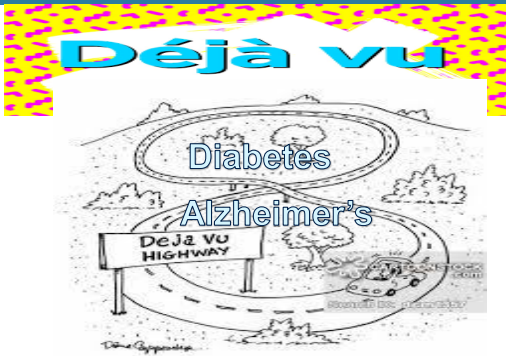


ALZHEIMER'S & DIABETES WHAT IS THE CONNECTION?





Quiz: True or False?

Alzheimer's disease can not be diagnosed without an autopsy of brain tissue.

Today there are medications that cure Alzheimer's disease.

Alzheimer's symptoms do not usually appear until 20 or more years from the onset.

Brain tissue does not regenerate.

Objectives

Learn epidemiology & pathogenesis of Alzheimer's Disease.

Understand the impact of uncontrolled diabetes mellitus (DM) on the pathology of Alzheimer's.

Recognize the importance of partnership between Alzheimer's Association and DM programs.

Evaluate appropriate Alzheimer's screening in clinical practice.

Dementia

Dementia is a set of symptoms with many causes.

Some forms of dementia, such as a drug interaction or a vitamin deficiency, are actually reversible or temporary.

<https://www.alzheimers.net/difference-between-alzheimers-and-dementia/>

Possible Causes of Dementia

- ◆ medication side effects
- ◆ chronic alcoholism
- ◆ tumors or infections in the brain
- ◆ blood clots in the brain
- ◆ vitamin B12 deficiency
- ◆ some thyroid, kidney, or liver disorders
- ◆ stroke
- ◆ Parkinson's disease
- ◆ Sleep disturbances

National Institute on Aging, last update May 4, 2017

National Institute on Aging Last Updated: May 4, 2017
https://vivacare.com/nwn/HealthTopic/Alzheimers_Disease_Overview

- Age major risk factor
- Damaged proteins
- Genetics (family history of Alzheimer's)
- Neuronal energy failure
- Neuro-inflammation
- Vascular disease



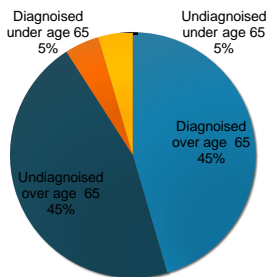
Alzheimer's

Alzheimer's disease (AD) is the most common cause of dementia and one of the leading sources of morbidity and mortality in the aging population

Alzheimer's is not a reversible disease. It is degenerative and incurable at this time.

<https://www.alzheimers.net/difference-between-alzheimers-and-dementia/>

5.5 million Americans living with Alzheimer's Disease





Costs

- \$259 billion in 2017
- Between 2017 and 2013 \$7.7 trillion in health care costs.

http://act.alz.org/site/DocServer/2012_Costs_Fact_Sheet_version_2.pdf?docID=7161



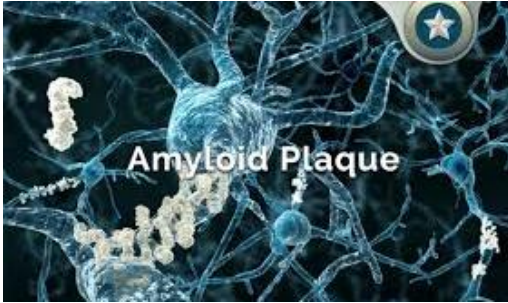
Diagnosis

Currently Dx is made 90% of the time using:
Questions about patient's health, past medical problems and ability to carry out daily tasks.
Cognitive tests including memory, problem solving, attention level and language.
Medical tests: brain scans



Pathogenesis

- The neuropathological hallmarks of Alzheimer disease include diffuse and neuritic extracellular amyloid plaques in brain that are frequently surrounded by dystrophic neurites and intraneuronal neurofibrillary tangles.

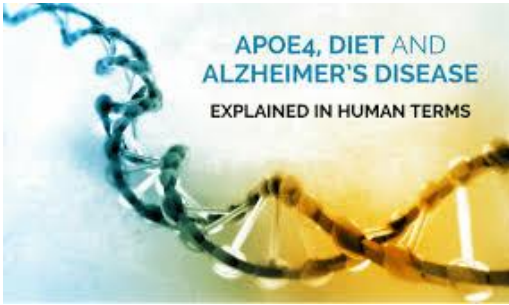


Diagnostic Markers

- MRI (magnetic resonance imaging)
- PET scan (positron emission tomography to measure amyloid in brain)
- Spinal Cord Fluid
- Glucose Metabolism in the Brain
- Genetic Markers

Genetics Markers

- APO-E 4 increases risk for Alzheimer's
- APO-E gene determines the type of protein produced to bind & transport fat particles to the liver.
- APO-E has three possibilities, 2,3,4 with APO-E3 most common.



