The Whole Person in Dementia

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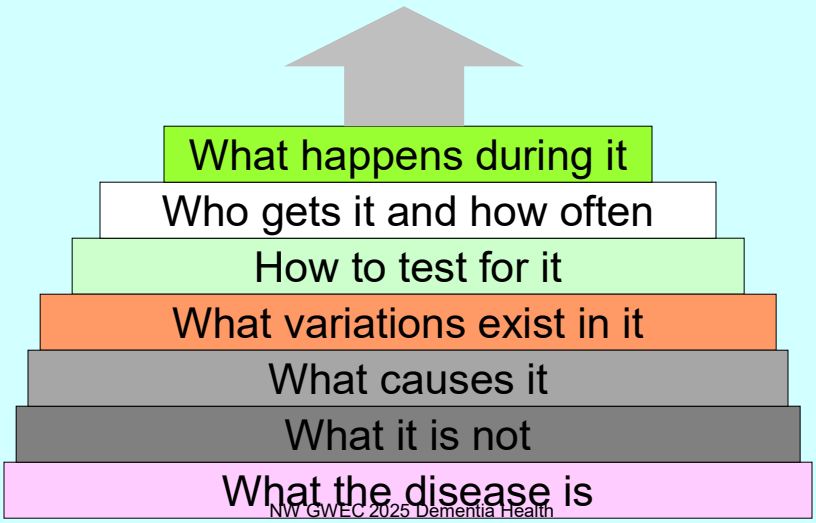
"BOOK LEARNING"



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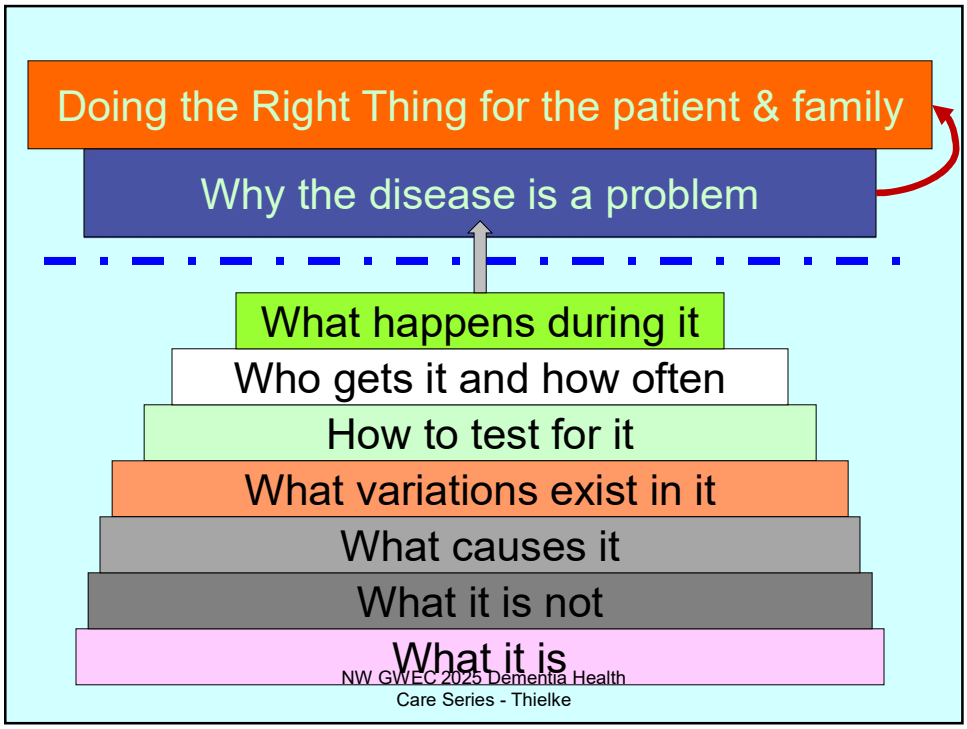


Scenario #1

One of your parents develops memory problems, cannot remember which pills they took, gets lost when driving, and is paranoid about neighbors stealing things. They left the stove on and almost burned the house down.

-Practically, what do you do?

-What are your main needs?

-How can medical care help you?

Scenario #2

Your parent requires assistance with dressing, eating, bathing, and toileting. They cannot remember your name. You are the only one available to care for them.

-Practically, what do you do?

-What are your main needs?

-How can medical care help you?

Scenario #3

You live with your parents, aunts, uncles, and cousins in a large multigenerational household. Someone is always home. People are flexible in their schedules. Your parent needs assistance with dressing, eating, bathing, and toileting. They cannot remember anyone's name.

-Practically, what do you do?

-What are your main needs?

