Alzheimer’s Disease and Dementia:
Diagnosis, Treatment, and the
Important Role of the Caregiver

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What is Needed
Humor
Hope
Help
Humility
Health
Test: True or False

This is a problem of “normal” aging

False!

It is a myth that if you live long enough, you’ll develop significant memory and cognitive impairment, Alzheimer’s disease or dementia.

Fact in 2016

• Alzheimer’s disease and other causes of dementia are not an inevitable part of aging.
• Almost everyone experiences some mild forgetfulness with aging.
• But not everyone develops a brain disease, such as Alzheimer’s, that significantly affects:
  – Memory
  – Judgment
  – Personality
  – Behavior
• Millions of people reach old age with intact memory and relatively little decline in mental abilities.
Significant Cognitive Decline is NOT Part of Normal Aging

When there is significant decline, there is something wrong!
That something may be dementia

What is Dementia?

Dementia refers to a new loss of memory and other cognitive functioning that results in significant impairment in social or occupational functioning.

That is, it gets in the way of routine independent living.

Dementia is Not an Illness or Disease
Causes of Dementia

• “Reversible”
  - Hypothyroidism
  - Vitamin B12 Deficiency
  - Clinical (Major) Depression

• Neurodegenerative/Progressive Disease
  - Vascular Dementia/Multi-Infarct
  - Frontotemporal
  - Dementia with Lewy Bodies
  - Chronic Traumatic Encephalopathy (athletes)
  - Alzheimer’s Disease (75-80% of all dementia)

Dementia is a Clinical Syndrome, Not A Disease

Alzheimer’s is a Brain Disease that Causes Dementia

Alzheimer’s Disease and Dementia

• **NOT** a continuum

dementia = mild  ➔  AD = severe
Alzheimer’s Dementia Numbers
• Every 67 seconds, someone in the US develops AD.
• In US, around 5.3 million people now have AD.
• By 2025, this number is expected to be >7 million and by 2050 will reach 14 million!
• 1 in 9 persons ≥65 currently have Alzheimer’s dementia
• 1 in 3 ≥85!!
• 6th leading cause of death in the country and the only cause of death among the top 10 in the US that cannot be prevented, cured or even slowed.

Alzheimer’s Disease is a Fatal Disease
• >700,000 deaths per year in U.S.
• Average time from diagnosis to death is 8 years.
• Can last up to 20 or more years.
• Some can be shorter
• It depends upon how advanced the disease was at time of diagnosis, age at diagnosis, overall health, etc.
• Most common causes of death are infections, such as pneumonia.
• But, someone can die from the brain being so destroyed that it can no longer sustain life.
What are the Cognitive Symptoms?

• **Memory Disorder: new learning**
  — Rapid forgetting, repeating stories, the information is NOT there
  — Older memories remain

• **Language Difficulties (aphasia)**
  — Significant difficulty with word-finding
  — Later on problems with comprehension and expression

• **“Executive” Functioning Deficits**
  — Planning, organization, multi-tasking, abstraction, decision-making, judgment

• **Anosognosia**
  — Poor awareness and insight

The Perfect Storm

• Cannot remember what happened five minutes ago...and...
• Is unable to be aware that she or he has a neurological problem

What are the Neuropsychiatric Symptoms

• Some of these changes are directly due to the part of the brain that is being hurt by the disease...
• Some are caused by the individual trying to make sense of their reality
• Apathy and Abulia
• Depression: is it Apathy and Abulia
  — often the presenting symptom
• Aggression and Agitation
• Impulsivity/Disinhibition
• Anxiety and Fear
• Delusions and “Paranoia”
• Hallucinations
What you see may not be what you think...or what they are experiencing

• Examples
  – Lying in bed or sitting in chair, not spontaneously engaging in activities
  – Talking about having a conversation with deceased spouse or parent
  – Blaming a loved one or aid for stealing from wallet or taking something
  – Not eating what is on their plate

