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SPECTRUM HEALTH

MICHIGAN STATE UNIVERSITY
College of Human Medicine

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

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Your Health Lecture Series

Living well with Alzheimer's Disease

Timothy Thoits MD, MPH

November 13, 2017

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Objectives

Definition of AD

Pathology of AD

Treatment for AD

Research

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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

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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

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Mild Cognitive Impairment (MCI)

Mild cognitive impairment-amnestic (aMCI)

- Cognitive decline with intact ADLs - corroborated
- Memory impairment

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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)

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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

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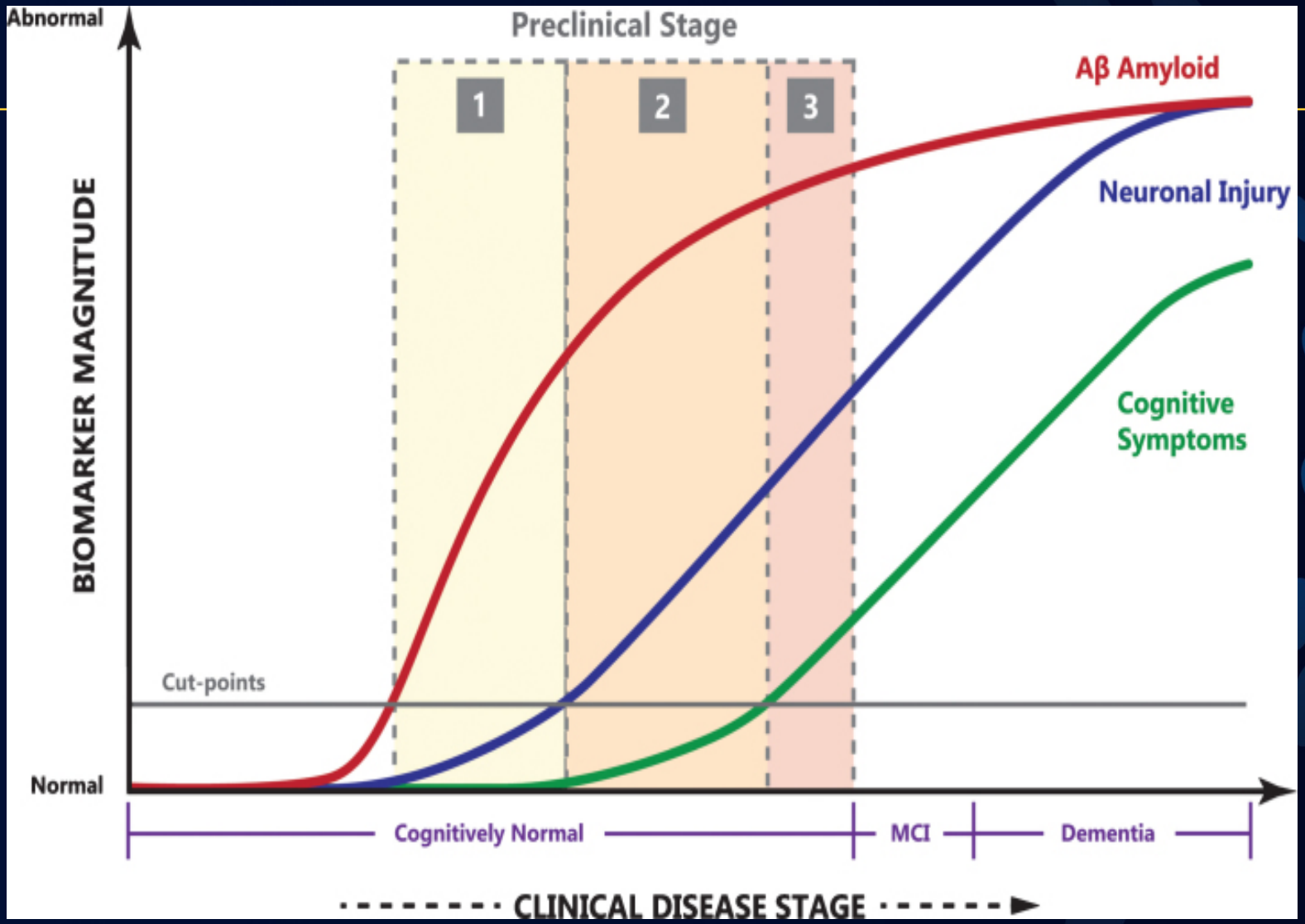

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Pathology of AD

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.