-How can medical care help you?

Definition of Dementia (#1)

A **significant**
chronic
loss
in **memory and/or mental functions**,
involving **structural damage** to the brain (= death of neurons)

Definition of Dementia (#2)

A progressive neurodegenerative condition with functional consequences.

NOT
-Lifelong
-Abrupt or acute
-Normal aging
-Insignificant

NOT NECESSARILY
-A problem with memory
-Alzheimer's
-Disturbed behavior
-Age-related
-Fatal

Definition #3: DSM-5 Criteria for Major Neurocognitive Disorder (Dementia)

- -Significant cognitive decline in one or more domains
- -The impairments interfere with independence (i.e. cause **FUNCTIONAL** problems)
- -The symptoms are not due to delirium or another mental disorder
- -Domains of cognition:
  - -Complex attention (multitasking)
  - -Executive function (complex tasks)
  - -Learning and memory
  - -Language
  - -Perceptual-motor (coordinated activities)
  - -Social cognition (appropriateness)

DSM-5 Major Neurocognitive Disorder (Dementia) Descriptors

- -Possible vs probable
- -With or without behavioral disturbance (psychosis, mood problems, agitation)
- -Severity: based on **FUNCTIONING**
  - -Mild: Instrumental activities of daily living (ADLs) are affected
  - -Moderate: Basic ADLs affected
  - -Severe: Fully dependent in ADLs

Delirium, Dementia and Depression

	Common Features	Hallmarks
Delirium	Subjective confusion Difficulty performing tasks "Not right" on interview Loved ones are worried	• Confusion / Impaired attention • Rapid onset; waxing and waning • Due to a medical cause
Dementia		• Problems in specific domains • Chronic and progressive, slow onset • Functional decline
Depression		• Decreased concentration and interest • Sensorium is clear

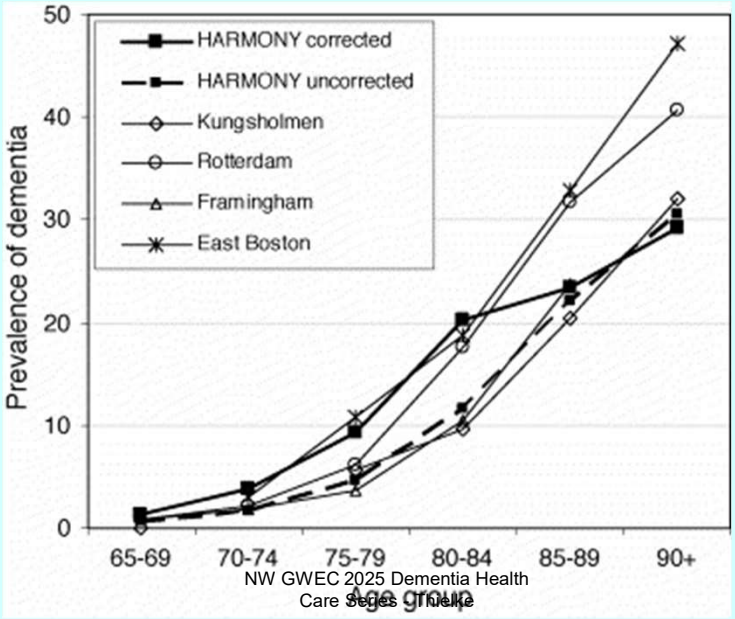
Dementia Prevalence

About 1% at age 65

6-8% if older than 65

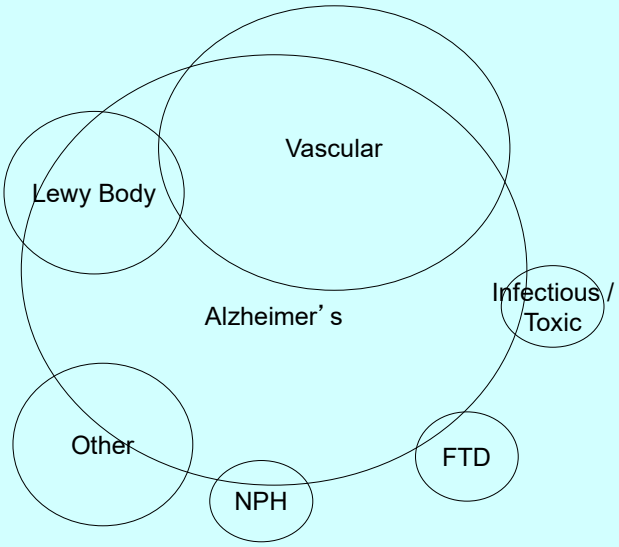
30% if older than 80

Frequency of Dementia



Types of Dementia:

