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

Accumulation of a protein (tau) within neurons

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

“PLAQUES”

“TANGLES”
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 ♥