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Pathology of AD

The oligomer formation Aβ 42 and aggregation results in a cascade of events:

-tau protein neurofibrillary tangle formation

-inflammatory response

-oxidative injury

Causing neurotoxicity and neurodegeneration

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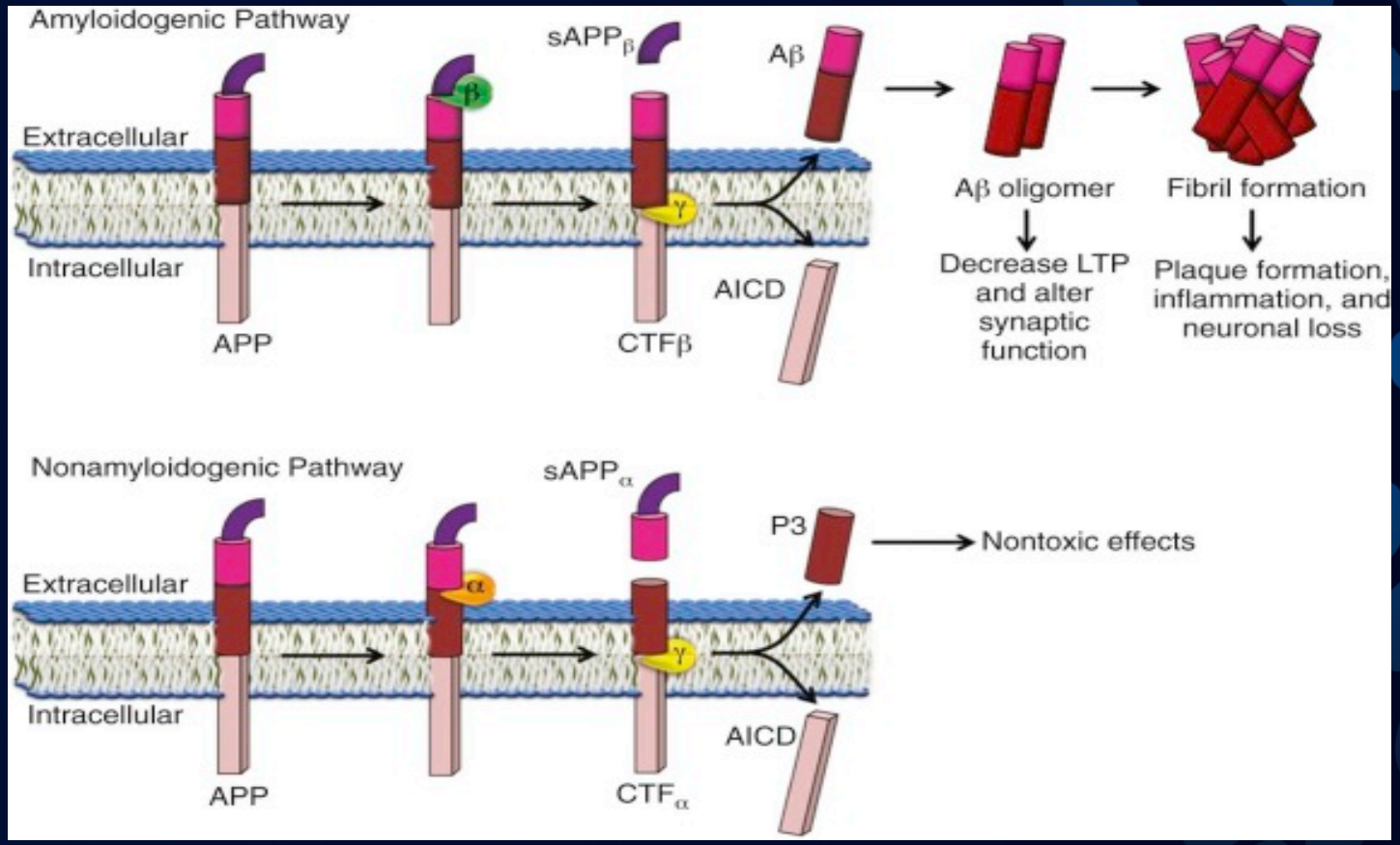
Amyloid Theory AD



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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

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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**

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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

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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

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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

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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.