- Alzheimer's
- Vascular
- Lewy Body
- Frontotemporal
- "Reversible"



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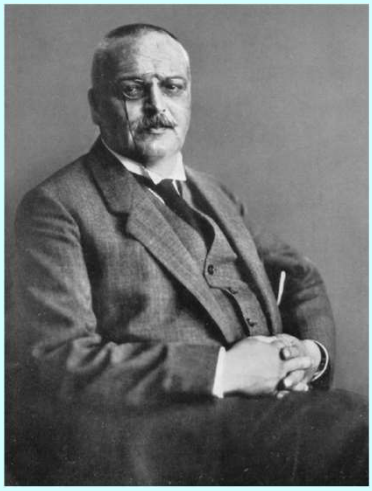
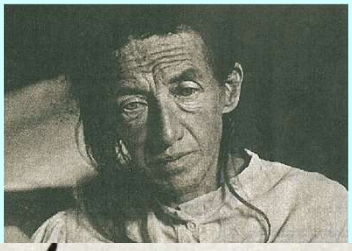
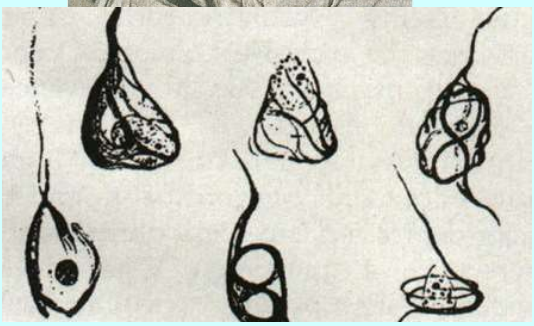
Alzheimer's Disease







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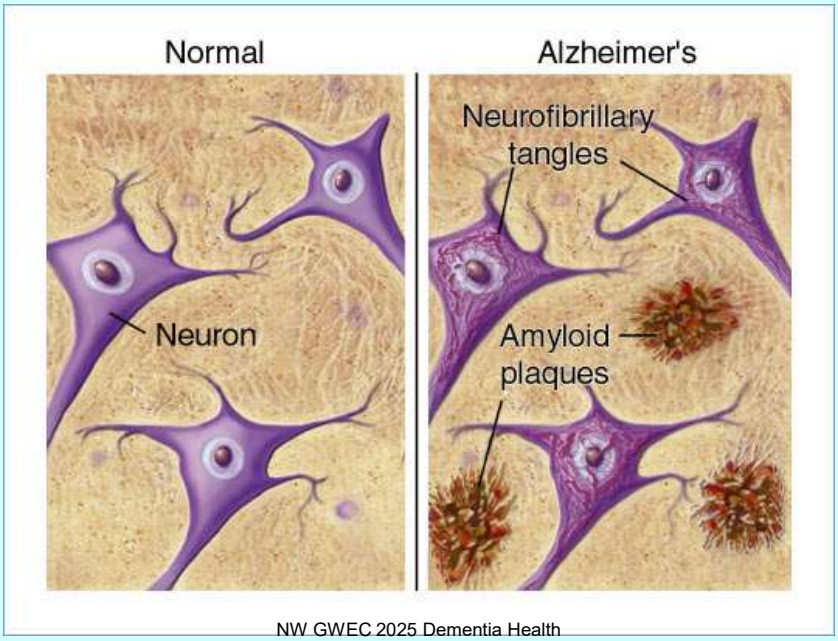
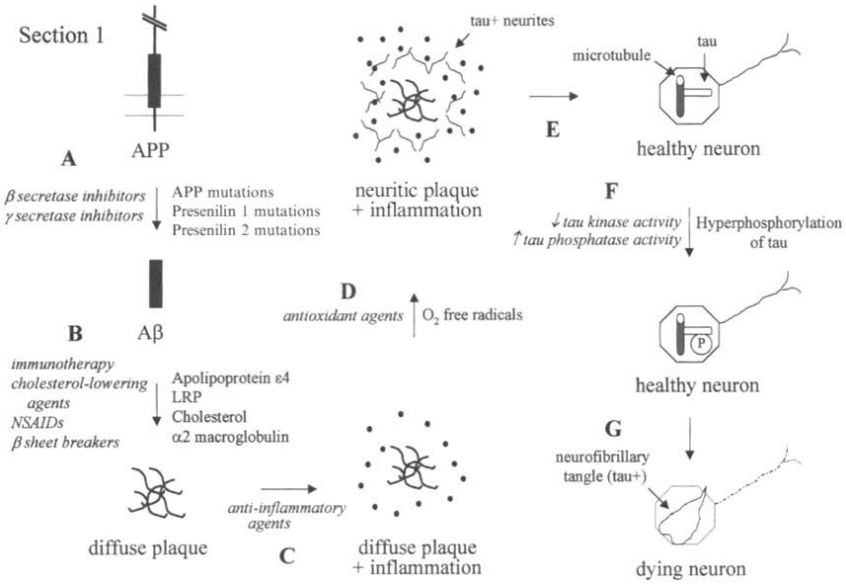
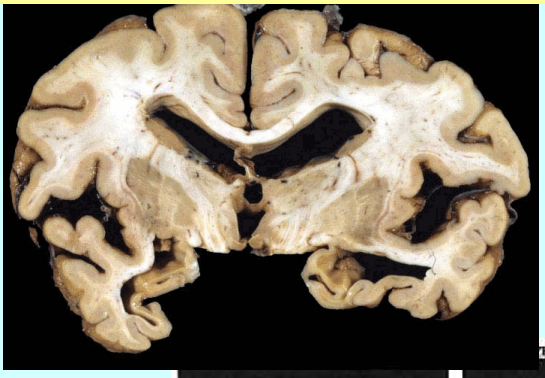
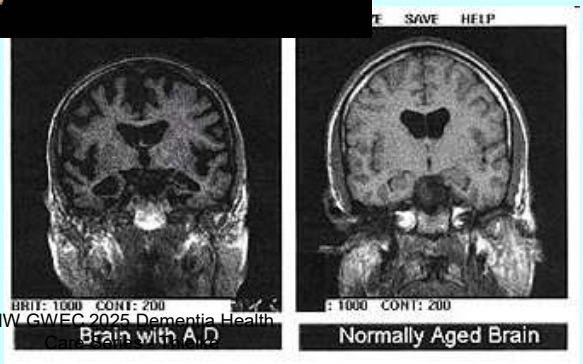

