



Family History of Alzheimer Disease

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Alzheimer disease (AD) is the most common form of chronic dementia in North America and Europe. AD is characterized by adult-onset, slowly progressive dementia. The first noticeable symptom is generally memory loss and a problem with attention. Other common symptoms include confusion, poor judgment, language disturbances, and behavior/personality disturbances. Death usually results from malnutrition, pneumonia, or other infections. Age of onset is variable, usually occurring between 50 to 75 years of age. The disease is often more severe in younger patients. The course of AD is usually 8-10 years, although the duration can range from 1 to 25 years.

There is no accurate clinical diagnostic test for most cases of AD, although imaging studies of the brain will show cerebral atrophy. The diagnosis is confirmed by characteristic changes in the brain tissue itself. These β -amyloid plaques and intraneuronal neurofibrillary tangles can only be identified by autopsy examination.

The cause of Alzheimer disease in most cases is unknown, and the contribution of genetic and environmental factors to the disease is unclear. It is thought that late-onset AD is the result of unknown environmental factors acting on a predisposing genetic background.

Most reported cases of AD are sporadic, with the affected person having no known family history. Approximately 25% of AD is familial, with multiple family members having the onset of dementia after the age of 65 years. This type of AD is a complex disorder that may involve multiple genes. First-degree relatives (parents, siblings, and children) of a single individual with AD have an approximately 20% lifetime risk of also developing AD. When several individuals in a family have AD, the risk is further increased.

Studies have shown a significant association between the *APOE* e4 allele and late-onset Alzheimer disease. However, the usefulness of *APOE* e4 testing in clinical diagnosis and risk assessment remains unclear. At this time, this testing does not appear to have a role for predicting disease.

Early-onset familial Alzheimer disease (EOFAD) refers to families with multiple affected individuals with the onset of dementia before 65 years of age. Less than 2% of families with AD have this type. Mutations in three different genes (*APP*, *PSEN1*, and *PSEN2*) have been found to cause the three subtypes of EOFAD. Molecular genetic testing for these mutations is clinically available. EOFAD is inherited in an autosomal dominant manner, with the offspring of affected individuals having a 50% risk to also develop EOFAD.

For additional information, please contact the Alzheimer's Association National Headquarters at 800-272-3900 or www.alz.org.