

Dementia

Jeanette Norden, Ph.D.

Professor Emerita
Vanderbilt University School of Medicine

What is “Dementia”?

Dementia is a *general term* referring to a decline in cognitive/mental functioning; this decline can be manifest as a difficulty in

- *memory
- *thinking and reasoning
- *language
- *judgment
- *personality
- *other “higher-order” functions

Diagnosis and Classification of Dementias

- **Generally a person is not diagnosed with dementia unless they show difficulties in at least 2 domains *and* the impairment interferes with daily activities**
- **Dementias can be classified by many different characteristics into “classes”; positive diagnosis within a class of dementias can be done (generally) only on autopsy**
- **Thus, a *specific type* of dementia is generally diagnosed during life as “definite, probable, possible”**

Classification of Dementias

- Dementias can be
 - **Primary**, meaning that the dementia is the *primary* condition; Alzheimer's disease would be considered a primary dementia
 - **Secondary**, meaning that the dementia is the result of some other disorder or condition; Parkinson's Disease Dementia would be considered a secondary dementia

Dementias (Secondary)

- Secondary dementias include:
 - Parkinson's Disease Dementia
 - Huntington's Disease Dementia
 - Wernicke-Korsakoff's Dementia
 - Normal Pressure Hydrocephalus Dementia*
 - Drug-induced Dementia*

****Potentially reversible***

Dementias (Primary)

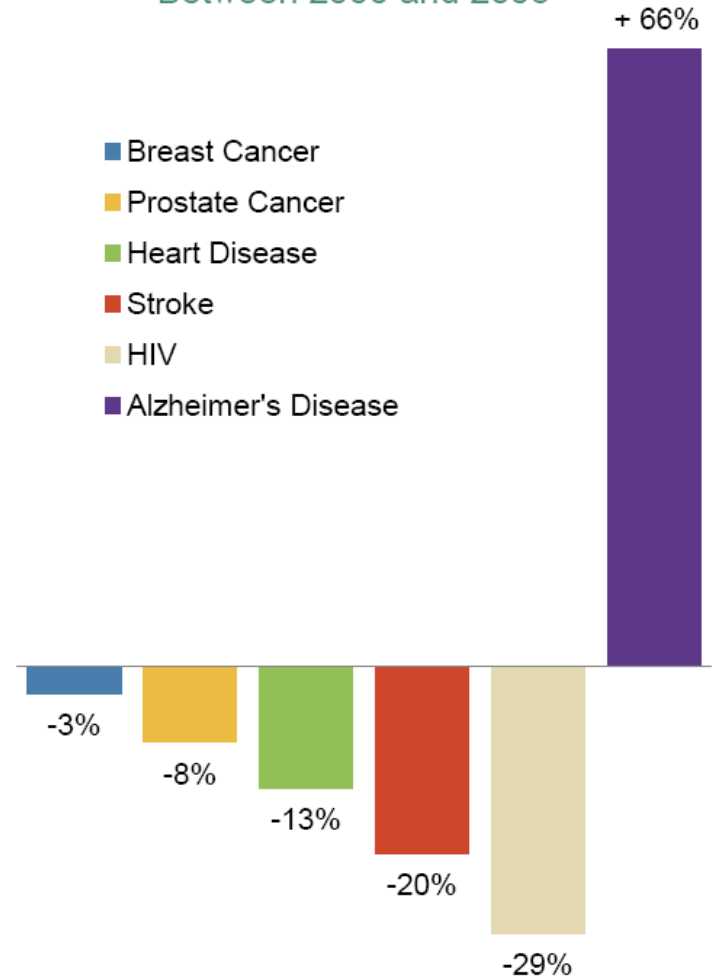
- Alzheimer's Disease
- Vascular Dementia
- Lewy-Body Dementia
- Frontotemporal Dementia
- Other rare dementias

Primary dementias are **chronic, progressive, and irreversible**

Alzheimer's Disease

- Is a **primary dementia**; except for **genetic forms, cause unknown**
- Is the most *common* type of primary dementia
- Is a fatal neurodegenerative disease affecting ~5 million Americans and ~25 million individuals globally, primarily in industrialized nations
- **Early-onset form (<65)** – familial - ~5% of cases; autosomal dominant
- **Late-onset form (>65)** – 95% of cases; sporadic

