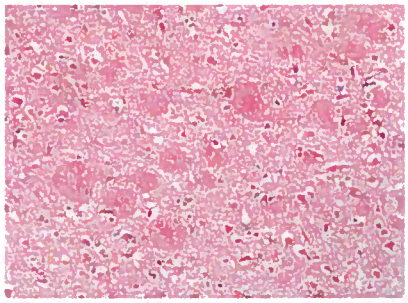
Alzheimer Disease

Background: Alzheimer disease (AD) is the most common cause of dementia, affecting more than 5 million Americans at any time. It was named after German psychiatrist Alois Alzheimer, who first described this disease in 1906. It causes devastating physical and emotional trauma to patients and their families, and is also a huge financial burden to the society. In 2012, the estimated costs of dealing with AD were about 200 billion dollars, without counting the unpaid care by family members. AD is an irreversible, progressive disease of brain that has no cure at this time.

Pathogenesis: Through autopsy, Alois Alzheimer discovered that there were abnormal structures in the brain of AD patients, which he named as "senile plaques" and "neurofibrillary tangles" (see figures). It was not until decades later that the biochemical composition of these structures was elucidated. The senile plaques are made of beta-amyloid protein, while the tangles have tau protein. Both plaques and tangles are typically seen in the hippocampus, a brain structure responsible for memory. Two leading theories of AD are amyloid hypothesis and tau hypothesis, depending on whether beta-amyloid or tau is regarded as the primary cause of disease. Neither hypothesis is perfect. In addition, tangles and plaques can be found in the brain of older individuals without AD.



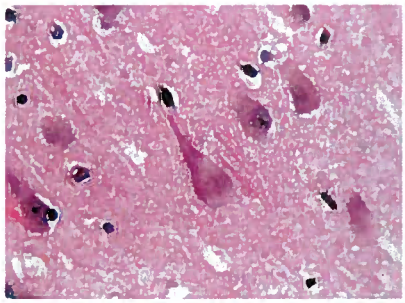


Figure 1. Senile plaques in the hippocampus are round and more eosinophilic than the background.
Figure 2. Neurofibrillary tangles in the cytoplasm of pyramidal neurons.

Diagnosis: The diagnosis of AD is primarily clinical. Imaging studies (CT, MRI) and laboratory tests may be used to rule out other causes of dementia. For patients with early onset AD and positive family history, genetic tests for mutations in amyloid precursor protein (APP) and presenilin genes may be indicated for familial AD. Recently, it was discovered that individuals carrying apolipoprotein E (APOE) e4 allele are at increased risk of developing AD. APOE genotyping could stratify the risks of AD. However, many experts believe this test should not be offered to individuals given its low predictive value.

Treatment: Current treatments for AD are for symptoms only. There have been many research efforts and clinical trials involving agents that can potentially lower or clean beta-amyloid and tau proteins in the brain. For example, various vaccines, monoclonal antibodies, and chelating agents have been tried. Unfortunately, none has succeeded beyond stage III clinical trial so far.

Submitted by: Dr. Jie Song