
Alzheimer's Disease

Alzheimer's Disease

- Alzheimer's disease (AD) is a devastating illness characterized by progressive memory loss, impaired thinking, personality change, and inability to perform routine tasks of daily living.
- The neural damage in AD is irreversible, and hence the disease cannot be cured.
- There is no effective drug for relieving symptoms, and no prospect of one in the near future.

Alzheimer's Disease

- Symptoms:
 - Progressive memory loss
 - impaired thinking
 - personality change
- Pathophysiology—unknown
 - Starts in hippocampus
 - Progresses to cerebral cortex

Alzheimer's Disease (contd..)

- Hippocampus serves important role in memory
- Cerebral cortex is important for speech, perception, reasoning, and other higher functions
- With advanced AD, the ACh levels are 90% below normal
 - Ach is an important neurotransmitter in hippocampus and cerebral cortex
 - Critical to forming memories

Alzheimer's Disease (contd..)

- **Neuritic Plaques**

- Form outside neurons- spherical bodies that are composed of beta-amyloid (may help to destroy neurons) and remnants of axons and dendrites

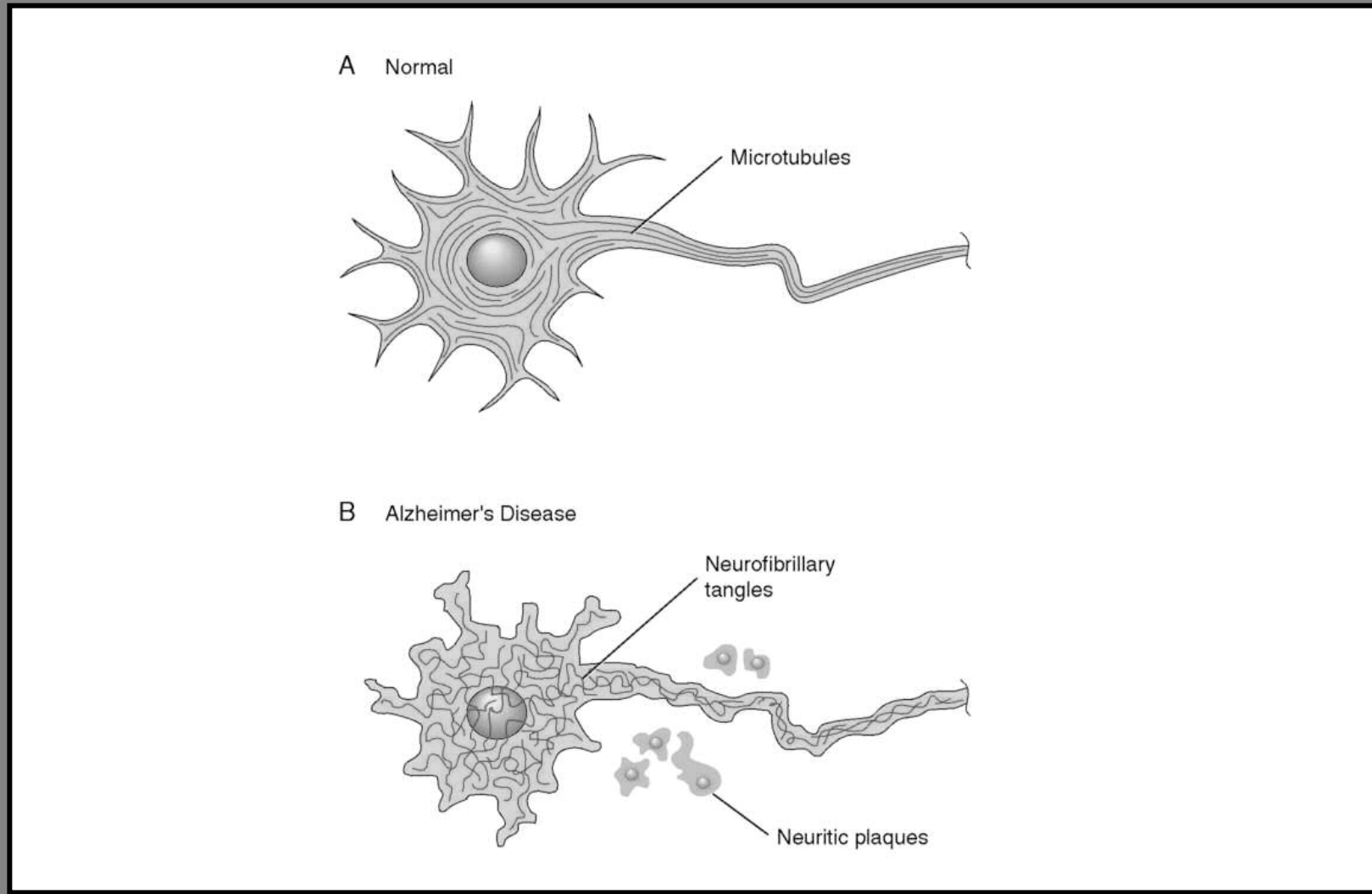
- **Beta Amyloid**

- Kills hippocampal cells (grown in culture)
- Can release free radicals
- Can disrupt potassium and calcium channels in cell membranes
- Cause vasoconstriction, blood vessel injury and leads to "starvation" of neurons and neuron cell death
- Injection of beta-amyloid into brains of monkeys leads to symptoms and characteristics of AD (old monkeys only, young monkeys not affected)

Alzheimer's Disease (contd..)

- **Neurofibrillary Tangles**
 - Tangles form inside neurons in cerebral cortex
 - Cause is production of abnormal form of *tau*, a protein that forms cross-bridges between microtubules and keeps them in stable configuration
- **Apolipoprotein E4 (ApoE)**
 - Role in cholesterol transport
 - E4 associated with AD but E2 is protective
 - ApoE4 promotes the formation of neuritic plaques; also binds to beta-amyloid to make it insoluble
 - E4 neither necessary nor sufficient to cause AD (many people have apoE4 gene, but do not have AD).

Figure 35-1: Histologic Changes in Alzheimer's Disease



Menu

T

Alzheimer's Disease (cont.)

- Risk factors
 - Advancing age
 - Family history
- Diagnosis
 - No specific test
 - Autopsy
- Drug therapy
 - Tacrine (Cognex)
 - Donepezil (Aricept)

Tacrine (Cognex)

- Cholinesterase inhibitor
- Increases acetylcholine
- Mild or moderate Alzheimer's disease
- Adverse effects
 - Hepatotoxicity
 - Nausea, vomiting, diarrhea