AD and the Economic Crisis: Now and in the Future

• The national cost of caring for people with AD is about $250 billion every year (i.e., >25% of famous Stimulus Bill). This will rise to $1.1 trillion by 2050.
• In 2015, Medicare and Medicaid will pay $153 billion in health care, long-term care and hospice for people with Alzheimer’s and other dementias.
• Out-of-pocket spending another $44 billion!
• Total per-person health care and long-term care payments in 2014 for Medicare beneficiaries with Alzheimer’s and other dementias were three times as great as payments for other Medicare beneficiaries in the same age group ($47,752 per person for those with dementia compared with $15,115 per person for those without dementia)
• Average cost for memory care assisted living is $59,250/yr.
• Costs to businesses for employees who are dementia caregivers is $37 billion/yr.

Caregivers

• ~15 million dementia caregivers.
• Caregivers not only suffer emotionally but also physically.
• Lost dreams
• But, the person with AD is not “dead” and both patient and spouse can benefit from maintaining emotional and physical closeness.
• ABC’s Good Morning America, September 16, 2011
Alzheimer’s Science 101 Class

AD is a Neurodegenerative Disease Marked by “Plaques and Tangles”

• Since Dr. Alzheimer first described the disease over 100 years ago, the hallmark features have been plaques and tangles seen in brain tissue.
• Plaques (neuritic plaques) are made up of an abnormal form of a protein called beta amyloid, and are found outside of the neurons.
• Tangles (neurofibrillary tangles) are made up of an abnormal form of another protein, tau, and are found inside neurons.
AD Doesn’t Just Come Out of the Blue

- It is likely that the plaques and tangles begin to accumulate many, many years before there is evidence of any cognitive impairment.
- Recent study found that the amyloid begins to accumulate ~25 years before symptoms!
**Current View of the Progression of AD**

1. Abnormal forms of Beta Amyloid (Aβ) begin to accumulate and clump together into neuritic plaques. This happens years before symptoms.
2. Tau begins to change from healthy to unhealthy/toxic form and leads to neuronal injury.
3. Structural changes (e.g., atrophy) occur.
4. Early symptoms begin (e.g., memory).
5. Progression of cognitive and neuropsychiatric symptoms lead to clinical dementia, i.e., impacting daily functioning and independence.

**Stages of Alzheimer’s Disease**

- **Preclinical**
  – No symptoms but the brain changes have begun

- **Mild Cognitive Impairment (MCI)**
  – The term used to describe the first symptoms of Alzheimer’s, before “dementia”
    - Memory or other cognitive complaints
    - Abnormal when formally tested
    - But, no “dementia,” i.e., the impairment is not bad enough to get in the way of daily functioning

- **Dementia**
  – Memory and other cognitive difficulties bad enough to impact daily life

**Progression of Alzheimer’s Disease**

**New Diagnostic Categories**

- Cognitively Normal = Preclinical AD
- Mild Cognitive Impairment (Due to AD)
- Dementia (Due to AD)

*From D. Knopman, Alzforum presentation 2011*

*Very Fuzzy!*
The Diagnosis of Alzheimer’s Disease

Current Clinical Diagnosis of Alzheimer’s Disease

• Without looking at actual brain tissue, the diagnosis of AD is never completely certain.
• The current “best” diagnosis is based on history, clinical examination, imaging (CT, MRI, PET), and formal memory/cognitive testing.
HELP!!!!!

• I don’t know the best way to “test” for it
• I don’t have time
• There’s nothing that can be done
• What do I tell the patient?
• Where can I get help?

How to Test???

• Patient
  – Test for reversible causes
  – Mental Status/Cognitive Testing
    • Rule out delirium
    • Orientation
    • Memory: ability to learn and recall new information
    • Executive Functioning: planning, organization, multitasking
• Informant!
  – Functional independence

The MMSE: Yuck!

