

# Understanding Genetics and Alzheimer's Disease

Alzheimer Society

Research

## What is Alzheimer's disease?

Alzheimer's disease is one type of a large group of disorders known as "dementias." Alzheimer's disease is a disease of the brain in which the progressive degeneration of brain cells causes symptoms of dementia such as memory loss, difficulty performing daily activities, and changes in judgement, reasoning, behaviour and emotions. These dementia symptoms are irreversible, which means that any loss of abilities cannot come back. There is currently no cure for Alzheimer's disease. **However, there are treatment options and lifestyle choices that may slow it down.**

**Young-onset Alzheimer's disease:** Symptoms become noticeable before age 60-65.

**Late-onset Alzheimer's disease:** Symptoms begin after age 60-65.

**Note:** All **bolded** words are found in a Glossary of Terms located at the end of this document.

## Alzheimer's disease is not the only form of dementia

Alzheimer's disease is a common form of dementia; however, there are many other forms of dementia. Other irreversible dementias include vascular dementia, Lewy body dementia, frontotemporal dementia, and Creutzfeldt-Jakob disease. These conditions can have similar and overlapping symptoms, and many of them can only be diagnosed with certainty by an autopsy of the brain. Sometimes people are concerned about a family history of Alzheimer's disease when, in fact, they have a family history of a different dementia.

## The genetics of Alzheimer's disease

*Most Alzheimer's disease does not run in families and is described as "sporadic"*

- The most common form of Alzheimer's disease is called **sporadic Alzheimer's disease**; it has no specific family link.
- Sporadic Alzheimer's disease is due to a complex combination of our **genes**, our environment and our lifestyle.
- Any of us might develop sporadic Alzheimer's disease in our lifetime, just as any of us might develop heart disease, cancer, diabetes, or other health problems.
- The single greatest risk factor for developing sporadic Alzheimer's disease is aging.
- Most sporadic Alzheimer's disease symptoms become noticeable after age 60-65.
- Researchers have found many genes that may increase the chance of developing sporadic Alzheimer's disease. These genes are called **susceptibility genes** because they do not directly cause Alzheimer's disease, but they make you more susceptible to developing it in your lifetime.
- The role of specific environmental factors in developing sporadic Alzheimer's disease is unclear. Some studies show that it may be possible to decrease the likelihood of sporadic Alzheimer's disease by keeping your mind and body active, avoiding head injury, reducing vascular disease risk factors, and effectively managing stress and depression. For more information on dementia risk factors, please visit [www.alzheimer.ca/riskfactors](http://www.alzheimer.ca/riskfactors). For more information about brain health, please visit [www.alzheimer.ca/brainhealth](http://www.alzheimer.ca/brainhealth)

- Research has not confirmed whether specific vitamins, substances or supplements can prevent or slow down Alzheimer's disease. Before trying any of these, be sure to discuss the possible risks and benefits with your doctor.
- Sporadic Alzheimer's disease usually does not run in families. However, people who have a family history of sporadic Alzheimer's disease have a greater chance of developing the disease than people with no family history of Alzheimer's disease.

***Rare cases of Alzheimer's disease are inherited or "familial"***

- Families with **familial Alzheimer's disease** have very strong family histories of Alzheimer's disease (many family members over many generations).
- Familial Alzheimer's disease has similar symptoms as sporadic Alzheimer's disease and can develop at any age.
- Familial Alzheimer's disease accounts for less than 5% of all cases of Alzheimer's disease.
- Familial Alzheimer's disease is due to changes or alterations in specific genes that can be directly passed on from parent to child.
- Three familial Alzheimer's disease genes have been discovered so far: two presenilin genes (PSEN1 and PSEN2), and an amyloid precursor protein (APP) gene. If you have an alteration in any one of these genes, you will almost certainly develop young onset familial Alzheimer's disease (before the age of 65). Alterations in the PSEN1, PSEN2, and APP genes are rarely known to cause Alzheimer's disease among persons 65 years and older.
- These three disease genes (PSEN1, PSEN2 and APP) together are responsible for about half of familial cases. This is why researchers are searching for other genes that might cause familial Alzheimer's disease.
- Familial Alzheimer's disease is hereditary. If a parent has any of the faulty genes (PSEN1, PSEN2 or APP), their children have a 50% chance of inheriting the disease. If a person does not inherit the disease-causing gene they cannot pass it on to their children.

**Is there genetic testing for Alzheimer's disease?**

For most of us, there is no genetic test that can definitely tell us whether we will develop Alzheimer's disease.

***Genetic testing for sporadic Alzheimer's disease is not recommended.***

Researchers have identified several susceptibility genes for sporadic Alzheimer's disease. However, a susceptibility gene called the APOE4 gene is believed to have the greatest impact on a person's chances of developing sporadic Alzheimer's disease. ApoE4 is also associated with an earlier age of onset.

Some people who are concerned about developing sporadic Alzheimer's disease might be interested in finding out if they carry an APOE4 gene. Advisory committees around the world have recommended against this type of genetic testing. This is because individuals who have an APOE4 gene might never develop Alzheimer's disease and individuals with no APOE4 genes can still develop Alzheimer's disease.

**Direct-to-consumer genetic testing:** Some internet companies provide APOE4 genetic testing. Experts caution against using these services. If you are considering any kind of genetic testing, make sure you talk to your doctor or a genetic counsellor beforehand.