Change in Number of Deaths
Between 2000 and 2008



Epidemiology (U.S.; Late-onset Alzheimer's)

- **By Sex: Women > Men**
- **By Ethnicity:**
 - **African-Americans**
 - **American Indians/Native Alaskans**
 - **Latinos/Pacific Islanders**
 - **Caucasians**
 - **Asian-Americans**
- **By Age: 1/9 >65; 1/3 >85**

BEHAVIORAL CHANGES IN ALZHEIMER'S DISEASE

- **MEMORY LOSS**
- **DECREASED INITIATIVE**
- **DEPRESSION; EMOTIONAL INSTABILITY**
- **INABILITY TO INHIBIT BEHAVIOR**
- **FAULTY JUDGMENT, LOSS OF INSIGHT**
- **SEVERE LANGUAGE DEFICITS**
- **LOSS OF “SELF” and ABILITY TO “ENGAGE” INTERNALLY**

Major brain areas affected in Alzheimer's Disease

Cortical/Subcortical

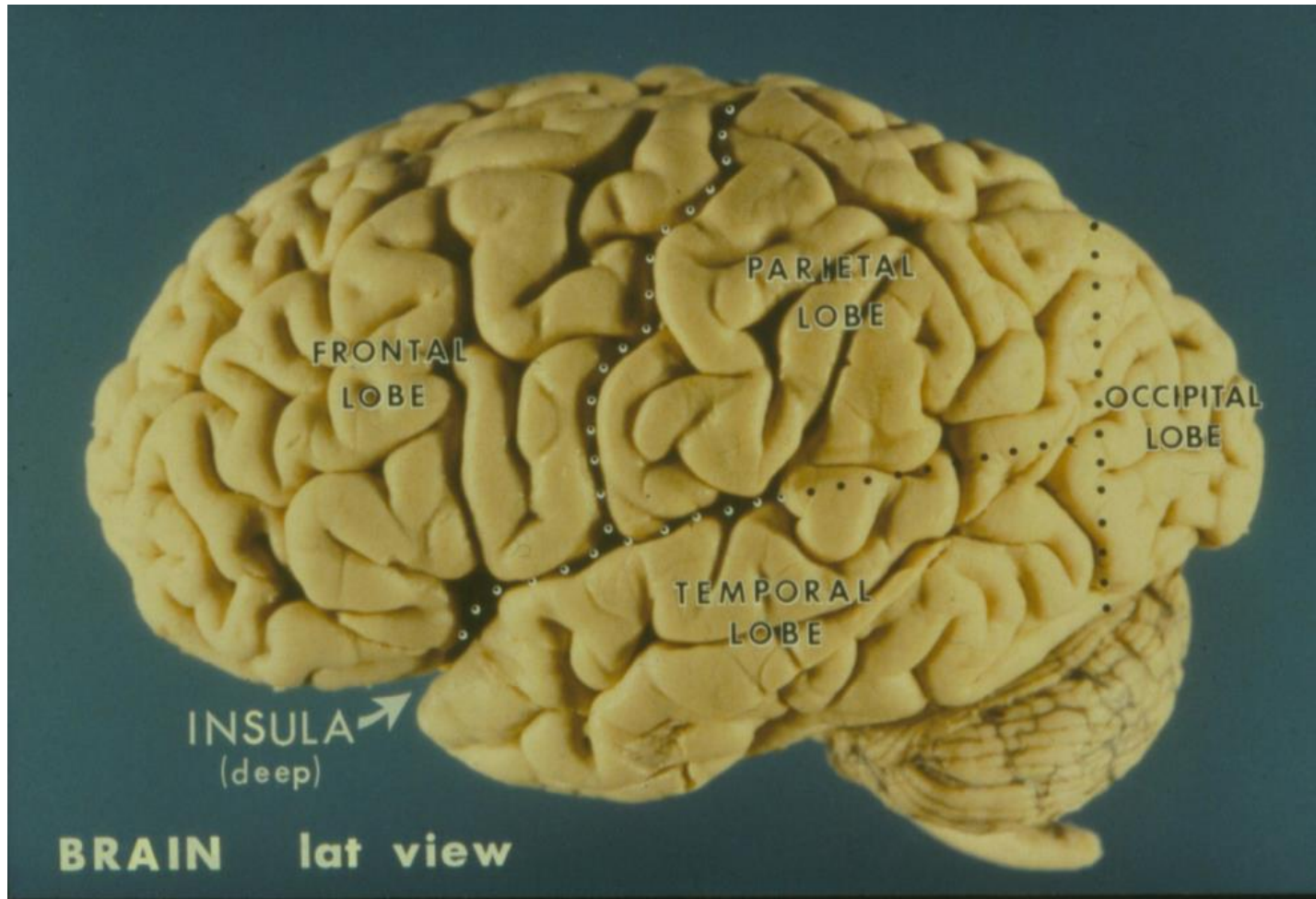
- **Neo-cortex** – higher-order cortical areas necessary for normal social and cognitive functioning
- **Medial cortex/cingulate gyrus** – default mode network – internal dialogue
- **Hippocampus** – an old cortical area critically involved in learning and memory and in the formation of an “autobiography”
- **Amygdala** – a subcortical area involved in emotional behavior/memory, especially “fear”