Normal
Alzheimer's
Neurofibrillary tangles
Neuron
Amyloid plaques


Section 1
APP
A
β secretase inhibitors
γ secretase inhibitors
APP mutations
Presenilin 1 mutations
Presenilin 2 mutations
Aβ
B
immunotherapy
cholesterol-lowering agents
NSAIDs
β sheet breakers
Apolipoprotein ε4
LRP
Cholesterol
α2 macroglobulin
diffuse plaque
anti-inflammatory agents
C
diffuse plaque + inflammation
tau+ neurites
neuritic plaque + inflammation
D
antioxidant agents
O2 free radicals
E
microtubule
tau
healthy neuron
F
↓ tau kinase activity
↑ tau phosphatase activity
Hyperphosphorylation of tau
P
healthy neuron
G
neurofibrillary tangle (tau+)
dying neuron



THE NEURONS HAVE DIED



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Alzheimer's Disease

Memory impairment + one of the following:

- -Aphasia (speech problem)
- -Apraxia (motor activity problem)
- -Agnosia (recognition problem)
- -Executive dysfunction

Functional impairment secondary to cognitive deficits

Not another cause

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Clinical Hallmarks of Alzheimer's

Slow, steady decline over **years**
Generally impaired insight into disease process
Generally a late presentation for medical care
Little waxing and waning
Death typically from medical causes in about 8-10 years

Mild Alzheimer's

- MMSE or MoCA 20-24
- Usually during the first 2-3 years after diagnosis
- Primarily memory, language, and problem-solving deficits
- Mild difficulty with day-to-day functioning, decision-making
- Often noticed, without any action taken

Conditions that can mimic early Alzheimer's

Delirium (including medication side effects and poorly managed medical conditions)

Sleep apnea

Vision and hearing problems

Mental health issues, especially PTSD

Moderate Alzheimer's

- MMSE or MoCA 11-20
- 3-6 years following diagnosis
- Speech and coordinated action decline
- Loss of IADLS and increased need for assistance with ADLs
- May show psychiatric symptoms such as paranoia

Severe Alzheimer's

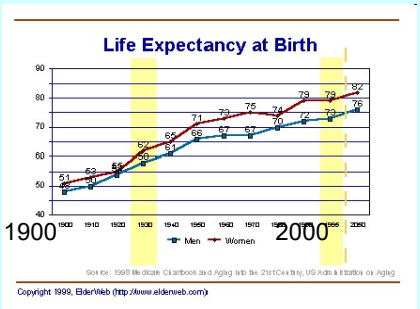
- Usually 6-10 years following diagnosis
- Severe language deficits
- May show pronounced behavioral symptoms such as agitation and aggression (not necessarily worsening)
- Very late in the course can see muscle rigidity, gait disturbances, incontinence, swallowing problems

"When you've seen one case of Alzheimer's, you've seen one case of Alzheimer's."

