

Alzheimer's Disease

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- Alzheimer's disease (AD), first characterized by Alois Alzheimer in 1907, is a gradually progressive dementia affecting cognition, behavior, and functional status.
- The exact pathophysiologic mechanisms underlying AD are not entirely known, and no cure exists
- Symptoms of AD can be reduced with drugs

Etiology

- Exact etiology of AD is unknown
- Alterations on chromosomes 1, 14, or 21-young-onset AD
- Most aggressive young-onset cases-mutations of a gene located on chromosome 14
- Genetic susceptibility to late-onset AD is primarily linked to the apolipoprotein E (APOE) genotype.
- Inheritance of the APOE*4 allele is believed to account for much of the genetic risk in late-onset AD.

Environmental factors

- Age
- Decreased reserve capacity of the brain
- Head injury, Down's syndrome, depression, mild cognitive impairment (MCI), and
- Risk factors for vascular disease (hypercholesterolemia, hypertension, atherosclerosis, coronary heart disease, smoking, elevated homocysteine, obesity, metabolic syndrome, and diabetes).

PATHOPHYSIOLOGY

- A β aggregation and deposition leading to the formation of plaques
- Hyperphosphorylation of tau protein leading to NFT development

PATHOPHYSIOLOGY

Amyloid Cascade Hypothesis

- Amyloid plaques are extracellular lesions found in the brain and cerebral vasculature.
- A β (amyloid beta) peptides are produced via processing of a larger protein, APP (amyloid precursor protein)
- The amyloid cascade hypothesis states
 1. An imbalance between the production and clearance of A β peptides
 2. Aggregation that causes accumulation of A β ultimately leading to AD
 3. Block the signals between neurons and activate inflammation

PATHOPHYSIOLOGY

Neurofibrillary Tangles

- NFT's are composed of abnormally hyperphosphorylated tau protein commonly found in the cells of the hippocampus and cerebral cortex in persons with AD
1. Microtubules-the cell's transportation and skeletal support system
 2. Tau protein provides structural support to microtubules
 3. Tau filaments undergo abnormal phosphorylation at a specific site
 4. They cannot bind effectively to microtubules
 5. The microtubules collapse
 6. Without an intact system of microtubules, the cell cannot function properly and eventually dies.

PATHOPHYSIOLOGY

Other mechanisms

- Synaptic failure and depletion of neurotrophin and neurotransmitters;
 - Loss of cholinergic activity is most prominent, and it correlates with AD severity.
 - Cholinergic cell loss seems to be a consequence of AD pathology, not the cause of it.
- Mitochondrial dysfunction
- Oxidative stress
- Serotonergic neurons of the raphe nuclei and MAO B activity increases
- glutamate pathway of the cortex and the limbic structure are abnormal
- excitatory neurotransmitters, including glutamate, may be neurotoxic in AD including

Clinical Presentation

- The patient may have vague memory complaints initially, or the patient's significant other may report that the patient is "forgetful." Cognitive decline is gradual over the course of illness.
- Behavioral disturbances may be present in moderate stages.
- Loss of daily function is common in advanced stages

Clinical Presentation

Symptoms

Cognitive

- Memory loss (poor recall and losing items)
- Aphasia (circumlocution and anomia)
- Apraxia
- Agnosia
- Disorientation (impaired perception of time and unable to recognize familiar people)
- Impaired executive function

Noncognitive

- Depression, psychotic symptoms (hallucinations and delusions)
- Behavioral disturbances (physical and verbal aggression, motor hyperactivity, uncooperativeness, wandering, repetitive mannerisms and activities, and combativeness)

Functional

- Inability to care for self (dressing, bathing, toileting, and eating)

Clinical Presentation

Laboratory Tests

- Rule out vitamin B12 and folate deficiency
- Rule out hypothyroidism with thyroid function tests
- Blood cell counts, serum electrolytes, and liver function tests

Other Diagnostic Tests

- CT or MRI scans may aid diagnosis

Thank you