• What does a score of 29 mean?
• What does a score of 15 mean?
• What does a score of 24 mean?!!!
• What is wrong with the patient who gets 0 of 3 words recalled?
• What is wrong with the person who cannot repeat “no ifs, ands, or buts”?
• What is wrong with a patient who has 2 points off for Orientation, including “County”?
Mini-Mental State Examination

• Brief, structured cognitive status examination
• 10 minutes to administer
• Typical deterioration of 3–4 points per year
• Sensitivity and specificity vary in different patient populations
• Adjustments for age, education and race may be necessary
• Beware: Many false positives and false negatives; does not make the Diagnosis!

<table>
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<th>Scores Range from 0–30</th>
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<td>≥27</td>
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<td>26 – 21</td>
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<tr>
<td>20 – 11</td>
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<td>10 – 0</td>
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My Recommendation

• Do not use the MMSE as a stand-alone screening
• Add to it or use something else
Clocks

- Draw the face of a clock
- Put in all the numbers
- Set the hands at 10 after 11
- Several Different Scoring Methods
  - Subjective, single score
  - Subjective, normal, questionable, impaired
  - Many formal, "objective" scoring systems
77 year old male with 10 yrs education.
Diagnosis: Probable AD

Montreal Cognitive Assessment (MoCA)

- Excellent for some patient groups (e.g., higher functioning, higher education, good vision and attention).
- Includes important areas of assessment (e.g., delayed recall, naming, verbal fluency – though it is phonemic and not semantic).
- Again, some limitations
And...If you have just a few minutes...

- “Tom and Bill went fishing. They caught three black bass.”
  - Seven individual pieces of information.
  - If not perfect from free recall, add cues, followed by multiple choice.
- Then do a clock.
- Ask some questions about current events (in areas of interest to the patient).
- Then do another recall of the two sentences.

The AD8 Informant Interview

- Informant-based questionnaire that can be administered at home or in waiting room
- Detects change compared with previous level of function
  - No need for baseline
  - Patients serve as their own control
  - Minimally affected by education, race, gender
- Brief (<3 minutes), yes/no format
  - 2 or more “yes” answers highly correlated with presence of dementia
  - Sensitivity 85%, Specificity 86%

Do Not Be Afraid to use the “A Word”
It is Okay to Give a Diagnosis of “Alzheimer’s Dementia”

• Okay to say:
  – “Based on my evaluation, I am confident that there are some pretty significant problems in your memory and other cognitive functions. The term that is used to describe this is “dementia.” In the large majority of cases, dementia is caused by a brain disease called Alzheimer’s disease. Although I cannot be completely sure that Alzheimer’s is the underlying cause of your dementia, I am pretty confident. There are many things that can be done to try and treat the symptoms and possibly slow down the progression. And, new research is providing tremendous hope.”

What NOT to Say to the Patient

• “Don’t worry... its just early dementia.”

• Heard as:
  • “Thank god it’s not Alzheimer’s.” OR
  • “It is not Alzheimer’s yet.”
Additional Statements to Avoid

• Sorry, but it is Alzheimer’s disease; have him take this Aricept and call me in a few weeks to see if we should increase it. You should probably get his affairs in order.
• It’s just normal aging...

Patient/Family Education and Support

• Integrate medical care and support
  — Do not try and manage all of the patient’s and family’s needs alone.
  — Alzheimer’s Association (800) 272-3900
    • www.alz.org
    • Care Consultation Program – Free!
  — Geriatric Care Managers
    — Be aware of caregiver stress and limitations
• Discuss diagnosis and treatment
• Involve early stage patients
• Discuss progression
• Discuss decisional capacity and end-of-life decisions

What to Tell Your Patients’ Caregivers About Communicating with Their Loved Ones

• Do NOT argue
• Do NOT use logic
• Do NOT belittle or treat like a child
• Do NOT expect YOUR reality
• Do NOT say, “remember...” or “I just told you...”
Dr. Stern’s Long List of DO’s

• Understand their reality
• Understand their reality
• Understand their reality
• Understand their reality
• Smile
• Smile
• Smile
• Smile