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BIOMARKERS

Imaging

Cerebral Spinal Fluid (CSF)

Plasma

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Imaging

Structural imaging: MRI hippocampal atrophy

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

Cerebral amyloid angiopathy (CAA)

Amyloid (Aβ) imaging (PiB)

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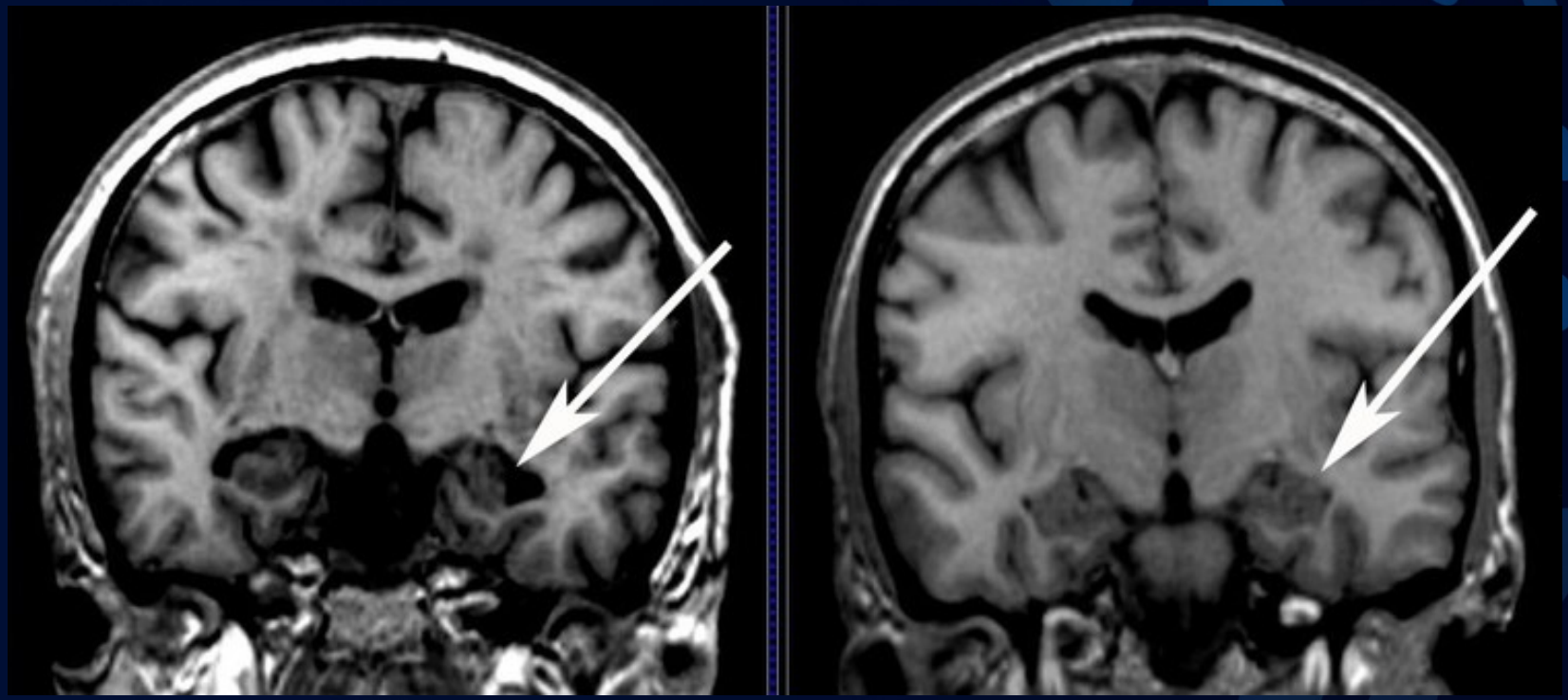
Structural MRI hippocampal atrophy



