

GENETIC TESTING

Background

Genetics and Alzheimer's disease

Genetics is the study of how a specific characteristic, such as a disease, is passed from one generation to another. The role of genetics in Alzheimer's disease is a subject of intense study for scientists and a major concern for people with Alzheimer's disease and their families.

Alzheimer's disease can be grouped into two types: Familial Autosomal Dominant Alzheimer's Disease (FAD) and Sporadic Alzheimer's Disease.

- **Familial Autosomal Dominant Alzheimer's Disease (FAD)**

This type of Alzheimer's disease is rare and accounts for approximately five to 10 per cent of all cases of Alzheimer's disease. It is known to be inherited. The disease will occur if the disease gene is present. In certain families, FAD is passed from one generation to another through a dominant inheritance pattern. This means that if a parent is affected, each child has a 50 per cent chance of inheriting the disease gene and developing Alzheimer's disease in adulthood. This form of Alzheimer's disease is usually associated with early onset of the disease, before age 65.

- **Sporadic Alzheimer's Disease**

This is the more common form of Alzheimer's disease and accounts for 90 to 95 per cent of all cases. It usually occurs after the age of 65. Many studies indicate that people with a relative (parent, brother or sister) with Alzheimer's disease have a greater chance of developing the disease than those with no family history. However, the role of heredity in Sporadic Alzheimer's Disease is unclear and continues to be the subject of research.

Genetic testing

There are two types of genetic investigation of a disease. Each has its limitations.

- **Predictive genetic testing**

This is a genetic test that can identify whether an unaffected person has a very high (approaching 100 per cent) or very low (approaching zero per cent) chance of developing a certain disease.

With Alzheimer's disease, predictive genetic testing can be used only in families that exhibit the very specific inheritance pattern associated with FAD. For the vast majority of families with Alzheimer's disease, predictive testing is not an option.

- **Genetic risk assessment**

This is the identification of genetic risk factors that could potentially increase a person's chance of getting an illness. The presence or absence of a genetic risk factor does not positively predict who will or will not get a disease. Therefore, a genetic risk assessment cannot be used to determine whether or not a person will get a disease in the future.

With Alzheimer's disease, one known genetic risk factor is the presence of the apolipoprotein E4

(APOE4) gene in a person's genotype (genetic makeup). The presence of APOE4 is associated with an increased risk of Alzheimer's disease. However, the gene, by itself, cannot predict that a person will develop Alzheimer's disease.

The meaning and accuracy of APOE testing is the subject of intense study. Advisory groups worldwide have stated that knowing a person's APOE genotype cannot be used to predict that the person will develop Alzheimer's disease in the future.

The issues

For people with Alzheimer's disease and their families:

Decision to be tested or not: Predictive genetic testing for Alzheimer's disease is an option only for people in families with a history of FAD. The decision whether or not to undergo genetic testing is difficult for many people. Will the information help people make decisions about personal relationships, having children, financial and lifestyle choices? Also, do people want to know their chances of developing a disease for which there may be treatment for symptoms but currently no cure and no prevention? What effect will this information have on the individual and other family members? For example, will it affect their access to insurance and employment benefits?

Right to know versus the right not to know: Within a family, one person may want to know whether or not he carries the gene or genetic risk factors for Alzheimer's disease; another may not. However, the assessment of one family member may reveal genetic information about other family members. Should informed consent be obtained from all family members before any type of genetic testing can occur?

Right to privacy and confidentiality: Who should be notified of the results of genetic testing? Should family members, insurance companies and employers be able to obtain the results? Should the information be kept confidential? Should the person who has been tested be allowed to prevent others from getting the results?

Potential exploitation of a person's desire to know: Some people are willing to buy any test that promises to tell the future, whether or not the test is sound or is accompanied by the essential components of consent, counselling and confidentiality. How should the potential exploitation of people concerned about developing Alzheimer's disease be addressed?

What does this mean for families concerned about Alzheimer's disease?

• Predictive testing

For the small group of families where the specific gene changes (on chromosome 21, 14 or 1) that cause FAD have been identified, predictive testing can be sought from clinical genetics units throughout Canada. Any predictive testing should be done with individual consent, counselling and confidentiality.

Consent: The person who is being tested or assessed must be aware of the type of test that is being done and the potential results, and must agree to undergo the test or assessment.

Counselling: Test results may have major psychological, legal and ethical implications for individuals and families. Counselling by trained professionals must be an integral part of the testing process.

Confidentiality: There must be guarantees that all test results remain confidential.



- **Genetic risk assessment**

At present, given the recommendations of several international committees, genetic risk assessment for Alzheimer's disease, based on APOE genotyping, is not performed as a clinical service in Canada.

In closing...

The field of genetics is a growing one. Each day, scientists are learning more about our genetic makeup. The challenge remains that, with every new discovery, consideration must be given to the effects on individuals, their families and society in general.

For the vast majority of people concerned about developing Alzheimer's disease, there is, at present, no test to determine if a specific unaffected person will or will not develop Alzheimer's disease.

For the small number of people for whom predictive testing is possible, the decision to know or not to know is a personal one. However, it should only be made in a setting that allows for informed consent, counselling and confidentiality.

Concerned individuals should contact the Alzheimer Society or their local clinical genetics unit for more information.

Resources:

From the Alzheimer Society of Canada:

1. [Alzheimer's Disease and Heredity](#)
2. [Alzheimer's Disease and Risk Factors](#)