Facts About Genes and Alzheimer’s Disease

Risk Factors for Alzheimer’s Disease (AD)
- The greatest risk factor associated with AD is increasing age.
- A family history of AD is also a risk factor. When people of the same age are compared, those who have a parent or a sibling with AD are 2 – 3 times more likely to develop AD than people who do not.

Two Forms of Alzheimer’s Disease
Sporadic AD
- genes, by themselves, do not cause AD, but may influence the risk of developing the disease
- occurs in a less predictable manner and in fewer family members
- most common form of AD
- most cases occur after age 60; often called late-onset Alzheimer’s

Familial AD
- genes are the direct cause of AD
- occurs in families with many members affected in multiple generations, and is very rare
- most cases occur before the age of 60; often called early-onset Alzheimer’s

Sporadic Alzheimer’s Disease/ late-onset AD
- Not caused by any particular gene that guarantees development of AD;
- slight variations in genes may, however, affect an individual’s susceptibility to sporadic AD
- Apolipoprotein E (APOE) is the best-studied susceptibility gene
  - there are 3 forms of APOE: APOE-ε2, APOE-ε3, and APOE-ε4
  - APOE-ε4 is associated with AD: people who inherit one APOE-ε4 (from one parent) or two APOE-ε4s (from both parents) have a higher risk of developing AD than people who have no APOE-ε4
- However, it is important to note that:
  - People with 2 copies of APOE-ε4 do not invariably develop AD
  - There are many cases of AD in people who have no APOE-ε4
- There is strong evidence that other susceptibility genes affect the development of AD. This is the most active area of research in AD.

Familial Alzheimer’s Disease/ early-onset AD
- Can be caused by mutations in one of three possible genes
  - the presenilin genes (PS1 and PS2)
  - the amyloid precursor protein gene (APP)
- These mutations are inherited
an individual who carries a mutation has a 50% chance of passing the gene on to children
- those who inherit the mutation will almost certainly develop AD
- The protein products of the PS1, PS2 and APP genes provide important clues about the biological cause of AD
  - all 3 genes are involved in the production of \( \beta \)-amyloid
  - \( \beta \)-amyloid is a sticky substance that clumps together in the brain and probably plays a role in the development of AD pathology

**Genetic Testing**

- Genetic testing is available for mutations in the 3 genes that cause *Familial/early-onset AD*; testing must be considered very carefully
  - these mutations are rare; only about 200 families in the world are known to carry such mutations
  - since no preventive treatment is available, results of testing will have no practical impact on medical treatment decisions
  - test results may have a significant effect on an individual’s psychological well-being and family relationships, and may affect employment, health and long-term care insurance matters
  - **It is very important to receive genetic counseling before a test is ordered and when results are obtained, in order to discuss these issues thoroughly with trained genetic counselors.**

- For individuals with no symptoms of dementia, genetic testing is not recommended for *Sporadic/late-onset AD*; a positive test of APOE-\( \varepsilon \)-4 does not provide useful information:
  - people with APOE-\( \varepsilon \)-4 may or may not develop AD
  - people with no APOE-\( \varepsilon \)-4 may still develop AD
  - there are medical, legal, social and ethical issues involved
  - testing positive for APOE-\( \varepsilon \)-4 may cause employment, insurance and psychological problems

- For individuals with dementia symptoms, **APOE testing has limited value**
  - in a thorough assessment, without APOE testing, AD can be diagnosed with approximately 90% accuracy
  - the accuracy of the diagnosis can only be slightly improved with APOE testing
  - test results may provide unwanted information for the children of the AD patient, in terms of their own genetic makeup.

- Genetic testing can be very important in a research setting. Such testing can be done so that results are kept confidential and not revealed to the study participant or their families.

**For More Information:**

*Genetic Testing: Ethical Issues in Alzheimer’s Disease.* This statement by the Alzheimer’s Association Ethics Advisory Panel can be found on the Association Web site at [www.alz.org/ResourceCenter/ByType/FactSheets.htm](http://www.alz.org/ResourceCenter/ByType/FactSheets.htm).

The Alzheimer’s Disease Education and Referral Center (ADEAR) at [www.alzheimers.org](http://www.alzheimers.org)

*Alzheimer’s Disease: What Causes It?* An interactive information page on AD symptoms, causes, treatment and testing at [http://www.yourgenesyourhealth.org/alz/cause.htm](http://www.yourgenesyourhealth.org/alz/cause.htm)