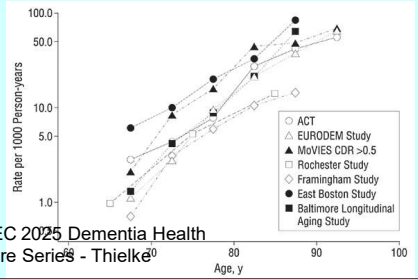
Genetics of Alzheimer's

- Early age of onset (< 60 years) is more likely to be inherited or "familial"
- Most Alzheimer's starts after age 70 and is "sporadic"
- Having a relative with "sporadic" Alzheimer's does not increase risk very much
- Several known genes (i.e. ApoE4) increase risk, but are not a guarantee
- Most forms are probably a consequence of multiple random brain changes that accumulate over time

Why is there more Alzheimer's? Because people live longer!



Incidence of Alzheimer's Disease by Age



Vascular Dementia

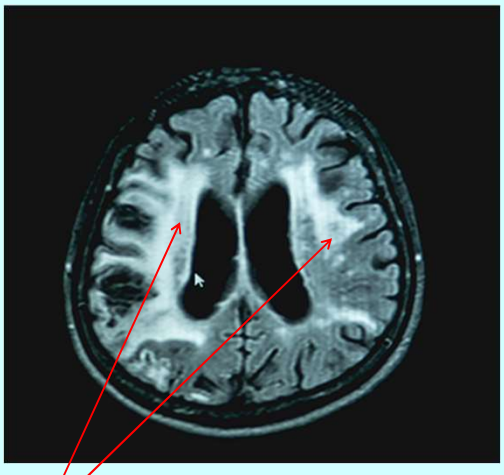
MICROVASCULAR (small blood vessel) pathology - different than strokes

Clinically similar to and overlaps largely with Alzheimer's

Risk factors: **hypertension**; smoking; hypercholesterolemia; diabetes; cardiovascular disease, BUT worsens even when these are treated -- ???

Not necessarily definitive findings on neuroimaging

Vascular Dementia

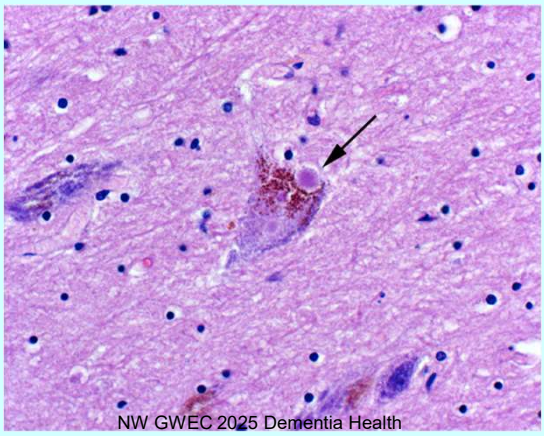


"Periventricular white matter hyperintensities"

Lewy Body Dementia

Occurs throughout the brain

Alzheimer's is mainly in the cortical (outer) layers



Lewy Body Dementia

Overall incidence 7-26% of dementia cases, often with Alzheimer's disease

"Parkinsonism" (stooped posture, shuffling gait, slow movements, cogwheeling, masked facies)

Visual hallucinations (usually not scary or bizarre)

Waxing and waning

Cognitive & memory impairment may come AFTER these other symptoms

Antipsychotics often worsen symptoms

Frontotemporal Dementia

Frontotemporal Dementia

Frontal brain atrophy: usually visible on brain imaging

Personality changes, disinhibition, executive dysfunction

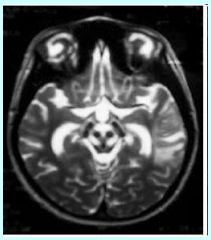
Later: memory and cognitive impairment

Earlier age of onset than Alzheimer's or vascular dementia

Usually familial

"Reversible" Dementias

Normal pressure hydrocephalus
Alcohol-related
B12 deficiency
Folate deficiency
Electrolyte abnormalities
Thiamine deficiency (Korsakoff)
HIV/AIDS
Advanced Lyme disease
Neurosyphilis
Carbon monoxide
Heavy metals
Wilson disease
Severe endocrinopathies
Creutzfeldt-Jakob disease
Autoimmune disease
Lipid storage diseases
Mass lesions or trauma



