ALZHEIMER'S DISEASE AND GENETICS

The role of genes in Alzheimer's disease

Alzheimer's disease is the most widespread of a large class of disorders which clinically are known as "dementias". It is a disease of the brain, characterized by deterioration of thinking ability and of memory, caused by the progressive death of brain cells.

Sporadic Alzheimer's disease

Alzheimer's disease is not a normal part of aging. It is a disease that can affect young adults but more often affects people as they get older. The majority of people with Alzheimer's disease have the "sporadic" or "late onset" form, with no specific family link. However, even in the sporadic form of Alzheimer's disease having a close relative (a parent or sibling) with the disease does increase the chances of a person developing Alzheimer's disease by a small percentage.

Familial Alzheimer's disease (FAD)

About seven per cent of people with Alzheimer's disease have "Familial" Alzheimer's disease (FAD), or "early onset" Alzheimer's disease. FAD is identical to the sporadic form, but it is largely attributable to the inheritance of specific genes which at some point in the history of certain families "mutated". This means that they changed their normal character to an abnormal one, in consequence making the members of those families very highly susceptible to Alzheimer's disease.

APOE

Aside from the mutated genes responsible for FAD, the most important genetic risk factor for both the familial and sporadic forms of Alzheimer's disease is the apoE4 gene. This gene is not, however, an abnormal one, i.e. it has not undergone a mutation that has impaired its ability to carry out its usual job. ApoE4 is one of the three variants of the apoE gene, the others being the benign apoE2 and apoE3 genes. Everyone has a double set of genes; one from each parent. If a person's pair of apoE genes include one apoE4, they have three times the normal risk of developing Alzheimer's disease, but if they carry two apoE4 genes the risk increases to ten times. It is important to note, however, that people with no apoE4 genes can still develop Alzheimer's disease, and people with two apoE4 genes may not. Researchers are actively looking for evidence of other quite normal genes that predispose one to Alzheimer's disease, but it seems unlikely that these still to be discovered genes will be as important a risk as the apoE4 one.

Genes are not the complete answer

Although one's genes are present from birth, they can't cause the disease on their own. Alzheimer's disease seems to develop when the combined effects of various "risk factors" cross a certain "threshold" and overwhelm the natural self-repair mechanisms in the brain that normally help to maintain nerve cells in a healthy state. The most important risk factor is aging. Even in FAD a minimum age needs to be reached for Alzheimer's disease to develop (family members do not get the disease in their teen years or even in their 20s).

For more information on risk factors, please refer to the Alzheimer Society's Information Sheet on **Alzheimer's Disease and Risk Factors**.

Alzheimer's disease and genetic testing

Predictive genetic testing can sometimes help identify whether a person has a high or low chance of developing Alzheimer's disease. The presence of the apoE4 gene gives an indication of susceptibility for developing Alzheimer's disease, even in the sporadic form. However, there is presently no reliable genetic test for the common sporadic form of Alzheimer's disease. Therefore, for the vast majority of families, predictive testing is not a recommended option.

For the small number of people for whom there are clear indications that the disease is transmitted through the family, predictive testing is often recommended though entirely at the discretion of the person concerned. In these instances it is important that an experienced clinical geneticist* is involved in the required medical assessment.

If the person suspected to have had Alzheimer's disease is no longer living, the "best estimate" diagnosis can be determined through a careful review of autopsy reports and medical records, if they are available.

* Contact your local Alzheimer Society for information about the availability of genetics clinics in your area.

What are the implications of testing for genetic factors?

The decision to participate in genetic testing is a personal one. Prior to consenting to genetic assessment or testing, it is important to consider the psychological, legal, social and ethical implications of genetic testing. If the decision is made that genetic testing is appropriate, the person should:

- give **informed consent** to the testing
- receive **counselling** from a trained professional
- be guaranteed that the test results will remain **confidential**

Need further information?

For more information on the ethical questions raised by testing, refer to "Genetic Testing and Alzheimer's Disease", part of the Alzheimer Society's *Ethical Guidelines*. Copies can be obtained from our website at www.alzheimertoronto.org.

Families with a history of Alzheimer's disease can inquire about participating in research through the Familial Alzheimer Disease Registry, Centre for Research in Neurodegenerative Diseases, Tanz Neuroscience Building, University of Toronto, 6 Queen's Park Crescent West, Toronto, ON, M5S 3H2; www.utoronto.ca/crnd; email: crnd.info@utoronto.ca.