Inside the Brain

In the Alzheimer brain:

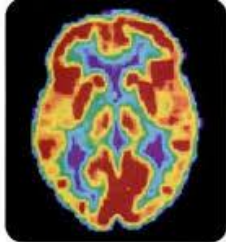
- The **cortex** shrivels up, damaging areas involved in thinking, planning and remembering.
- Shrinkage is especially severe in the **hippocampus**, an area of the cortex that plays a key role in formation of new memories.
- **Ventricles** (cerebrospinal fluid-filled spaces within the brain) grow large



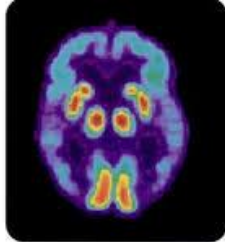
Brain
Hippocampus

Hippocampus
"Sea Horse"

PET Scans



PET Scan of Normal Brain



PET Scan of Alzheimer's Disease Brain

Can Brain Cells Regenerate?

- ◆ Conventional medical wisdom has held that people are born with all of the brain cells they will ever have, and once they are gone, they are permanently gone.
- ◆ Now, however, scientists have found that cells in the region of the brain responsible for memory and learning (hippocampus) are capable of being regenerated in a laboratory.
- ◆ Although there are currently no practical applications for this new finding, it could have implications in the future for the treatment of neurodegenerative diseases and brain trauma.

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Do Brain Cells Regenerate?



University of Pennsylvania in 2010 reported that aerobic exercise among 120 older adults increased the actual size of the hippocampus by two percent and effectively reversed the aging-related cell loss by one to two years.

Erickson, A., Voss, M., Prakash, R. et al. "Exercise training increase size of hippocampus and improves memory." PNAS. 2010, 108(7):3107-22; DOI: 10.1073/pnas.1015985108.

Glucose Levels and Risk of Alzheimer's

"It may be that with the brain, every additional bit of blood sugar that you have is associated with higher risks. It changes how we think about thresholds, how we think about what is normal, what is abnormal."

Published 2013, New England Journal of Medicine

Crane, P.K., Walke, P., Hubbard, R.A., Li, E., Nathan, D.M. et al. "Glucose Levels and Risk of Dementia" N Engl J Med 2013; 369:540-548
DOI: 10.1056/NEJMoa1215740

3rd TYPE OF DIABETES?

Specific types of diabetes due to other causes.
2017 Standards

http://care.diabetesjournals.org/content/diacare/suppl/2016/12/15/40_Supplement_1_DC1/DC_40_S1_final.pdf . found 4/18/2018.
Diabetes Care 2017;40(Suppl. 1):599-S104|DOI:10.2337/dci17-S014. Older Adults. Found 4/21/2018.

Multistep System

Stage 1

Stage 1	Presentation	Markers
Preclinical Alzheimer's disease	Un-noticeable. May not display clinical signs of cognitive deficits as memory loss.	<ul style="list-style-type: none"> Measurable changes in the brain. Cerebrospinal fluid Blood biomarkers
National Institute on Aging & Alzheimer's Association	Changes can occur 20 years prior to symptoms.	Reduce confusion in diagnosing and care for patient's with cognitive disorders.

https://www.huffingtonpost.com/entry/the-importance-of-revamping-the-guidelines-for-alzheimers_us_5981deede4b0b35d274c5ef6

Stage 2

Stage 2	Presentaton	Biomarkers
<u>Mild cognitive impairment</u>	Easier to identify mostly areas of cognitive and social functioning. Changes from previous level. Impairment in: orientation, language, attention, executive function, memory, problems in performing complex tasks.	MRI shows atrophied gray matter especially in the hippocampus and entorhinal cortex. PET scans show reduced metabolism in tempoparietal cortex and decreased glucose metabolism in posterior cingulate cortex

Memory+ Cognition+ Personality = Totally "ME"



Stage 3

Stage 3	Clinical Presentation	Markers
<u>Dementia due to Alzheimer's disease</u>	Distinct presentation in episodic memory, executive function, language, social dysfunction severe enough to impair the ability to function in daily life.	MRI Pronounced atrophy of the hippocampus and middle temporal lobe

Just once I would like to read a medication label that says: **WARNING' May cause permanent weight loss, remove wrinkles and increase energy."**



Current Rx Treatment for AD

Cholinesterase Inhibitors stop destruction of neurotransmitter acetylcholine.