### *Genetic testing for familial Alzheimer's disease is available in some cases.*

Genetic testing is only an option for families that have young-onset familial Alzheimer's disease.

If you are interested in genetic testing for young-onset familial Alzheimer's disease, the first step of this process should be a detailed review of your family history by a **genetic counsellor** or physician to make sure that your family fits the pattern of young-onset familial Alzheimer's disease (several family members with Alzheimer's disease beginning before the age of 60-65). These families are rare.

If your family fits the young-onset familial Alzheimer's disease pattern, a sample of **DNA** (genetic material) would need to be taken from a family member who has been diagnosed with young-onset Alzheimer's disease. This DNA sample would then be tested for alterations in the three known young-onset familial Alzheimer's disease genes (PSEN1, PSEN2, and APP genes).

If this family member is found to have an alteration in one of the three young-onset familial Alzheimer's disease genes, other relatives can choose to have genetic testing to find out if they carry the same alteration, even if they have no symptoms of Alzheimer's disease. This is called **presymptomatic or predictive genetic testing**. This testing can only be done after meeting with a genetic counsellor to review all the risks and benefits.

Testing of the three known young-onset familial Alzheimer's disease genes can be done at Canadian research laboratories or commercial laboratories in the United States. Commercial testing is costly and may not be covered by your provincial healthcare plan.

### **Help is available**

If you are thinking about genetic testing for Alzheimer's disease it is important to get help from a healthcare professional like your doctor or a certified genetic counsellor. They will help you find out whether genetic testing is relevant for you based on your family history. If it is relevant, they will also help make sure you understand the testing process and all the things you should think about before getting tested.

**For more information about genetic testing, please contact the Alzheimer Society of Toronto, your family doctor, or the Canadian Association of Genetic Counsellors ([www.cagc-accg.ca](http://www.cagc-accg.ca)).**

**This document is for information only; it is not intended to replace the advice of a healthcare professional.**

**There is a lot to think about before having a genetic test for familial Alzheimer's disease, including:**

- **Motivations:** Why do you want the test? Will it change life decisions such as financial planning or having children?
- **Informed consent:** Do you fully understand what the test will and will not tell you? Do you fully understand the possible benefits and risks of having the test?
- **Confidentiality:** Will your test results be kept private? Who will you share them with?
- **Risks:** Will the test results affect family relationships? Your mental or emotional wellbeing? Insurance or employment applications?

## Glossary of terms

**DNA:** The human body contains about 25,000 to 35,000 genes. Each gene has a special job to do. Genes are made up of DNA. The DNA in a gene holds the instructions for building proteins, which are the building blocks for everything in your body. You can think of DNA as a cookbook recipe, in which the DNA contains all of the instructions needed to “cook” something in your body, such as muscles.

**Familial Alzheimer’s disease:** Familial Alzheimer’s disease accounts for less than 5% of all cases of Alzheimer’s disease. This form of the disease runs in families. If a person has familial Alzheimer’s disease, each of their children has an increased chance of inheriting the disease-causing gene and developing Alzheimer’s disease.

**Genes:** Genes carry the information that determines many of your traits (such as your hair colour and your height). Genes are passed on to you from your parents, and you have two copies of each gene, one inherited from each parent. Genes also provide your body with the instructions that it needs to build and maintain itself. Although genes play a role in the development of some diseases, it is important to know that your environment and lifestyle can have an equal or greater impact on your health.

**Genetic counsellor:** Genetic counsellors are health professionals that provide individuals and families with support and information on genetic disorders to help them make informed medical and personal decisions.

**Genetic testing:** Genetic testing is a type of medical test that looks at your genes. A genetic test can help confirm or rule out a suspected genetic condition, or help determine a person’s chance of developing a genetic disorder, such as familial Alzheimer’s disease. A genetic test may also help when choosing treatments or to evaluate how your body will react to a treatment.

**Informed consent:** An informed decision is made when you:

- have all the information available
- can understand the information provided
- can communicate your wishes
- understand the consequences of your decisions

**Presymptomatic or predictive genetic testing:** A genetic test performed on a person who has a family history of a disease, such as Alzheimer’s disease, but does not have symptoms of the disease at the time of testing.

**Risk factor:** Risk factors are characteristics of your lifestyle, environment and genetic background that increase the likelihood of getting a disease. Risk factors, on their own, are not causes of a disease. Rather, risk factors represent an increased chance, but not a certainty, that dementia will develop.

Similarly, having little or no exposure to known risk factors does not necessarily protect a person from developing the disease. Some risk factors are modifiable, meaning that they can be changed (e.g., smoking and high blood pressure). Other risk factors are non-modifiable, meaning they cannot be changed, such as age or genetic makeup.

**Sporadic Alzheimer’s disease:** This is the most common form of Alzheimer’s disease; it has no specific family link. Sporadic Alzheimer’s disease is due to a complex combination of our genes, our environment and our lifestyle. The single greatest risk factor for developing sporadic Alzheimer’s disease is aging. Most symptoms become noticeable after age 60-65 years.

**Susceptibility genes:** Genes that may increase the chance of developing sporadic Alzheimer’s disease. These genes are called susceptibility genes because they do not directly cause Alzheimer’s disease, but they make you more susceptible to developing it in your lifetime.

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