Major Brain Areas affected in Alzheimer's Disease

Brainstem

- **Locus coeruleus (norepinephrine)** – attention & arousal
- **Raphe nuclei (serotonin)** – mood regulation
- **Nucleus basalis of Meynert (acetylcholine)** – function unknown; degeneration is always associated with dementia

CORTEX: the outer 1-4 mm of nerve cells surrounding the hemispheres – **responsible for voluntary action & thought, executive function, higher-order functions and subjective experience**



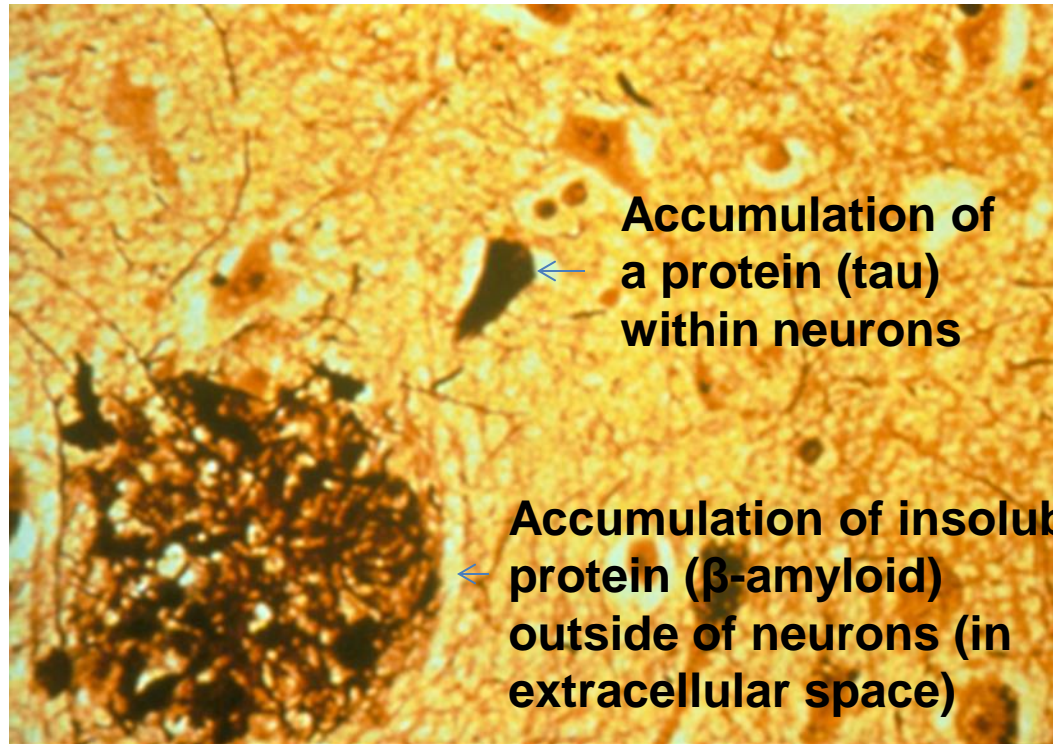
***Alzheimer's Disease causes death of cortical neurons,
especially those involved in higher-order functions***