Treatment

• Non-pharmacological approaches for treatment and prevention of symptoms that have some research to support them:
  – Exercise
  – Mediterranean Diet
  – Social Interactions
  – Intellectual Stimulation: Kind of....
  – Music
  – Arts, in general

Currently Available FDA-Approved Medications

• There has not been a new FDA approved drug for AD for over 12 years!
• Existing medications:
  – Razadyne® (galantamine)
  – Exelon® (rivastigmine)
  – Aricept® (donepezil)
  – Namenda (memantine)
• The Three Somes:
  – Some symptom improvement
  – Some small amount of time
  – Some people
• They do not modify the disease course in any way
New Treatments Under Study

- Over 100 currently active Phase 2 and 3 clinical trials of new medications.
  - Anti-amyloid
  - Anti-tau
  - Anti-inflammation
  - Neuroprotective
  - Others

Clinical Trial “Failures”

- Over the past several years, some high profile clinical trials, especially of anti-amyloid antibody medications, have “failed.”
- But….stay tuned
Prevention

- If we can delay the onset of Dementia from AD by just five years, we can cut in half the number of people with the dementia!
- So, Prevention and/or Delay is critical.
Prevention Clinical Trial
For People at Risk for Sporadic AD

• A4: The Anti-Amyloid Treatment in Asymptomatic Alzheimer's Disease Trial
  – The A4 trial is studying the effectiveness of solanezumab, in 1,150 symptom-free volunteers WITHOUT genetic predisposition for AD, whose PET scans show abnormally high levels of beta-amyloid in the brain.

The Brain is the Only Part of the Body that Cannot Easily be Tested for Injury or Disease
Biomarkers

- Objective biological tests of an illness, injury, condition, disease
  - Heart = EKG, cholesterol, blood pressure
  - Diabetes = blood sugar, HA1C
  - Pneumonia = Chest X-ray
  - Cancer = biopsy
  - Orthopedic injury = X-ray/MRI
  - Kidney disease = blood tests
  - Liver disease = blood tests

Biomarkers for AD

- MRI
  - Hippocampal/Temporal lobe atrophy
- LP
  - Decreased CSF amyloid/Increased Tau
- PET (FDG)
  - Bilateral temporal or parietal lobe hypometabolism
- Three FDA approved PET amyloid imaging tests
  - Amyvid: florbetapir F 18 injection; Avid Radiopharmaceuticals
  - Vizamyl: flutemetamol F 18 injection; GE Healthcare
  - Neuraceq: florbetaben F 18 injection; Piramal Imaging
- New PET scans for p-tau in clinical trials

MRI showing Hippocampal Atrophy
PET Scan showing Beta Amyloid

PET Scan showing p-Tau!

A Blood Screening Test?  
Measurement of Tau in Plasma

- Plasma Tau (Quanterix Simoa Platform)
  - Promising preliminary results, but what does it mean to measure tau that is in the blood and not from the brain???
- Plasma exosomal tau!
  - Exosomes are nanovesicles that are released from all cells and contain the “cargo” from the parent cells (including proteins)
  - Cross blood-brain barrier
  - Isolated in plasma
  - Measure tau
Biomarkers in Addition to Clinical Evaluation Should Make the Diagnosis Much More Accurate

- Clinical examination and cognitive testing
- Biomarker for amyloid deposition (LP or PET)
- Biomarker for neurodegeneration (atrophy)
- Future: measure of p-tau!

From Jack et al. (2010)
What is Needed?

• With the growing number of seniors, AND with modification of the disease course, there will be more and more individuals living with the disease, and at earlier stages of severity.
• Quality of Life issues are critical for both the patient and the caregiver.

Translation

• Increased training of primary care clinicians
• More support and facilities
  – Adult Day Care, specialized for dementia and personalized for age and symptoms
  – Assisted Living Facilities and Memory Support residences, specialized in dementia and based on scientifically-based programming
  • Music and Arts
  • Intellectual stimulation
  – Research Participation
  – HOPE!!!!! And..........