AD Normal

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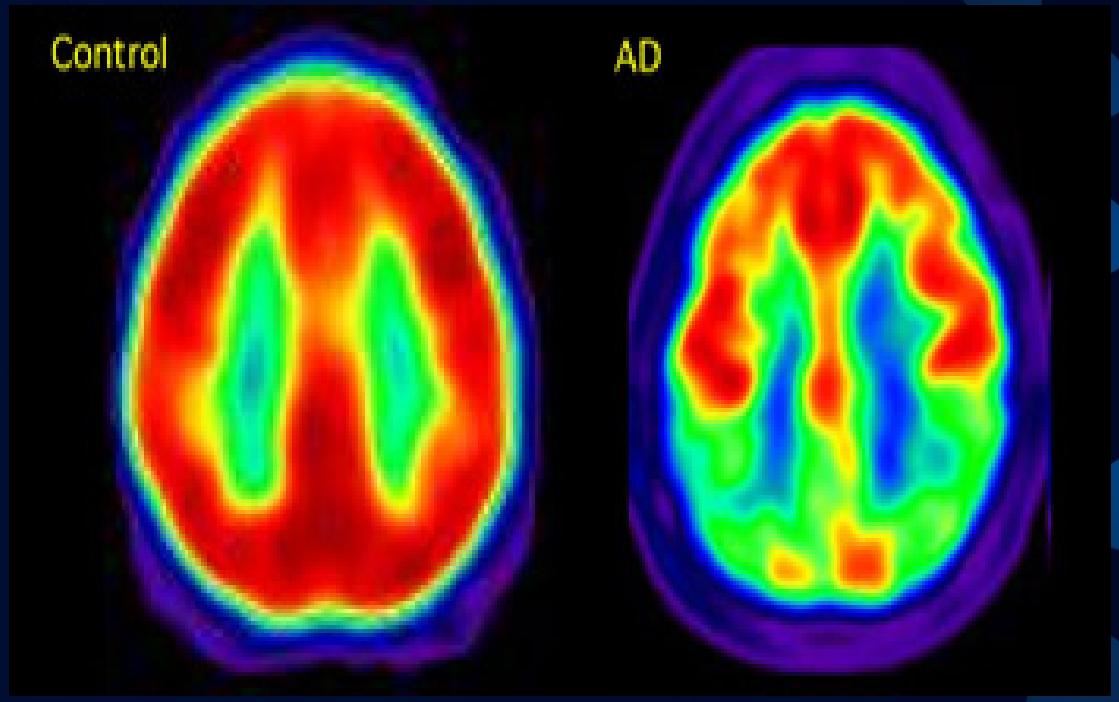
Functional FDG- PET glucose use



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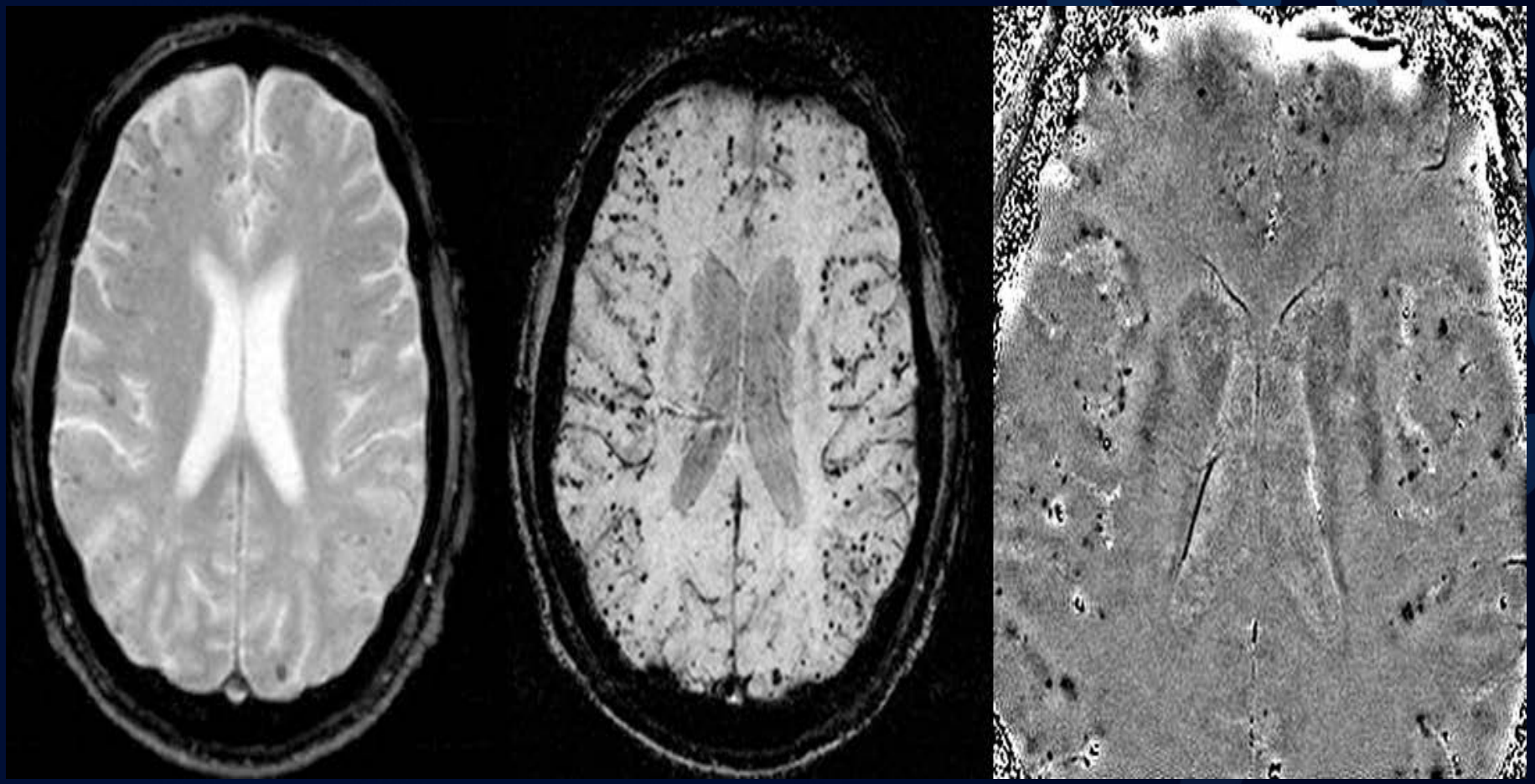
Cerebral Amyloid Angiopathy CAA