- Donepezil (Aricept®)
- Rivastigmine (Exelon®)
- Galantamine (Razadyne®)

Memantine (Namenda®) used with Cholinesterase Inhibitor

Namzaric® (memantine HCl and donepezil HCl) Combination of Aricept and Namenda.

126 drugs in Clinical Trials

Trials	
Immune System	Epigenetics harness gene alterations
Amyloid-Beta	
Tau (protein)	AADvac1 Vaccine
Brain Blood Glucose	pioglitazone and exanatide
Reduce inflammations	Antioxidant agents
Improving Cognition	Serotonin

Pharmaceutical Targets

- ◆ Amyloid: clumps of abnormal proteins- leading target of pharmaceutical companies. Aim to remove from brain. A hallmark of Alzheimer's.
- ◆ Tau: tangles of abnormal proteins causing cell death. A hallmark of Alzheimer's and other nerve cell disorders. Target for new drug development.
- ◆ APOE (apolioproteom E) genetic risk factor for late-onset. Target for AADF-funded scientists developing drugs to modify risk.
- ◆ Inflammation & Vascular: Target for drugs to protect against injury-induced inflammation.

Research with Victoza

- King's College London, University of Cambridge, University of Southampton, University of Bristol, Birmingham University, University of Brighton, St Georges University of London evaluating the novel diabetic drug, liraglutide in the treatment of Alzheimer's disease (ELAD study) 2017.

Cost of Victoza: \$800-\$1,000. Some insurances pays 50% Manufactory's coupon

Research with Brain Ketones Metabolism

Ketogenic Interventions in Alzheimer's

Found that 40% decrease glucose metabolism in some area of the brain.

Recent studies show the brain is able to use ketones in place of glucose.

A Ketogenic Diet is being tested by Dr. Swerdlow, University of Kansas Alzheimer's Disease Center.

PDF File: "Mediterranean Diet Deconstructed: Evidence-based Culinary Medicine and Practical Applications."

Breaking News

February 2018

- Enzyme, BACE1 inhibitor shown to "completely" reverse build up of beta-amyloid plaque in the brain.
- Study on mice only by scientists at Cleveland Clinic Research Institute in Ohio.
- Further study needed.

Recent Findings

1. Possible that low Serotonin is involved in Alzheimer's.
2. Potential use of extremely low frequency electromagnetic waves to treat Alzheimer's.

Low-Frequency Pulsed Electromagnetic Field Is Able to Modulate miRNAs in an Experimental Cell Model of Alzheimer's Disease. by E. Capelli - 2017
<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5434238/>

Serotonin: A New Hope in Alzheimer's Disease?
 Claeysen S, Bockaert J, Giannoni P.
 ACS Chem Neurosci. 2015 Jul 15; 6(7):940-3. Epub 2015 May 26.

Prevention

- Diet**
- Exercise**
- Brain Health**

Resource for Diet Mangement:
 Sherry Christiansen January 15, 2018
<https://www.alzheimers.net/alzheimers-prevention-tools/>
 Diet management for prevention.

Prevention is “Brain Health”

- The American Heart Association and American Stroke Association have issued an advisory on maintaining optimal brain health throughout life.
- After reviewing 182 scientific studies of brain and heart health, they issued a seven step plan for helping to keep the brain in top working order and to keep Alzheimer's at bay in old age.
- The advisory reflects a growing body of evidence that what's good for the heart is good for the brain.

Steps to brain health

Diet: Mediterranean, Dash

Don't smoke: Smoking can damage blood vessels throughout the body, including in the brain.

Exercise: Regular physical activity is good for the heart and the brain.

Healthy weight. Obesity at midlife is a risk factor for Alzheimer's disease and other forms of dementia

Blood pressure. Below 120/80, the same risk factors for stroke are also risk factors for Alzheimer's disease,

Maintain a healthy cholesterol. High cholesterol is a known risk factor for Alzheimer's.

Control blood sugar: Type 2 diabetes, a risk factor for Alzheimer's disease

ALZinfo.org: The Alzheimer's Information Site. Reviewed by Marc Flagler, Ph.D., Fisher Center for Alzheimer's Research Foundation at The Rockefeller University.
 Photo © Corbis. Karen L. Fink, Cassandra Isabella, et al. Defining Optimal Brain Health in Adults: A Presidential Advisory From the American Heart Association/American Stroke Association. Stroke, Sept 7, 2017

Add Brain Games
 to Your Daily Routine



<https://www.brainhq.com/welcome>

Brain Training and Dementia

A newly published paper shows that one particular type of brain training exercise—called “speed of processing training” in the study—cut the long-term risk of dementia by 29%.

