

## *FREQUENTLY ASKED QUESTIONS ABOUT...*

# **Gene Testing for Hereditary Ataxia**

This fact sheet provides an overview of gene testing for ataxia. It also addresses commonly asked questions about gene testing for ataxia, and offers general guidelines for testing of the hereditary ataxias. Keep in mind that the answers and information given here are general. Your physician and a genetic counselor should be consulted for more specific recommendations pertaining to your care and genetic testing.

### **What is ataxia?**

Ataxia is defined as a lack of muscle coordination. It can affect almost all of your movements, including walking, speech, eye movements, and hand control. Ataxia is a symptom that can occur as the result of strokes, head injuries, illness, and hereditary disease.

### **What is hereditary ataxia?**

Ataxia is one of the symptoms in more than 300 hereditary conditions. However, inherited conditions where ataxia is the primary symptom are much less common. These inherited forms of ataxia are often referred to as “hereditary ataxias.” Hereditary ataxia means the condition is caused by changes in genes that are inherited from parents and may be passed to children.

### **What is genetic information?**

We are all born with genetic instructions of how to grow and develop. We inherit our genetic information through chromosomes passed to us from our parents. We have 23 pairs of chromosomes because we receive one copy of each chromosome from our mom and one from our dad. 22 pairs are the same in males and females and are called autosomal chromosomes. The 23rd pair differs between males and females and the chromosomes in this pair are called the sex chromosomes. There are a number of different

genes that can cause ataxia and at this time most are located on autosomal chromosomes. Chromosomes are made up of substances known as nucleotides. These nucleotides, identified by letters, are linked together in chains. A group of nucleotides together form genes. There are thousands of genes located on each chromosome.

Many of the genes that cause dominant forms of ataxia have a mutation resulting from expanded sections in these nucleotide chains called “trinucleotide repeat expansions.” For instance, a mutation in the SCA1 gene on the sixth chromosome results in extra copies of a series of nucleotides identified by the letters C-A-G. In some conditions, the number of trinucleotide repeats is associated with the severity of the disease and the age of onset.

### **For which of the hereditary ataxias is gene testing available?**

Discovery of specific ataxia genes makes it possible to develop blood tests to facilitate the diagnosis of both symptomatic individuals and at risk family members. In 1993, the first ataxia gene was identified by a research team led by Drs. Harry Orr and Huda Zoghbi. This gene is responsible for spinocerebellar ataxia type 1 (SCA1). Its discovery paved the way for the identification of many additional ataxia genes. The list continues to grow as we discover new forms of ataxia.

As of 2015, genetic testing is available for dozens of forms of ataxia including dominant ataxias (e.g. SCA1, SCA2, SCA3, SCA6 and others), recessive ataxias (e.g. Friedreich ataxia, AOA1, AOA2, and others), X-linked ataxias (e.g. Fragile X tremor ataxia syndrome), and mitochondrial ataxias (e.g. MELAS). New genetic testing technologies have enabled the discovery of many new ataxia genes and the list of available tests is constantly growing.

## **What is the preparation for gene testing?**

NAF recommends that you research your family tree and record as much information as possible about your family, including your parents, siblings, grandparents, uncles, aunts, and cousins. This can help your doctor as he or she tries to determine the cause of ataxia in your family. NAF also highly recommends that you consult with a genetic counselor as you consider genetic testing for diagnostic or predictive purposes. A counselor can help collect your family history and discuss how ataxia is being inherited in your family. In addition, a genetic counselor will discuss the risks, capabilities, limitations, accuracy, costs, and requirements of genetic testing. Genetic counseling should be made available to all family members because genetic testing has direct implications for the affected individual as well as other family members (siblings, parents and children).

Meeting with a genetic counselor allows you the opportunity to explore important issues such as the reason for pursuing testing at this time, possible outcomes of learning the results, clarification of your support system, and appropriate timing for testing.

## **What are the purposes of genetic testing?**

**Diagnostic testing** – Testing is performed when symptoms are present. The purpose of diagnostic testing is to confirm or rule out a specific hereditary ataxia. A careful evaluation by a physician will help determine which genetic tests to perform and rule out the possibility of other medical problems. If a gene test has already shown the specific type of ataxia present in a family, it is not necessary to test every affected person. However, if for any reason the diagnosis is uncertain in a family member, a diagnostic test will be useful. When ataxia is sporadic (there is no known family history of affected relatives), gene testing should be considered only after non-genetic causes of ataxia have been excluded. In these cases, tests for known ataxia genes often come back normal. However, as more genes are identified, gene tests may provide a definitive diagnosis in a greater number of cases.

**Predictive testing** – Testing is performed when there are no ataxia symptoms in an individual, but they are at risk for developing a known form of ataxia. The purpose of predictive testing is to determine whether a gene mutation is present and whether you will develop symptoms or not. People elect predictive testing to help plan and prepare for their future. To be eligible for predictive gene testing, you must know which specific type of ataxia runs in your family and be 18 years or older.

There are a number of other issues to consider before having a predictive gene test, including the possible psychological effects of the results on you or your family and the impact of results on your insurance and employment. It is best not to rush into a predictive test. Once you know the answer, you can never “unknow” it. Predictive testing will not tell you when symptoms of ataxia will begin or how severe your symptoms will be.

**Prenatal testing** – Prenatal testing is another form of predictive testing. When a family has a history of a specific hereditary ataxia, prenatal testing will determine whether the abnormal gene is present in a fetus. Prenatal testing is performed through an invasive procedure, such as an amniocentesis. If you have or are at risk of having a child with ataxia and are of childbearing age, NAF recommends that you talk to your physician and a genetic counselor regarding reproductive options. A variety of options currently exist for couples at risk for hereditary ataxia.