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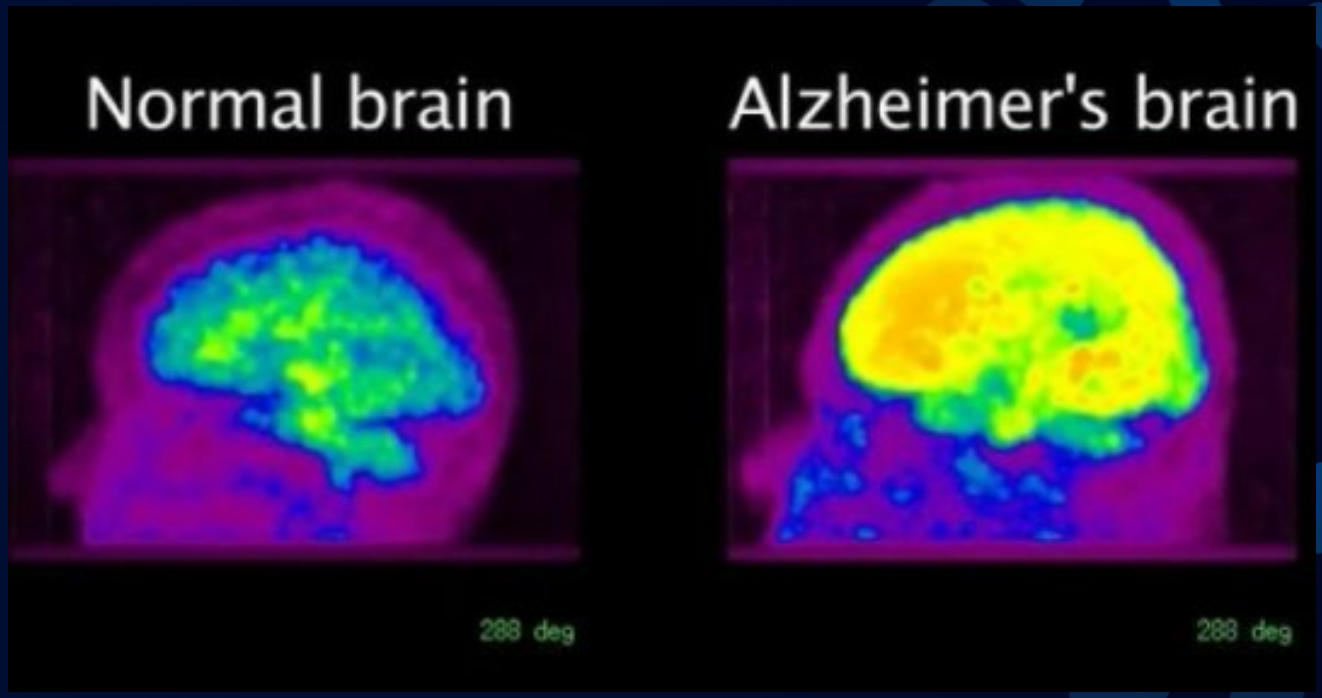
Amyloid (Aβ) binding PiB-PET