These new results are from a gold-standard randomized controlled clinical trial—and allow scientists for the first time to say that doing the brain training directly reduces the risk of dementia.

Brain HQ
https://www.brainhq.com/welcome?signup=success#challenges/memory_basics_1_challenge

Case Study: Type 1 DM

Type 1 Dx adult onset
Accountant, wife, mother of 4, 2 granddaughters

Early age Alzheimer’s DX; age 50 MRI & PET SCAN testing at Hospital in Seattle specializing in Alzheimer’s
Early onset of aphasia & word finding problems
Died age 54 of Alzheimer’s complications

Case Study: Type 2 DM

Type 2 for 38 years A1C 14% at (diagnosis 245 lbs. 6’4)

Age 78
Current wt. 190
A1C 5.7%
Metformin BID
Glipizide 5mg BID
Aspirin
Lisinipril
Multivitamin with B12
No cardiac problems
Good health besides arthritis
Stage 2 Alzheimer’s DX MRI & multiple testings
Attending various Alzheimer’s Associations Ed classes & support groups, participating in early stage clinical trial.

What Can You Do?

Early detection

- Observe for questionable behavior
- Refer for screenings

Education

- Include in diabetic education programs:
 - Risk factors for Alzheimer's
 - Brain Health Techniques
 - Importance of sleep
- Enjoying life** (music, dancing, games, learning second language, yoga, Sudoku)

MMSE Test

• Mini-Mental State Examination (MMSE) or Folstein test is a 30-point questionnaire that is used extensively in clinical and research settings to measure cognitive impairment. Commonly used in medicine and allied health to screen for dementia.

- https://www.parinc.com/webuploads/permission_request/Permission_Req_Form_distributed.pdf
- <http://www.dementiatoday.com/wp-content/uploads/2012/06/MiniMentalStateExamination.pdf>

SAGE Self-Administered Assessment

Self-Administered Gerocognitive Exam (SAGE)

<http://www.elderguru.com/download-the-self-administered-geocognitive-exam-sage-alzheimers-test/> (found 4/17/2018)

- SAGE Test 1
- SAGE Test 2
- SAGE Test 3
- SAGE Test 4
- Scoring instructions
- Explanation of SAGE scoring

Additional Resources

Edwards JD, Xu H, Clark DO et al. (in press) Speed of processing training results in lower risk of dementia. *Alzheimer's & Dementia: Translational Research & Clinical Interventions*.

Ball K, Unverzagt FW, Rebok G et al. (2014) ACTIVE: Advanced Cognitive Training for Independent and Vital Elderly (ACTIVE). *ClinicalTrials.gov*.

Try Double Decision—A Brain-Training Exercise. *BrainHQ.com*.
<https://www.alzdiscovery.org/cognitive-vitality/newsletter>

<https://www.youtube.com/watch?v=jBvWadjwXs&feature=youtu.be>

The Self-Administered Gerocognitive Exam (SAGE) was developed by Ohio State University College of Medicine, Department of Neurology. The test is a cognitive screening instrument used to identify Mild Cognitive Impairment (MCI) and early dementia. The test is self-administered, so people questioning their own cognitive abilities can take the exam privately.
www.elderguru.com/download-the-self-administered-geo...

**Beat the Heart Attack Gene:
The Revolutionary Plan to Prevent Heart Disease, Stroke,
and Diabetes**

Paperback – February 4, 2014
by [Bradley Bale M.D. \(Author\)](#), [Amy Doneen ARNP \(Author\)](#), [Lisa Collier Cool \(Contributor\)](#), [Larry King \(Contributor\)](#)

<https://www.verywell.com/complementary-and-alternative-therapies-for-dementia-98671>

Mediterranean Diet Deconstructed:
Evidence-based Culinary Medicine and Practical Applications. PDF file found on 4/19/2018
https://www.google.com/search?Source=hp&ei=gOnYWsjQH4218AOa0KGwDQ&q=Mediterranean+Diet+Deconstructed%3A+Evidence-based+Culinary+Medicine+and+Practical+Applications&oeq=Mediterranean+Diet+Deconstructed%3A+Evidence-based+Culinary+Medicine+and+Practical+Applications&gs_l=psy-ab.3...5352.5352.0.7588.1.1.0.0.0.123.123.0j1.1.0...0.1.2.64.psy-ab.0.0.0...0.0-F1C442jo
