100 Years of Progress in Research on Alzheimer's Disease

**Age of Discovery (1880-1907)**
- 1906: Dr. Alois Alzheimer first reports the hallmark pathological changes of AD in the brain of patient Auguste D.

**Dark Ages of Alzheimer's Disease (1907-1963)**
- 1929-1932: Fliegel, Schottky, and Lowenberg independently identify what appear to be familial patterns of inheritance of AD and senile dementia.

**Age of Rediscovery (1963-1976)**
- 1963: The first ultrastructure of plaques and tangles in the brains of AD patients are examined with electron microscopy.

**Psychodelic Era (1976-1987)**
- 1976: Davis publishes a study on selective deficits in cortical markers of cholinergic neurons in AD patients, which demonstrates the importance of cholinergic transmission in memory formation.

**Molecular Genetic Era of Alzheimer's Disease (1987-Today)**
- 1987: Gene coding for amyloid precursor protein (APP) is identified on chromosome 21 and sequenced.
- 1993: ApoE is associated with AD. A cholinergic therapy is approved for AD.
- 1995-1998: In 1995, presenilin mutations are cloned as loci for early onset AD. One year later, presenilin mutations are shown to alter APP processing. In 1998, presenilins are shown to be central components of atypical amyloid proteins, complexes responsible for β-secretase, which cleave to generate amyloid precursor protein (APP).

1966: Alzheimer's disease is now the most common neurodegenerative disease, with over 20 million cases diagnosed worldwide.

2003: α5 and 6 vaccine trials begin, but are halted because of serious cranial side effects.

2006: Alzheimer's disease is now the most common neurological disorder.

1999: Extensive amyloid-β deposition is found to occur in the neocortex and is reported to precede severe tangle pathology. Haplotypes H1 and H2 are found to characterize the Tau gene in populations of European descent.

**1906: Dr. Alois Alzheimer first reports the hallmark pathological changes of AD in the brain of patient Auguste D. in a meeting at Tubingen. He was the first to describe the fibrillar tangles associated with the disease.**

**1910: Emil Kraepelin names Alzheimer's disease in the Textbook of Psychiatry.**

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