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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

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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)

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Risk Factors

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

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Treatment

Pharmacological

Nonpharmacological

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Treatment

Cholinesterase inhibitors: donepezil (Aricept)

rivastigmine (Exelon)

galantamine (Razadyne)

Mild-Mod AD by the FDA

NMDA receptor antagonist: memantine (Namenda)

Mod-Severe AD

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Treatment

Physical activities- daily

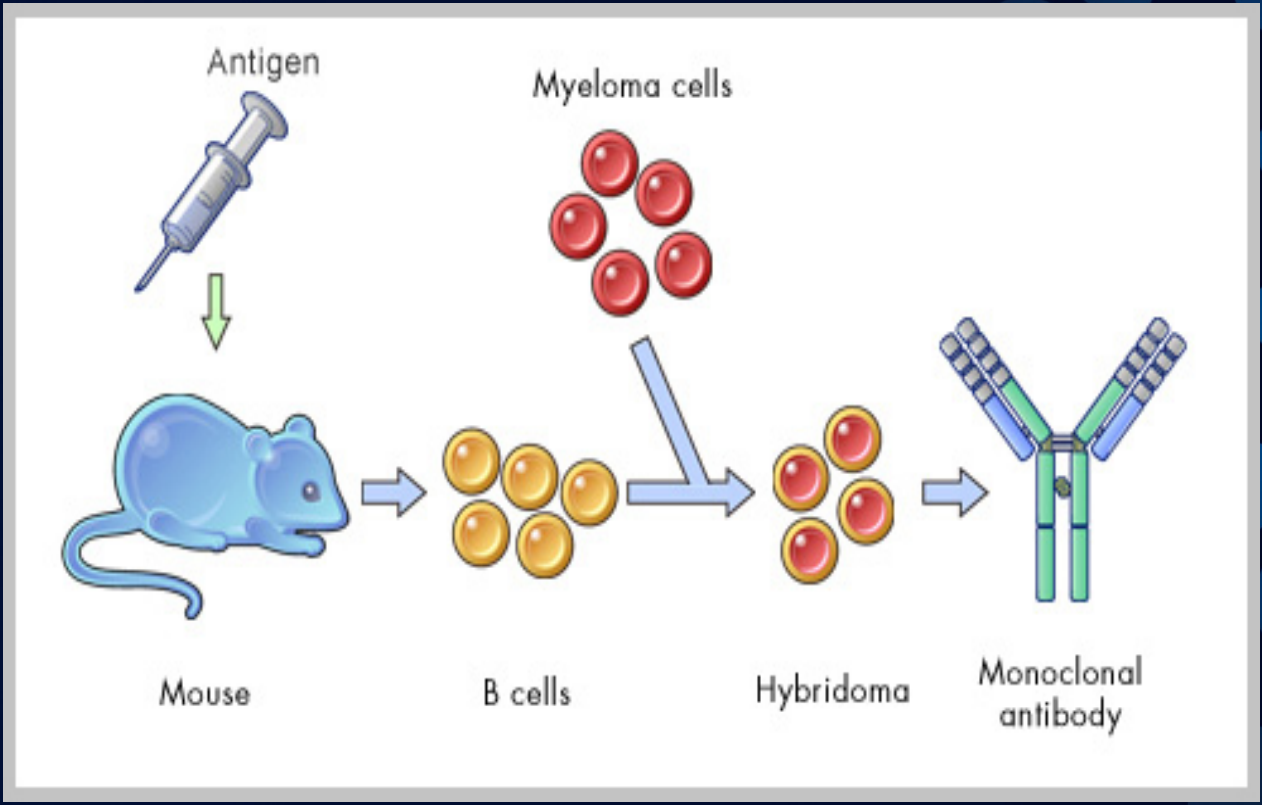
Cognitive activities- daily

Mediterranean diet

- Yes: olive oil, vegetables, fish, legumes, nuts
- No: red meat, dairy

Maintain good control over BP, serum glucose

Production of monoclonal antibodies



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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

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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

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References

Eur J Neurol. 2017 Jul 28. doi: 10.1111/ene.13374. [Epub ahead of print]. Moonga I1, Niccolini F1, Wilson H1, Pagano G1, Politis M1; Alzheimer's Disease Neuroimaging Initiative. Hypertension is associated with worse cognitive function and hippocampal hypometabolism in Alzheimer's disease.

