Alzheimer’s Disease
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• 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

A  Normal

B  Alzheimer’s Disease

- Microtubules
- Neurofibrillary tangles
- Neuritic plaques
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