

GENETIC TESTING FOR ALS

ALS is a rapidly progressing and fatal neuromuscular disease. Since ALS paralyzes the body's voluntary muscles and may not impact the mind, sufferers of ALS are often aware of what is happening to their bodies. Approximately 3,000 Canadians are currently living with the disease and every day, two or three Canadians die of ALS. Since the majority of people with ALS do not have the hereditary version, an ALS diagnosis does not involve a genetic test. A neurologist will make the diagnosis after symptoms are reviewed, a neurological exam is conducted and results on nerve and muscle function tests have been examined. Clinically, familial ALS is identical to non-familial. Approximately ninety percent of people with ALS do not have a family history of the disease. However, in a small percentage of families, ALS is directly hereditary. Currently, the best way to identify familial ALS is through an examination of the family history. Humans have 23 pairs of chromosomes. In each chromosome pair, one chromosome is inherited from the mother and the other from the father. 'Autosomal dominant' is the name for the most common inheritance pattern for familial ALS. With this inheritance pattern, it is equally likely for a male or female to obtain the disease because a mutated gene is located on a chromosome that men and women have in common. A mutation is an error in the genetic code, resulting in the gene working abnormally. A child who is born to someone who has familial ALS has a 50 per cent chance of inheriting the gene mutation. In this case, the 50 per cent chance is derived from the fact that parents randomly pass on only one of the paired genes. Therefore, either the gene with the mutation or the one without it will be passed on. Approximately five to 10 per cent of ALS cases are hereditary and approximately 20 per cent of these have a mutation of the superoxide-dismutase (SOD1) gene, located on chromosome 21. The normal function of this gene is to detoxify the free radicals that can be harmful to the body's cells. Other candidate genes relevant to ALS are being actively sought and include genes that are involved in the assembly of neurofilaments and in the transport of glutamate.

People who may be carriers of the mutated gene (SOD1) may want to know in order to help them with decisions about marriage and having a family; also, if it is known that they have the gene and it becomes possible to prevent ALS, then the most can be made of future measures. There are also reasons why someone may not wish to know they are a carrier. It could be extremely difficult to live with the knowledge that the gene is present and ALS might develop, especially since, to date, ALS is not preventable nor is there a cure. For the familial ALS test, a blood sample is taken and sent to a laboratory where the DNA is removed. Specialized techniques allow for the SOD1 gene to be duplicated and then tested. One of the methods used for testing the DNA is to create bands by running the sample on a type of gel. The bands will be in a different location as compared to the control sample – which does not have a genetic change in the SOD1 gene – if a genetic change is present. The name of this method is single strand conformation polymorphism (SSCP). A second method is called sequencing and involves viewing the DNA on a finer scale so that changes to the gene can be seen. A positive result on the genetic test would signify that the hereditary cause of familial ALS has been identified. A mouse model with the same gene mutation has been developed by researchers so that the change in the SOD1 gene that leads to ALS symptoms can be better understood. At the present time, new therapies – designed to slow or halt the progression of ALS – are being tested on the mouse model. Gene therapy to correct the genetic mutation, while still in the future, is also being investigated. It is important to remember that a person's inheritance of the gene for familial ALS is not in any way a guarantee that they will develop symptoms of ALS. In general, it is not recommended that children under the age of 18 be tested; consent for this test must be given and the implications of the result must be fully grasped. Some people who have ALS of a non-familial type also have mutations in their SOD1 genes. Mutations in other genes, to date unidentified, may cause familial ALS. Researchers are currently carrying out studies to understand how ALS is caused by mutations in SOD1 and to discover ways of preventing and treating ALS.