

FREQUENTLY ASKED QUESTIONS ABOUT...

Friedreich's Ataxia (FRDA)**What is Friedreich's ataxia (FRDA)?**

Friedreich's ataxia (FRDA) is an inherited disease of the central nervous system. It was named after Nikolaus Friedreich, who first described it in 1863, and it was the first form of hereditary ataxia to be distinguished from other forms of ataxia.

What are the symptoms of FRDA?

Difficulty with balance (disequilibrium), impaired coordination of the legs or arms, and thick or slurred speech (dysarthria) are usually the first symptoms of Friedreich's ataxia.

Over time, problems with coordination and speech are likely to worsen. Curvature of the spine (kyphoscoliosis) and high arches in the feet (pes cavus) commonly develop. Affected individuals might notice difficulty knowing where their feet or hands are in space (impaired position sense) and they may develop weakness in the legs and hands.

Enlargement of the heart, irregular heartbeat, or other symptoms of heart trouble (cardiomyopathy) occur in many individuals with Friedreich's ataxia. Heart problems range from mild to severe. Diabetes mellitus is not uncommon.

Later in the course of the disease about 10 percent of individuals with FRDA have hearing loss, and a similar percentage develop loss

of visual acuity or changes in color vision. Another late-stage symptom in about 50 percent of affected people is difficulty with bladder control (incontinence).

What causes FRDA?

Friedreich's ataxia is a genetic disorder, which means it is an inherited condition. It is caused by an abnormality of a single gene called the Frataxin, (FXN) gene. The abnormality can be passed from generation to generation by family members who carry it.

Inherited diseases like FRDA occur when one pair of the body's 100,000 genes does not work properly. (Genes are microscopic structures within the cells of our bodies that contain instructions for every feature we inherit from our parents. Two copies of each gene are inherited, one copy from the mother and one from the father.)

FRDA is autosomal recessive, which means that an individual only develops symptoms of the disease if both copies of his or her frataxin gene are not working properly. An individual who has one copy of an altered or nonfunctioning FXN gene does not develop any neurologic symptoms and is called a carrier. In people who are carriers, the normal frataxin gene compensates for the nonfunctioning copy of the gene. However, a child whose parents are both carriers can inherit a "double dose" of the altered FXN gene and will therefore develop FRDA. ➤

HOW AN AUTOSOMAL RECESSIVE DISORDER IS PASSED ON IN A FAMILY

When both parents are carriers, each of their children has a 25 percent chance of having FRDA and a 50 percent chance of being a carrier.

FATHER WITH ONE **F** AND ONE **f**
(DOES NOT HAVE FRDA)



MOTHER WITH ONE **f** AND ONE **F**
(DOES NOT HAVE FRDA)



F = normal gene
f = disease gene

The above parents each have one recessive FRDA-causing gene. Each of their offspring could inherit one of four possible gene combinations:



F from father, **f** from mother
(child doesn't have FRDA but can pass disease gene on to future children)



f from father, **F** from mother
(child doesn't have FRDA but can pass disease gene on to future children)



F from father, **F** from mother
(child doesn't have FRDA and has no disease gene to pass on to future children)



f from father, **f** from mother
(child will have FRDA and will pass disease gene on to all future children)

Most of the time carriers have no idea that they have an abnormal FXN gene because there are no symptoms or medical problems that go along with being a carrier. It is often only when a child is diagnosed with FRDA that the parents learn they are both carriers. When both parents are carriers, each of their children has a 25 percent chance of having FRDA and a 50 percent chance of being a carrier. The illustration above shows how an autosomal recessive disorder like Friedreich's ataxia can be passed on.

When do FRDA symptoms appear?

Males and females are equally likely to inherit the genes that cause FRDA. Symptoms

usually begin between ages five and 25 but occasionally appear in younger children or adults in their 30s or 40s.

How common is FRDA?

