Certified Specialties**
  - Clinical Psychologists
  - Clinical Neuropsychologists
  - Forensic Psychologists

* American Board of Medical Specialties
** American Board of Professional Psychology
**Problems in Assessing Clinical Capacity**

- Inter-rater reliability of physician capacity judgments is low
- Overall agreement of 56% in one study of mildly demented individuals (Marson et al., 1997a).
- Physicians differ in terms of which cognitive process they focus on when making judgments of clinical capacity (Marson et al., 1997b).

**Assessing Clinical Capacity**

  - Provides detailed guidelines for conducting clinical capacity exams for six different capacities.
  - Companion manuals were published for lawyers and judges.

**Assessing Clinical Capacity: The ABA/APA Model**

Nine components of ABA/APA Model

1. Legal Standards
2. Functional Elements
3. Diagnoses
4. Cognitive underpinnings
5. Psychiatric or Emotional Issues
6. Values and preferences
7. Risk of Harm and Level of Supervision Needed
8. Means to Enhance Capacity
9. Clinical judgment
Directing your legal and healthcare decisions when you lack capacity to do so

Advance Directives

- Today’s Topics
  - How to let others know your healthcare preferences
  - How to arrange for someone to make healthcare decisions for you if you can’t.
  - How to arrange for someone to make financial decisions if you can’t.
Advance Directives

• Advance Directives we will discuss today
  • Living Will
  • Durable Power of Attorney for Health Care
  • Power of Attorney for Financial Affairs
• Note: In most cases the services of an attorney are not necessary complete and execute advance directives.

What is a living will (declaration)?

• Document created expressing your wishes should you enter into a permanently unconscious or terminally ill state, addressing the use, continuation, withholding, or withdrawal of life-sustaining treatment when you are unable to express such wishes.
• This must be executed before a person loses legal capacity to perform this action.

Permanently Unconscious

• An irreversible condition in which a person is unaware of his/her surroundings and unable to feel pain or suffering.
• Requires diagnosis by two physicians, who must agree that it is not reasonably possible that the person will regain consciousness and that he or she is unable to feel pain or suffering.
Terminally Ill

- irreversible, incurable and untreatable condition caused by disease, illness or injury.
- Requires diagnosis by two physicians, who must agree that recovery is not reasonably possible and death is likely within a short period of time if no life-sustaining treatment is given.

Why have a living will?

- To ensure a person's wishes about life-sustaining treatment are followed when he or she can no longer voice his or her own wishes.

Key characteristics of Living Wills

- A Living Will has priority over other advance directives, e.g., Durable Power of Attorney
- It identifies actual wishes.
- It's important to tell physicians, family, and friends about living wills and where they are located.
- A living will is revocable.
DURABLE POWER OF ATTORNEY FOR HEALTH CARE

- Allows an individual to name an agent to act on his or her behalf to make health care decisions for him or her if he or she becomes unable to make such decisions.
- The agent may be any adult except:
  - The patient's attending physician
  - The physician's employees
  - Nursing home administrator
  - Employees of healthcare institution where the patient is receiving care (unless relatives or members of same religious order)
  - An alternate agent may be designated

Durable Power of Attorney for Healthcare: Some key characteristics

- The designated agent has the power to authorize and refuse medical treatment for the patient.
- The patient's physician should consult with the agent when the patient is unable to make and express healthcare decisions.
  - This includes when incapacity is temporary and immediate attention is needed.
- The agent and healthcare workers must abide by the patient's living will (the living will has priority).

Durable Power of Attorney for Healthcare: Bases for Decision-Making

- If the agent knows the patient's wishes: The agent should make healthcare decisions based primarily on the patient's wishes.
- If the agent does not know the patient's wishes: The agent should make healthcare decisions based primarily on the best interests of the patient.
DURABLE POWER OF ATTORNEY FOR HEALTH CARE

- A key difference between a living will and a durable power of attorney for healthcare:
  - A Living Will is only effective when you are permanently unconscious or terminally ill and unable to express your wishes for end-of-life care.
  - A Durable Power of Attorney for Health Care is effective when a person lacks capacity and is unable to make and/or to express his or her health care wishes.