J Neural Transm (Vienna). 2017 Aug 1. doi: 10.1007/s00702-017-1763-2. Riederer P1, Korczyn AD2, Ali SS3, Bajenaru O4, Choi MS5, Chopp M6. The diabetic brain and cognition.

Gatz et al, 2006. Gatz M., Reynolds C.A., Fratiglioni L., et al: Role of genes and environments for explaining Alzheimer disease. Arch. Gen. Psychiatry 2006; 63: pp. 168-174

Lautenschlager et al, 1996. Lautenschlager N.T., Cupples L.A., Rao V.S., et al: Risk of dementia among relatives of Alzheimer's disease patients in the MIRAGE study: What is in store for the oldest old?

Mapstone M, Cheema AK, Fiandaca MS, Zhong X, Mhyre TR, MacArthur LH, Hall WJ, Fisher SG, Peterson DR, Haley JM, Nazar MD, Rich SA, Berlau DJ, Peltz CB, Tan MT, Kawas CH, Federoff HJ (2014) Plasma phospholipids identify antecedent memory impairment in older adults. Nat Med 20, 415–418.

Schneider L, Dagerman K, Higgins J, McShane R (2011) Lack of evidence for the efficacy of memantine in mild Alzheimer disease. Arch Neurol 68, 991–998.

Schrijvers EMC, Koudstaal PJ, Hofman A, Breteler MMB (2011) Plasma clusterin and the risk of Alzheimer disease. JAMA 305, 1322–1326.

Brier MR, Gordon B, Friedrichsen K, McCarthy J, Stern A, Christensen J, Owen C, Aldea P, Su Y, Hassenstab J, Cairns NJ, Holtzman DM, Fagan AM, Morris JC, Benzinger TL, Ances BM (2016) Tau and A-beta imaging, CSF measures, and cognition in Alzheimer's disease. Sci Transl Med 8, 1–10.

Livingston G, Sommerlad A, Orgeta V, et al. **Dementia prevention, intervention, and care** Lancet July 20, 2017

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Rebecca Davis, PhD, RN
Grand Valley State University
Kirkhof College of Nursing

Living Well With Alzheimer's Disease

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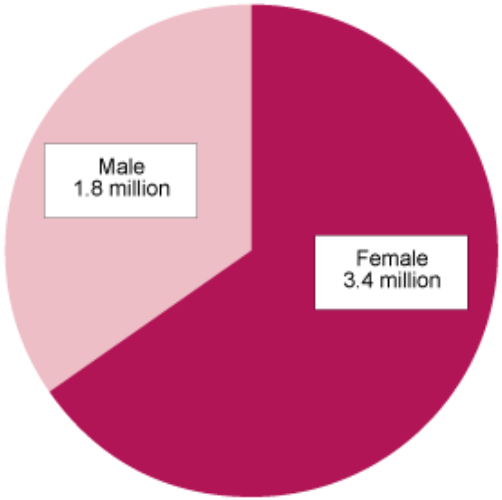
The future

More than 5 million Americans are living with Alzheimer's disease.

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



*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.

Source: Alzheimer's Association. 2012 Alzheimer's Disease Facts and Figures. Retrieved from http://www.alz.org/alzheimers_disease_facts_and_figures.asp Accessed 06/11/12.

* What can be done after diagnosis?

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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?