Almost none of these happen commonly or go a long time without being identified

General Workup

Take a good history, relying on other sources

Rule out delirium

Perform basic cognitive testing

Rule out reversible causes

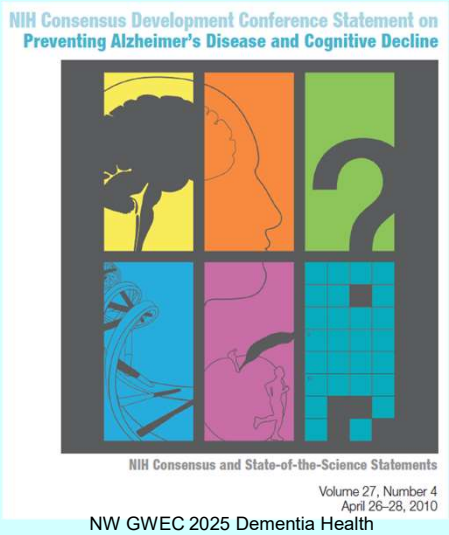
Symptom-Diagnosis mismatch:

Low → less workup High → more workup

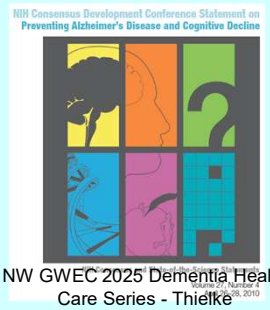
Basic tests: CBC, Chem-7, B12, folate, thyroid, calcium

Neuroimaging (CT, MRI) are not routinely indicated

Prevention of Dementia?



"Currently, firm conclusions cannot be drawn about the association of any modifiable risk factor with cognitive decline or Alzheimer's disease. Evidence is insufficient to support the use of pharmaceutical agents or dietary supplements to prevent cognitive decline or Alzheimer's disease."



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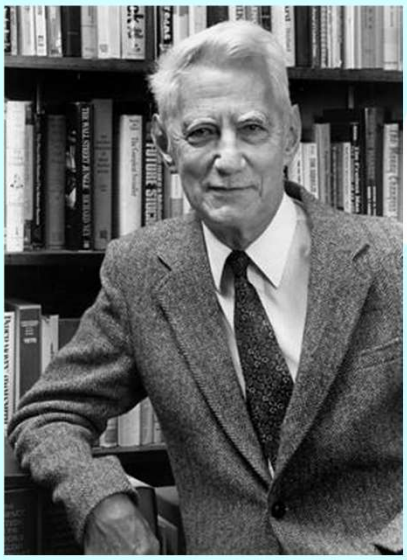

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Screening for Dementia?

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New blood test predicts Alzheimer's, dementia

Researchers have developed a new blood test that can predict with 90% accuracy whether a healthy person will develop Alzheimer's or cognitive decline within 3 years. They report how they identified and validated the 10 biomarkers that form the basis of the test in a study published in *Nature Medicine*.

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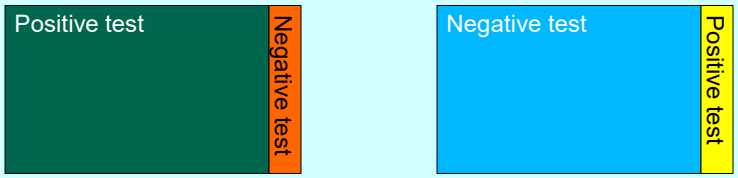
Screening for dementia

Test predicts with 90% accuracy

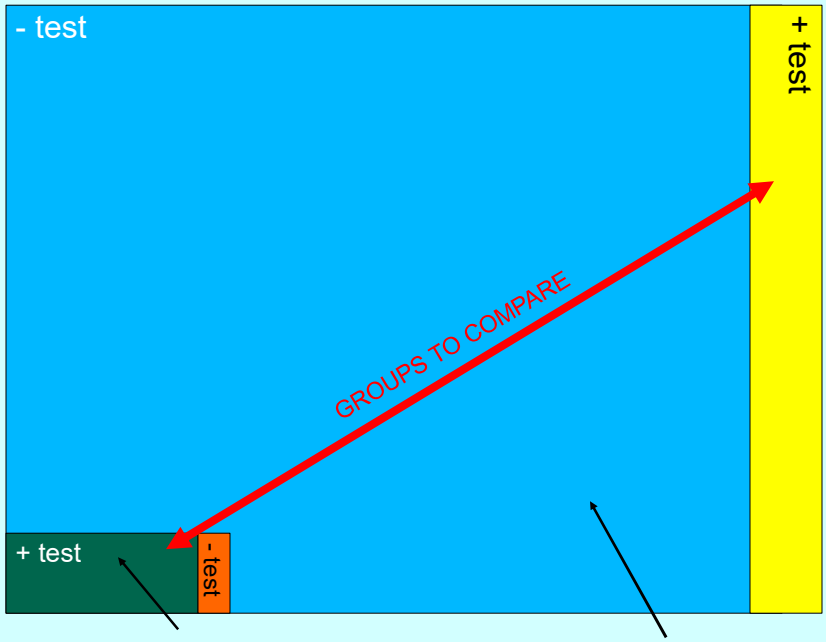
→ if you have the disease, you will get a positive test 9 out of 10 times

