ONE IN THREE OF YOU WILL GET DEMENTIA!
ALZHEIMERS : the symptoms.

- Memory loss
- Misplaced things
- Changes in personality and behavior
- Poor judgment
- Problems with language
- Difficulty perceiving spatial relationships or finding one's way
How Alzheimers disease is diagnosed.

- Mental status test -- questions/tests to evaluate the amount of decline in mental functioning, including orientation, memory and language skills
- Neuropsychological testing
- Magnetic resonance (MR) scan of the brain
- Blood tests – blood counts, vitamin levels, liver and kidney function, mineral balance, thyroid gland function
- Positron emission tomography (PET) metabolic or amyloid scanning in some patients

NO UNEQUIVOCAL DIAGNOSIS
Alzheimers: dementia and the brain.

Cortex (Cerebral Hemisphere) and Cerebellum affected.
Distribution of plaques

Plaques

Glucose use
Schematic of plaque formation between nerve cells
Plaques and tangles in AD. (biopsy)
• PLAQUE FORMATION CAUSES THE NERVE CELLS TO DIE

• RESULTING IN DECREASED BRAIN FUNCTION.
• PURIFY AND CHARACTERIZE THE PLAQUES.
THE PLAQUES CONTAIN A FRAGMENT OF THE AMYLOID PROTEIN
Genes causing early onset Alzheimers

• APP Amyloid b (A4) protein precursor.

• PSEN1 Presenilin 1 (SUBUNIT OF GAMMA SECRETASE)

• PSEN2 Presenilin 2 (IBID)

• APO E4
Cleavage of APP by secretases:
Early onset Alzheimer gene effects.
Front Cell Neurosci. 2015 May 28;9:186. The Maze of APP Processing in Alzheimer's Disease: Where Did We Go Wrong in Reasoning?

Chen M1.
Acta Neuropathol Commun. 2014 Sep 18;2:135

Inconsistencies and controversies surrounding the amyloid hypothesis of Alzheimer's disease.

Morris GP, Clark IA, Vissel B1.
Beta amyloid uptake into mitochondria
Genetic Mutations
- APP
- PS1
- PS2

Risk Factors – APOE4, Sortilin related receptor 1, Clusterin, Complement component receptor 1, CD2AP, CD33, EPHA1, & MS4A4/MS4A6E

Aging (and DNA Alterations) and Lifestyle Activities

Phosphorylated Tau

Aβ40
Aβ42
Aβ43

Oxidative DNA Damage

P53 activation

Telomere Shortening

Synaptic Damage

Neuronal Dysfunction and Neuron Loss

Alzheimer’s Disease
A model in which tau starts and beta amyloid accelerates Alzheimer's progression.
Involvement of Tau in Alzheimer's.
The Tau, beta amyloid...mitochondrial connection.

- Amyloid-beta peptide (Abeta) binding alcohol dehydrogenase (ABAD), an enzyme present in neuronal mitochondria, is a cofactor facilitating Abeta-induced cell stress. We hypothesized that ABAD provides a direct link between Abeta and cytotoxicity via mitochondrial oxidant stress. Neurons cultured from transgenic (Tg) mice with targeted overexpression of a mutant form of amyloid precursor protein and ABAD (Tg mAPP/ABAD) displayed spontaneous generation of hydrogen peroxide and superoxide anion, and decreased ATP, as well as subsequent release of cytochrome c from mitochondria and induction of caspase-3-like activity followed by DNA fragmentation and loss of cell viability.
• The U.S. Food and Drug Administration (FDA) has approved two types of medications — cholinesterase inhibitors (Aricept, Exelon, Razadyne) and memantine (Namenda) — to treat the cognitive symptoms (memory loss, confusion, and problems with thinking and reasoning) of Alzheimer's disease.