**Pre-implantation genetic diagnosis** – Genetic screening for mutations associated with ataxia can be performed on embryos produced through in vitro fertilization. If you are at risk of having a child with ataxia, in vitro fertilization is a technology that can be used to conceive embryos outside of the body using genetic material from both parents. Embryos can be tested for genetic mutations before they are implanted into the uterus. This screening process allows couples at risk for hereditary ataxia to greatly reduce the risk of their child inheriting the condition. In order to perform PGD, doctors will need to know the type of ataxia that is in your family.

**Exome or Genome sequencing** – Some individuals have a family history of ataxia, but diagnostic tests for known ataxia genes cannot explain the ataxia in their family. In recent years, scientists have developed technologies to sequence thousands of genes at the same time. This allows specialists to find ataxia-causing genetic mutations in many families. However, since these tests provide such a large amount of genetic information, they may identify some unexpected findings in your genes. If you are considering exome or genome sequencing, it is important to consider the following possibilities:

- **Variants of uncertain significance** – Exome or genome sequencing may identify changes in genes that are difficult to interpret. In some cases, these changes may be the cause of a person's ataxia. In other cases, these changes turn out to be normal variations. It often takes years to figure out the significance of these findings.

- **Incidental findings** – When looking at such a large amount of genetic information, it is possible that the results will show the presence of a genetic mutation that is not linked to ataxia, but may provide you with information about other serious health concerns. For example, the testing may find a genetic variation that increases your risk for cancer or heart disease.

- **Portions of the genome not sequenced** – Current testing cannot completely analyze all of your genes. This means that there may be variants or mutations in your genome impacting your condition that testing will not detect. Testing is expected to improve with time.

### **What are the key considerations before undergoing gene testing?**

If you are considering a predictive gene test for ataxia, it is important to locate a clinic that provides the following services:

- **Genetic counseling** – Before gene testing, a geneticist or genetic counselor should explain genetic principles important for understanding the test and its results. He or she should clarify what the test does and does not provide, the implication of the results, and the alternatives to genetic testing. The reasons for seeking

predictive testing, in particular, are complex and the outcome of such a test (favorable or unfavorable) can potentially impact many aspects of life, including work, ability to obtain life and health insurance, and relationships with family and friends. Finally, the logistics (cost and payment, clinical protocol, resources, etc.) of a gene test should be reviewed.

- **Psychological assessment/Counseling** – prior to testing, psychological evaluation is recommended to ensure the person being tested is as prepared as possible to receive the test results, and to ensure connection with a professional in the event that further support is needed after the results are given. As part of the assessment, the psychologist or psychiatrist will review support resources and stress management, as well as anticipated benefits of the gene test results. In some cases, this may be provided by a genetic counselor and does not require an additional visit to a psychologist.

- **Neurologic evaluation** – Before gene testing is ordered, the coordinating physician may choose to perform neurologic examinations, MRI scans, or other tests. It is important to be informed about the reason for the exam or tests, the possible outcomes, and the nature of information they will provide.

- **Time** – It is wise to allow a span of time between the request for genetic testing and the actual drawing of blood to proceed with the test. This provides the opportunity to carefully consider the input from the counseling sessions before deciding to actually proceed with the test.

- **Results and follow-up** – Predictive test results, favorable or unfavorable, should always be given in person rather than by telephone or mail. Follow-up should be discussed at the time that results are given. A physician or counselor should be available, or called on, to respond to additional questions or concerns. If test results indicate the presence of an abnormal gene, the person tested should be referred to a neurologist or ataxia center for a baseline neurological evaluation.

**Where can I find more information?**

NAF does not endorse any specific physician or genetic testing center, but can help you find a health care professional in your area who can provide the services you need. Some neurologists work with a genetic counselor, and most medical schools have one or more geneticists or genetic counselors who can help you obtain more information about gene testing.

**What is GINA?**

The Genetic Information Nondiscrimination Act of 2008, also referred to as GINA, is a federal law that protects Americans from being treated unfairly because of differences in their DNA that may affect their health. The law prevents discrimination from health insurers and employers. In general, Title I of GINA prohibits health plans from discriminating against covered individuals based on genetic information. “Genetic information” includes family medical history and information regarding individuals’ and family members’ genetic tests and genetic services. Title II of GINA, prohibits employers from discriminating against employees based on genetic information. There are exceptions to this law; to find out more of what the law provides and does not provide, please visit the National Human Genome Research Institute’s web site, at [www.Genome.gov](http://www.Genome.gov) and select the “Issues in Genetics” tab.

**How can I participate in research?**

Whether you test positive for a specific type of hereditary ataxia, are at risk for ataxia, or have a sporadic form of ataxia (no known genetic cause), you can be involved in important research to help investigators discover new genes, understand the disease mechanism and the natural history of the

disease, and ultimately find effective therapies to treat and cure ataxia. Anyone affected with ataxia or at risk to develop ataxia is encouraged to enroll in the ataxia patient registry administered by Coordination of Rare Disease at Sanford (CoRDS). The goal of the registry is to connect ataxia patients and researchers to help advance treatments and a cure for ataxia. To enroll in the registry go the NAF website at [www.ataxia.org](http://www.ataxia.org) and click on “Ataxia Patient Registry”.

**How can the National Ataxia Foundation help?**

The National Ataxia Foundation is interested in all forms of hereditary ataxias and sporadic ataxia. NAF has been on the forefront for over 55 years funding promising worldwide research to find answers. NAF is committed to education about ataxia, services to individuals affected with the various forms of ataxia, and promoting research to find the causes, better treatments, and a cure for ataxia. You are encouraged to visit the website at [www.ataxia.org](http://www.ataxia.org) for additional information, a listing of ataxia support groups and social networks, and more. For additional questions, contact NAF at:

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