→if you do not have the disease, you will get a negative test 9 out of 10 times

→Assume that 4% of people have dementia



Has dementia No dementia



Has dementia No dementia

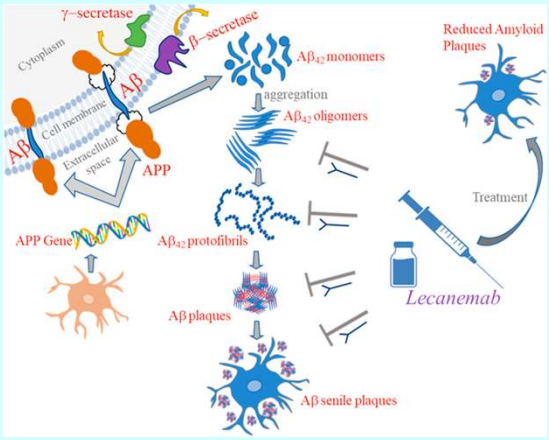
- If you get a **negative** test (868 people did), your likelihood of **having dementia is 0.4% (false negative)**
- If you get a **positive** test (132 did), your likelihood of **not having dementia is 73% (false positive)**
- **More than two out of three** people who are told they have dementia by this test will **not** in fact have it

Screening

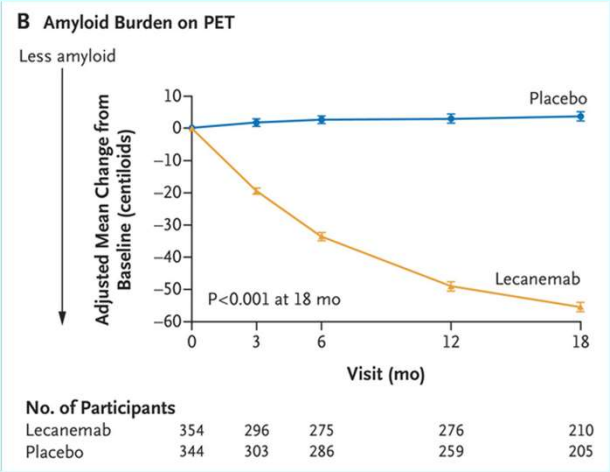
- Given the high false positive rate, routine screening for dementia is <u>not</u> recommended
- It works better to wait until people observe that they are having concerns or problems

Antibodies to Treat Dementia

Aducanumab
Lecanemab
Donanemab

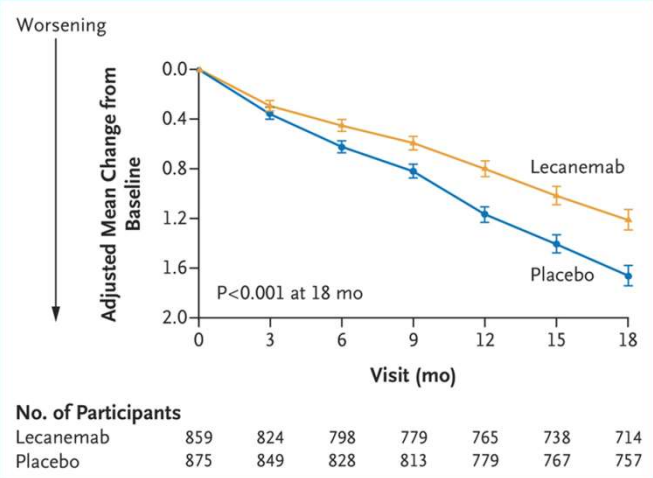


Change in Amyloid



Van Dyck et al, Lecanemab in Early Alzheimer's Disease. *N Engl J Med* 2023; 388:9-21

Change in "CDR-SB"

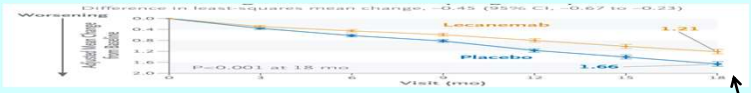


Van Dyck et al, Lecanemab in Early Alzheimer's Disease. *N Engl J Med* 2023; 388:9-21

CDR "Boxes"