- An Agent may order the withdrawal of life-sustaining treatment if
  - The patient is in a terminal condition or a permanently unconscious state, and
  - If two physicians have confirmed the diagnosis, and
  - Both physicians have determined that the patient has no reasonable possibility of regaining the ability to make decisions

General (Financial) Power of Attorney

- Allows a person to designate an agent to make financial decisions for him or her including
  - Personal property transactions
  - Real Estate transactions
  - Securities transactions
  - Banking transactions
  - Collect and pay debts
  - Pursue and defend against legal actions
  - Borrow money
  - Make gifts
  - Keep financial records
General (Financial) Power of Attorney

- Notes:
  - The power of attorney may be immediate (unlike the durable power of attorney for healthcare) or "springing," i.e., come into effect upon a particular event (such as illness, etc.).
  - The agent is expected to follow the principal's wishes, if known.
  - The agent is expected to be a fiduciary
    - Act in the principal's best interests
    - Not engage in self-dealing
  - This power of attorney is also revocable.

Advance Directives: Important Points

- Advance directives and other legal documents should be completed while the person still has the capacity to execute them!
  - Ideally before a person show any signs of cognitive deterioration
  - Persons may retain sufficient capacity to understand the transaction in the early stages of dementia.
  - One or more alternate agents should be designated in case the primary agent is unable to serve due to death, illness, unavailability.

What happens if a person does not have advance directives and lacks legal capacity due to dementia?

- A hearing may be necessary to declare the patient incompetent and appoint a guardian
  - This can be expensive
- If the person is in the hospital
  - A surrogate decision-maker may be consulted.
  - Hierarchy of decision-makers is determined in law.
Ohio Revised Code: Hierarchy of Presumed Surrogate Decision-Makers
1. Attorney in Fact in written document.
2. Guardian (if patient has one)
3. Patient’s spouse
4. Adult child or majority of adult children
5. Patient’s Parents
6. Adult sibling or majority of adult siblings
7. Nearest adult not related by blood or adoption (friend) who is available within a reasonable period of time.

Guardianship or Conservatorship
• Some states use these terms interchangeably
• Other states use them to define two different legal relationships
  • Guardian = Guardian of the person
  • Conservator = Guardian of the person’s estate
• Ohio prefers the use of the term guardian to cover both guardian of the person and guardian of the person’s estate.

Definition of a Guardian
• A person appointed by the court (usually probate court) to serve as a representative of a person with legal disability,
  • Once appointed, the guardian can make decisions and execute actions for the person without judicial involvement provided the guardian follows the procedures and rules specified by state law and any special conditions imposed by the court.
  • Usually reporting to the court at regular intervals is required.
  • The legal disability is defined in Ohio as “Incompetence.”
Guardians

- Guardian are expected to be fiduciaries
- Act in the Ward's best interests
- Not engage in self-dealing

Definition of “Incompetent”

- Ohio Revised Code (O.R.C.) 2111.01(D):
  - “'Incompetent' means any person who is so mentally impaired as a result of a mental or physical illness or disability, or mental retardation, or as a result of chronic substance abuse, that the person is incapable of taking proper care of the person's self or property or fails to provide for the person's family or other persons for whom the person is charged by law to provide, or any person confined to a correctional institution within this State.”

Appointment of Guardians

- Two Step Process
  1. Declaration of incompetence
     - Typically involves a “Statement of Expert Examination” completed by a physician or clinical psychologist attesting to the ward's physical and/or mental disability.
  2. Appointment of the guardian
     - Basic criterion is “best interest of the ward.”
Guardianship and Power of Attorney Compared

- Appointment process
  - Power of attorney – By the principal
  - Guardianship – By the court
- Relation to Legal Capacity
  - Power of attorney – Requires legal capacity
  - Guardianship – Requires lack of legal capacity usually supported by an expert evaluation
- Revocability
  - Power of attorney – Revocable by the principal
  - Guardianship – Terminated only by the court

Guardians

- May or may not be a family member
  - In some cases family members may be in conflict with each other
  - The interests of family members may be in conflict with the interests of ward
- Professional guardians – Typically lawyers who serve as guardians for several persons.
- Volunteer guardians – Often vetted by social agencies and approved by the court.

Types of Guardianships

- Guardians of the person
  - May make medical decisions for the ward in the absence of advance directives.
  - Oversee the residential placement of their ward (with court approval)
  - Ensure the ward receives proper professional services.
  - Release medical records and other medical information
  - Assist the ward in developing maximum independence and self-reliance.
  - Serve as a surrogate decision-maker
Types of Guardianships

- Guardian of the Estate
  - Make financial decisions
  - Enter into contracts
  - File lawsuits
  - Engage in Estate Planning
  - Sell real estate
  - Apply for government benefits

Types of Guardians

- Short-term or temporary guardians
  - Appointed for specific needs
  - Temporary incapacity
  - Temporary replacement of a guardian who dies or resigns.
  - Medical emergencies
  - For court orders and proceedings – “Guardian Ad Litem”
- Limited Guardianships
  - Example – For financial transactions over $500

Thank You

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- WellsBrooke
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- HCR ManorCare