Welcome to the Your Health Lecture Series!

Tonight’s Lecture:
Living Well with Alzheimer’s Disease

Lecture Begins @ 6:30pm

Moderator: Dr. Jean Nagelkerk
Vice Provost for Health
Grand Valley State University
Dr. Timothy Thoits, MD
Neurologist
Spectrum Health Medical Group

Clinical Associate Professor
Michigan State University College of Human Medicine

Tonight’s focus areas:

- Definition and Pathology of Alzheimer’s Disease
- Treatments
- Research
Dr. Rebecca Davis, PhD, RN
Professor
Kirkhof College of Nursing
Grand Valley State University

Tonight’s focus areas:

• Health Promotion
• Psychosocial Health
• Everyday Decision Making
Your Health Lecture Series

Living well with Alzheimer’s Disease

Timothy Thoits MD, MPH

November 13, 2017
Objectives

Definition of AD
Pathology of AD
Treatment for AD
Research
DSM V  Diagnostic Criteria for AD

Evidence of a decline in >1:

Learning and memory   Language
Executive functioning   Complex attention
Perceptual motor   Social cognition

Interferes with daily life

Not in delirium   Not schizophrenic   Not depressed

Insidious onset & gradually progressive
Mild Cognitive Impairment (MCI)

MCI refers to an in-between state: normal aging --- dementia.

- Cognitive change is greater than expected for age
- Able to maintain independence in the community
- Ability to carry out activities of daily living is preserved
Mild Cognitive Impairment (MCI)

Mild cognitive impairment-amnestic (aMCI)

Cognitive decline with intact ADLs - corroborated

Memory impairment
Mild Cognitive Impairment (MCI)

Mild cognitive impairment-nonamnestic (naMCI)
Cognitive decline with intact ADLs—corroborated
Non-memory cognitive impairment (language, attention, executive function, visual-spatial)
Preclinical AD

The stage of AD in which the molecular pathology of AD is present in the brain- years before symptoms appear.

Stage 1  No cognitive deficits, amyloid deposition begins

Stage 2  CSF changes noted, imaging changes noted

Stage 3  Biomarkers increase and cognitive deficits appear, not dementia
Pathology of AD

Amyloid Plaques

Aβ 42 deposited extracellularly in the brain, in a sequential manner starting in the cortex, followed sequentially by the hippocampus, basal ganglia, thalamus, and basal forebrain before finally reaching the brainstem and cerebellum.

Neurofibrillary Tangles

The major component of the neurofibrillary tangle (NFT) is tau within neurons and their cell processes. First, pretangles form in the neuron cytoplasm. Then, tau is organized into fibrils as neurofibrillary tangles. In neurofibrillary tangles, tau has become hyper-phosphorylated and abnormally conformed.
Pathology of AD

The oligomer formation $\text{A}\beta$ 42 and aggregation results in a cascade of events:

- tau protein neurofibrillary tangle formation
- inflammatory response
- oxidative injury

Causing neurotoxicity and neurodegeneration
Amyloid Theory AD
Genetics of AD

The lifetime risk of AD dementia in first degree relatives is approximately 39%.

Risk increases to 54% by age 80 if both parents have AD.

Twin study from Sweden based on 392 pairs of twins, the genetic component of AD was estimated to be 58%–79%.

Three fully penetrant gene mutations have been described to cause early onset AD.
Genetics of AD

**Early onset:** Amyloid Precursor Protein (APP) Chromosome 21

(<65 yo) Presenilin 1 (PSEN1) Chromosome 14
Presenilin 2 (PSEN2) Chromosome 1

**Late onset:** Apolipoprotein E (APOE)

APOE has 3 isoforms:  ε4 associated with **high risk**
 ε3 associated with **neutral risk**
 ε2 which is **protective**
Apolipoprotein E (APOE)

Genetic risk factor for late onset AD

APOE functions primarily in the transport of lipids/cholesterol from astrocytes to neurons.

The presence of the APOE ε4 allele is associated with:

- decreased CSF Aβ 42
- increased brain Aβ burden
- increased risk for developing AD
Diabetes

Type 2 DM is a risk factor for both AD and VaD, by causing inflammation and small vessel disease (cerebrovascular pathology)

80% of AD patients have DM or show abnormal blood glucose levels (Zhao and Townsend, 2009)

Insulin resistance is associated with:

• lower regional cerebral glucose metabolism and impaired memory performance (Willette, 2015)
• faster rates of atrophy and possibly neurodegeneration
• impaired amyloid clearance
Diabetes

Insulin resistance leads to activation of glycogen synthase kinase.