Alzheimer's disease

Normal (age-matched)

At Autopsy, Abnormal Cellular and Extracellular Accumulation of “Altered” Proteins can be Identified



Accumulation of
a protein (tau)
within neurons

“TANGLES”

Accumulation of insoluble
protein (β -amyloid)
outside of neurons (in
extracellular space)

“PLAQUES”

Other Abnormalities

- **Accumulation of β -amyloid insoluble protein; soluble β -amyloid normally cleared from brain during restful sleep**
- **Mitochondrial abnormalities**
- **Changes in blood vessels and blood-brain barrier**
- **Abnormalities in insulin receptors (some scientists consider Alzheimer's disease to be a Type III diabetes)**

Factors that **Increase Risk** for Late-onset Alzheimer's Disease

- **SEX, ETHNICITY, AGE**
- **INHERITANCE OF E4 ALLELES FOR ApoE**
- **HEAD INJURY**
- **OBESITY**
- **HIGH FAT DIET; ELEVATED BLOOD CHOLESTEROL**
- **ATHEROSCLEROSIS, DIABETES, HYPERTENSION**
- **HISTORY OF UNTREATED DEPRESSION**
- **HORMONE REPLACEMENT THERAPY (if started >65)**
- **CHRONIC STRESS (HIGH BLOOD CORTISOL)**
- **DIAGNOSIS OF MCI (Mild Cognitive Impairment)**
- **HEARING LOSS**

Factors that **Decrease Risk** for Late-onset Alzheimer's Disease

- **GOOD GENES!**
- **BEING YOUNG!**
- **HEALTHY DIET**
- **RESTFUL SLEEP**
- **CONTINUING MENTAL *CHALLENGE***
- **MAINTAINING STRONG SOCIAL CONNECTIONS**
- ****EXERCISE****

“The Nun Study”

Physical Benefits of Exercise

■ *Increases*

**Endurance
Strength (muscle & bone)
Flexibility
Balance & posture
Restful sleep
Resistance to stress
Overall cardiovascular fitness
Weight control**

■ *Decreases*

**Hypertension
Heart disease
Type II diabetes
Osteoporosis
Falls**

Cognitive Benefits of Exercise

■ *Increases*

- ❖ **Generation of new neurons in hippocampus and prefrontal cortex**
- ❖ **Survival of neurons (by ↑ neurotrophic factors and ↑ blood supply)**
- ❖ **Synaptic Plasticity**
- ❖ **Restful sleep (promotes memory consolidation and ↑↑ amyloid clearance from the brain)**
- ❖ **Production of Neurotransmitters/Substances that play a role in Attention, Arousal, Mood & Well-Being**

■ *Decreases*

- ❖ **Age-related loss of neurons in cortex**
- ❖ **Death of new baby neurons in prefrontal cortex and hippocampus**
- ❖ **Age-related decline in cognitive performance**
- ❖ **Risk for Alzheimer's Disease**

Factors that **Decrease Risk** for Alzheimer's Disease

- *Not under your control*
 - Choosing good parents 😊
 - Not aging (!)
- *Under your control*
 - Eating a healthy diet (stay close to the earth and sea; fruits, veggies, nuts, whole grains, fish high in omega 3 oils)
 - Maintaining a healthy weight; controlling HBP, cholesterol, etc.
 - Restful sleep
 - Continuing mental challenge
 - Maintaining strong social & personal connections
 - **PHYSICAL EXERCISE!**

**Dachsie Wisdom: EXERCISE AND CHALLENGE
YOURSELF mentally, emotionally and physically -
One Step at a Time ♥**