FRDA is the most common form of childhood-onset ataxia. In the United States it is estimated that about 1 in 100 people is a carrier of the altered FXN gene and one out of every 20,000 to 50,000 is affected with Friedreich's ataxia. In some regions or ethnic groups this number might be a little higher or lower.

How is the diagnosis made?

When symptoms resembling those of FRDA appear it is important to receive a thorough medical evaluation by a neurologist. Generally, an evaluation will involve a physical exam and tests to search for abnormalities in the brain and spinal cord. Many of these tests are done to rule out other possible causes of symptoms. (Other possible causes might include nutritional deficiencies, infections, multiple sclerosis, herniated disk in the neck, stroke, brain and spinal cord tumors, and other degenerative diseases.)

Some tests that might be included are a CT or CAT scan (a sophisticated x-ray technique for imaging the brain or spinal cord), an MRI (magnetic resonance imaging of body tissues, including the brain and spinal cord), and EMG (electromyography, a test that records the electrical activity of muscles and nerves). Depending on the symptoms present, other tests might be done such as analysis of spinal fluid, blood, and urine. Appropriate specialists may be consulted such as a heart specialist, ophthalmologist, audiologist (hearing specialist), orthopedist (bone doctor), urologist, or endocrinologist (diabetes).

Since the discovery of the FXN gene in 1996, it has been possible to make a specific diagnosis of FRDA by a gene test. In almost all cases, scientists are able to identify the abnormality in the frataxin gene that causes FRDA. The FXN gene is responsible for directing the production of the frataxin protein, which is one of the thousands of proteins needed for the body to function properly. Levels of frataxin in the spinal cord and brain are much lower than normal in individuals with FRDA. However, it is more practical to test the FXN gene in blood cells than to measure frataxin protein levels

in the nervous system.

Some individuals develop classic FRDA symptoms but have a normal FRDA gene test. It is not clear yet whether these FRDA-like conditions are the result of a slightly different alteration in the frataxin gene that is not detected by the current gene test, or whether the symptoms are caused by an alteration in a different gene that plays a role in the nervous system similar to that of the frataxin gene. This is a question researchers are still working to answer.

What happens after the diagnosis?

It is helpful for patients and families with FRDA to undergo genetic counseling since they typically have questions about the chances that other family members will acquire the disease or be carriers of the abnormal FXN gene. Questions about genetic testing can also be answered by a genetic counselor.

An individual with FRDA should find a physician who will follow him or her on a regular basis to help address the neurologic changes that are likely to occur over the course of the disease, to anticipate and screen for possible complications (such as diabetes and heart disease), and to make appropriate referrals to other specialists as needed, including physical, occupational or speech therapists.

What kind of support is available for people with FRDA and their families?

Before and after the diagnosis, psychological counseling or participation in support groups is often beneficial for the affected person and family members. Symptoms



of FRDA are often similar to those of other forms of ataxia and there are numerous ataxia support groups throughout the United States.

Support groups—People with Friedreich’s ataxia are welcome to participate in any of the support groups affiliated with the National Ataxia Foundation. Support groups throughout the United States can be found on the National Ataxia Foundations web site: www.ataxia.org.

What type of research is being done on FRDA?

The National Ataxia Foundation funds promising world-wide research in all the types of ataxias including Friedreich’s ataxia. The National Ataxia Foundation’s Young Investigator Award is awarded for research only in Friedreich’s ataxia or Spinocerebellar ataxia type 3. In 2007 NAF established the Friedreich’s Ataxia Special Projects Award for new and innovative studies for Friedreich’s ataxia research relevant to cause, pathogenesis or treatment of Friedreich’s ataxia.

In 2008, it was announced that a Phase III clinical research trial is studying the effects of idebenone on the nervous system and heart of patients with Friedreich’s ataxia.

The National Ataxia Foundation is committed to education about ataxia, service to individuals affected with all forms of ataxia and promoting and funding research to find the causes, better treatments and a cure for ataxia. For questions regarding on-going research, clinical trials or other information about FRDA, contact the National Ataxia Foundation.

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