Glycogen synthase kinase activity promotes:

- oxidative stress
- DNA damage
- higher levels of amyloid (Aβ 42) binding on PiB PET scans
- more Aβ 42 deposition in the brain
- higher tau levels in the spinal fluid and brain
Hypertension

Hypertension is the leading cause of small vessel disease (cerebrovascular pathology)

Patients with AD and hypertension have worse cognitive function than AD patients without hypertension

Maintaining very good control over hypertension may slow progression of AD.
BIOMARKERS

Imaging
Cerebral Spinal Fluid (CSF)
Plasma
Imaging

Structural imaging: MRI hippocampal atrophy

Functional imaging: SPECT (blood flow), FDG-PET (glucose use)

Cerebral amyloid angiopathy (CAA)

Amyloid (Aβ) imaging (PiB)
Structural MRI  hippocampal atrophy

AD  Normal
Functional FDG-PET glucose use
Cerebral Amyloid Angiopathy (CAA)
Amyloid (Aβ) binding  PiB-PET
CSF AD Biomarkers

- Reduction in the CSF Aβ 42
- Elevation in the CSF tau protein or p-tau

Sensitivity 85% + specificity 86%

Normal CSF levels of Aβ 42 and tau have been reported in autopsy-proven AD patients
Plasma Biomarkers

To date, none of the plasma biomarkers have the sensitivity or specificity to detect AD pathology.

10 different lipids from serum used to predict conversion from MCI to AD within 2-3 years with >90% accuracy (Mapstone, 2014)
35% of dementia attributable to combination of 9 risk factors:

- Education to a maximum of age 11–12 years
- Midlife (45-65 yo) hypertension, obesity, and diabetes
- Hearing loss
- Late-life depression
- Physical inactivity
- Smoking
- Social isolation
Treatment

Pharmacological

Nonpharmacological
Treatment

Cholinesterase inhibitors: donepezil (Aricept)
    rivastigmine (Exelon)
    galantamine (Razadyne)

Mild-Mod AD by the FDA

NMDA receptor antagonist: memantine (Namenda)

Mod-Severe AD
Treatment

Physical activities - daily

Cognitive activities - daily

Mediterranean diet

Yes: olive oil, vegetables, fish, legumes, nuts

No: red meat, dairy

Maintain good control over BP, serum glucose
Production of monoclonal antibodies
Research

Bapineuzumab

- binds amyloid proteins, improves amyloid removal from the brain
- lowers p-tau levels in CSF
- no improvement clinically

Solanezumab

- binds Aβ protein
- No improvement or slowing of cognitive deficits
Research

aducanumab

n = 165  monthly infusions
binds Aβ aggregates, including oligomers and insoluble fibrils
slows progression of Aβ plaque deposition
slows cognitive decline in prodrome or mild AD
Hypertension is associated with worse cognitive function and hippocampal hypometabolism in Alzheimer's disease.

Riederer P1, Korczyn AD2, Ali SS3, Bajenaru O4, Choi MS5, Chopp M6. The diabetic brain and cognition.


Living Well With Alzheimer’s Disease
The future
More than 5 million Americans are living with Alzheimer’s disease.

Adults Aged 65 and Older with Alzheimer’s Disease,* By Sex, 2012

- Male: 1.8 million
- Female: 3.4 million

*Estimates are based on the Chicago Health and Aging Project incidence rates converted to prevalence estimates and applied to population projections; assumes the same proportion female as in 2010.

What can be done after diagnosis?
I have a memory problem, what should I do?

- “I don’t want to know” – common problem

- Memory problems under-diagnosed by many
  - Ageism
  - Poor training
  - Under-reported problems by patients

- Diagnosis uncertain
  - No definitive test for Alzheimer’s disease, MCI, etc.
  - What does it mean if I have a diagnosis?
Current Model of Care

* **Good care!**
  - Management of existing comorbid conditions
  - Some prevention
  - Management of problems as they occur

* **Medications**

* **Opportunities**
  - Health promotion and planning
Why should we care?