CDR Score	0 Healthy	0.5 Very Mild Impairment	1 Mild	2 Moderate	3 Severe
Memory	No memory loss or slight inconsistent forgetfulness	Consistent slight forgetfulness; partial recollection of events; "benign" forgetfulness	Moderate memory loss; more marked for recent events; defect interferes with everyday activities	Severe memory loss; only highly learned material retained; new material rapidly lost	Severe memory loss, only fragments remain
Orientation	Fully orientated	Fully orientated except for slight difficulty with time relationships	Moderate difficulty with time relationships; may have geographic disorientation elsewhere	Severe difficulty with time relationships; usually disorientated in time, often to place	Orientated to person only
Judgment Problem Solving	Solves everyday problems and business affairs well; judgment good in relation to past performance	Slight impairment in solving problems, similarities, differences	Moderate difficulty in handling problems, similarities, differences	Severely impaired in handling problems, similarities, differences	Unable to make judgments or solve problems
Community Affairs	Independent function at usual level in job, shopping, volunteer and social groups	Slight impairment in these activities	Unable to function independently at these activities though may still be engaged in some	No pretense of independent function outside home Appears well enough to be taken to functions outside a family home	No pretense of independent function outside home Appears too ill to be taken to functions outside a family home
Home & Hobbies	Life at home, hobbies, intellectual interests well maintained	Life at home, hobbies, intellectual interests slightly impaired	Mild but definite impairment of function at home; more complicated hobbies abandoned	Only simple chores preserved; very restricted interests, poorly maintained	No significant function in home
Personal Care	Fully capable of self-care	Fully capable of self-care	Needs prompting	Requires assistance in hygiene, keeping of personal effects	Requires much help with personal care

Clinical Dementia Rating Scale – Sum of Boxes

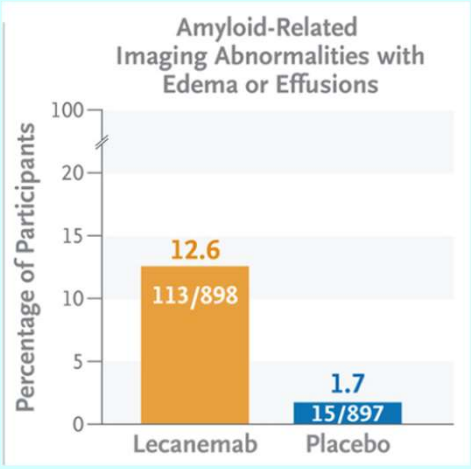


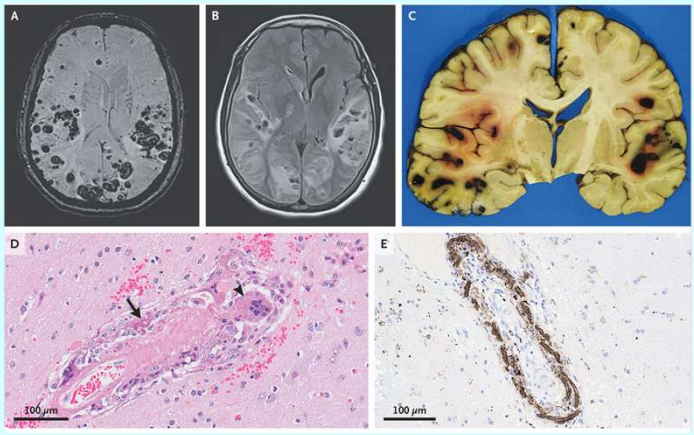
0.45-point difference

18 point scale

0.5 points is considered the smallest clinically meaningful change

Brain Edema or Bleeding





Reish et al. Multiple Cerebral Hemorrhages in a Patient Receiving Lecanemab and Treated with t-PA for Stroke. *N Engl J Med* 2023; 388:478-479

The truly important issues:

Why is dementia a problem?

How can we help people with dementia?

Caring for the Whole Patient, the Family, and the Environment

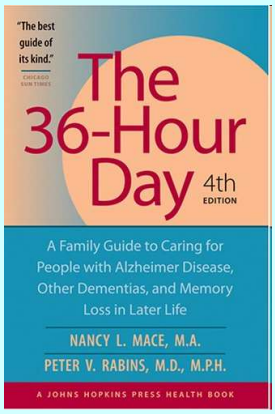
Listen

Don't make assumptions about what is easy or difficult

Screen caregivers and family members for depression

Focus on aggregate quality of life for the whole family unit

Recommend the Alzheimer's Association, County Senior Services, private social workers



Agitation

Figure out what is going on **before** turning to medications

Main reasons for agitation:

-Delirium

-Unmet needs

-Conditioning

-Natural response to the circumstances

Antipsychotic medications have a **black box** warning for dementia (about double risk of death)

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