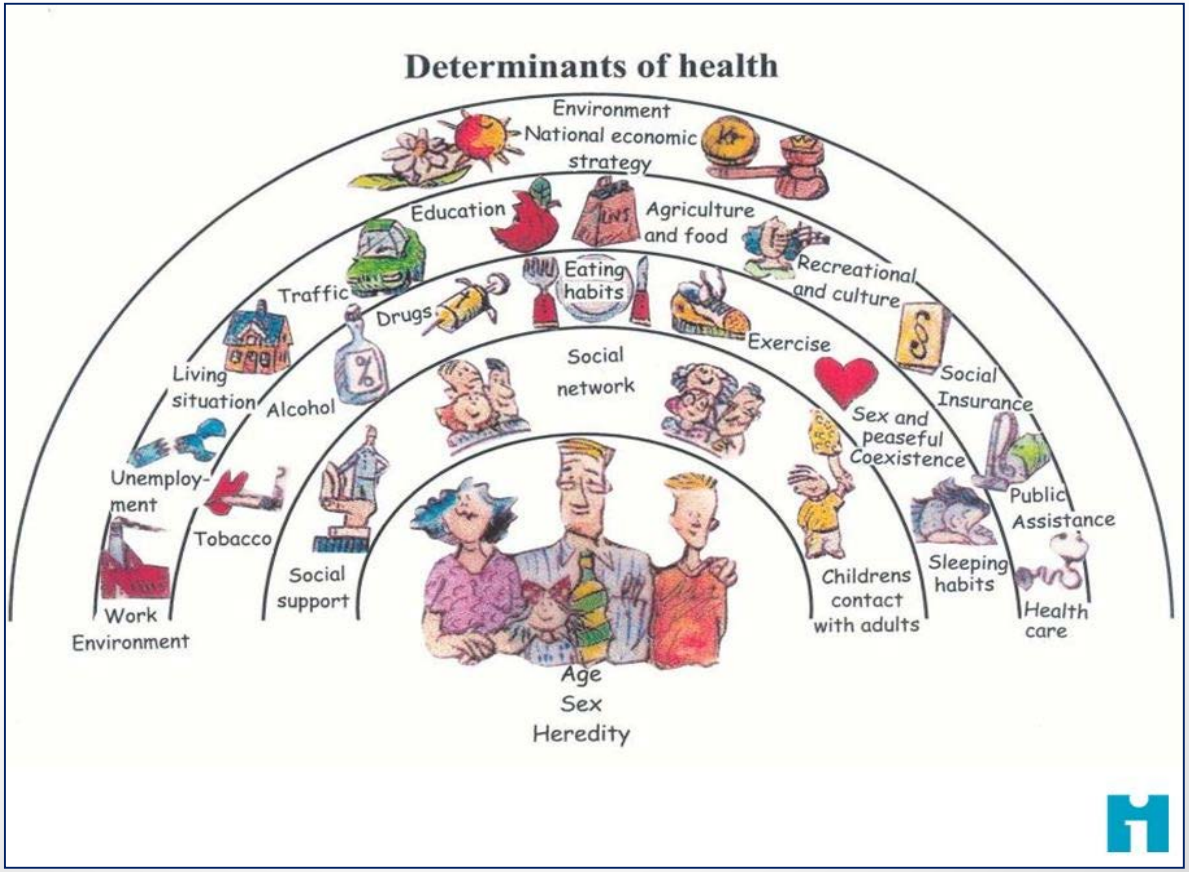
Current Model of Care

* 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?



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* **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

http://www.miraclealternatives.com/SUNBOX-Light-Box-SunRay-II-_p_264.html

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McCurry, Susan M., et al. "Increasing Walking and Bright Light Exposure to Improve Sleep in Community-Dwelling Persons with Alzheimer's Disease: Results of a Randomized, Controlled Trial." Journal of the American Geriatrics Society 59.8 (2011): 1393-1402.

Exercise

- Increases overall health
  - Cardiovascular
  - Function
  - Endurance

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

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Potter, Rachel, et al. "A systematic review of the effects of physical activity on physical functioning, quality of life and depression in older people with dementia." International journal of geriatric psychiatry 26.10 (2011): 1000-1011.

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*

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*Adams, K., Kohlmeier, M., Seisel, S. (2010) Nutrition education in US medical schools: Latest update of a national survey. *Academic Medicine,* 85, 1537-1542

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

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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

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Buettner, L., & Ferrario, J. (1998). Therapeutic recreation-nursing team: A therapeutic intervention for nursing home residents with dementia. *Annual in Therapeutic Recreation*, 7, 21-28.

Watermemories Swimming Club

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http://www.uq.edu.au/ami/watermemories-swim-club

* Supportive Environment

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

* **Decision Making**
  * Resources
    * Legal
    * Financial
    * Personal
    * Health
    * Information
  * Requires open communication and acceptance of diagnosis

Decision Making

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

* 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!

http://ilc.com.au/services/occupational-therapy-driver-assessment/

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

Every Day Decisions

* 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".

Summary

* 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

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Questions?

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