- Possibility to delay symptoms
- Increased quality of life
- Decreased illness burden
Health Promotion

- Increasing well-being

- Moving towards being healthy

- Moving away from unhealthy behaviors
Why consider health promotion with dementia?
Health Promotion

Specific to Dementia

**Psychosocial Health**
- Supportive environments
- Activities
- Decision making
- Social Networks
- Relationships

**Physical Health**
- Sleep
- Exercise
- Nutrition
Sleep

* Sleep is essential for well-being

* Over half of persons with dementia have sleep changes... even in early stages

* Improved sleep helps with memory

* Must screen for common sleep related disorders (i.e. sleep apnea)
* Sleep Remedies

* Keep sleep diary
* Some Evidence for:
  * Bright light therapy
  * Increased daily activity
  * Exercise
  * Clubs/Groups/Events
* Structured bedtime routines

Exercise

- Increases overall health
  - Cardiovascular
  - Function
  - Endurance

- Some evidence for
  - Improved cognition in persons with Alzheimer’s
  - Slowed progression of the disease

- Nutrition

- Frailty and decreased weight common in AD (and aging)

- Malnutrition common in AD and in aging (30-50%)

- Providers often not well versed in nutrition*

* Nutrition: Recommendations

* Observe for weight loss or muscle mass

* Recognize that overweight does not rule out malnourished

* Eat a healthy, well balanced diet

* Keep food diary if concerned

* Discuss with a nutritionist and provider if concerned
Psychosocial health

Promoting good relationships, maximizing independence, social networks, activities, and other factors related to well-being
Social Networks

* The people in your circle
  * Friends
  * Family
  * Paid help

* People you can rely on when you need them
Social Networks

- Maintaining bonds with others can help!
- Making new connections
- Sharing the news
- Asking for support
* Relationships

* Roles may change as disease progresses

* Many adapt in “isolation”

* Caregiving; yet maintaining life as a dyad
* Relationships: Example

* SHARE intervention
* Couples meet with counselor
* Develop individualized goals, plan
* Make decisions about future
* Communicate
* Recreation

* Activities (individualized)
* Recreation “Clubs”
* Results:
  * Decreased medications
  * Decreased isolation
  * Improved nutrition
  * Improved fitness
  * Enjoyment
  * Memories from past

Watermemories Swimming Club
Supportive Environment

- Early diagnosis and quality care and support
- Specialized memory loss services
- Dementia-aware and responsive client services
- Welcoming and supportive spiritual environment
- Dementia-aware and responsive customer service
- Suitable transportation and public spaces
- Emergency preparedness and response
- Independent living and quality of life support

http://actonalz.org/sites/images/ACT-CommunityGraphic-1.jpg
* Decision Making

* Resources
* Legal
* Financial
* Personal
* Health
* Information

* Requires open communication and acceptance of diagnosis
Big Decisions

* Financial decision making
* Medical decision making
* Living circumstances
* Caregiver involvement
  * Acting in best interest
  * Taking care of issues legally
  * Planning from early on in the disease
  * Don’t hide in the sand
  * Seek help from social worker/health care provider if needed
Driving is a complex skill

- Requires cognitive and physical abilities
- Driving ability usually declines over course of disease
- Often is very difficult to give up
Driving Warning Signs

* Family notice problems
* Does not obey traffic rules and/or signs
* Can’t stay in lane
* Confusing the pedals
* Getting lost
* Getting angry while driving
What to do if driving becomes a problem?

- Talk to person with dementia
- Indicate your concerns
- Plan for transportation
- Talk to HCP
- HCP can order an evaluation if needed
- Don’t wait too long!

Taking Medications

* Keep good records
* Make a schedule
* Keeping a routine
* Use pill boxes
* Medication reminder systems
* Reducing unnecessary medications

http://ep.yimg.com/ca/I/epill_2267_1968352
Every Day Decision Making

- Input into daily decisions
  - What to wear
  - What to eat
  - What to do, when to do it
  - Other daily decisions
- These decisions occur multiple times per day

http://www.nipic.com/show/10895915.html
Participating in EDDM is important for people with dementia

- Allows sense of control
- Personhood
- Quality of life

Persons with dementia can make many decisions

- May need support as the disease progresses.

“Would you like to wear the green dress or the red dress.”
People with dementia can have a good quality of life
Must maintain “normal” as much as possible
Health promotion is important
Some decisions require help from caregivers
Persons with dementia can make some everyday decisions
Questions?
Thank you for attending the Your Health Lecture Series!