Friedreich Ataxia

Friedreich Ataxia is a rare condition, yet is the most common form of inherited ataxia, with one-in-50,000 people affected. Compiled by Miriam Rodrigues.

Friedreich Ataxia (FA or FRDA) is a slow, progressive disorder of the nervous system and muscles, which results in an inability to co-ordinate voluntary muscle movements (ataxia).

This condition is caused by the degeneration of nerve tissue in the spinal cord and of nerves that extend to peripheral areas such as the arms and legs. FA affects the upper and lower limbs as well as the head and neck. There is a loss of sensations in the arms and legs, but mental capacity is not affected.

The onset of symptoms of FA usually occurs in childhood between the ages of five to 15 years, however may appear as early as 18 months or as late as 40 years of age.

It is a rare condition, yet is the most common form of inherited ataxia, with one-in-50,000 affected. FA affects males and females equally.

FA reduces normal life expectancy of the individuals, usually due to associated conditions, such as heart disease and diabetes. However, some people with less severe symptoms of FA often live through into their 60s or 70s.

What are the features of Friedreich Ataxia?

The first symptom to appear in FA is usually difficulty walking (gait ataxia).

This gradually worsens and eventually spreads to the arms and the trunk.

Individuals may over- or under-extend the leg when it is brought forward in walking, and feet may be lifted higher than necessary and brought down too hard. The use of a cane or other walking aids may be required.

Over time, muscles begin to weaken and waste away, particularly in the feet, lower legs, and hands. Frequent falls and difficulty controlling the hands will result in increased clumsiness. It may become increasingly difficult to perform tasks such as writing, getting out of chairs and climbing stairs.

FA affects the upper and lower limbs as well as the head and neck.

Foot deformities such as club foot, involuntary bending (flexion) of the toes, hammer toes (curled toes), or foot inversion (turning inward), high arches of the foot (pes cavus) may develop. These usually do not pose a problem in themselves, though if problems do arise, bracing or surgery can be beneficial.

Although progression varies from individual to individual, the ability to walk is often lost within eight to 10 years from the onset of symptoms, making it necessary to get a wheelchair. Options can be assessed by an occupational and/or seating therapist.

Other symptoms include loss of tendon reflexes, especially in the knees and ankles. There is often a gradual loss of sensation in the fingers and toes, which may spread to other parts of the body.

The muscles controlling speech can be affected, resulting in slow and slurred speech (dysarthria). Speech therapists may provide beneficial support for this.

Rapid, rhythmic, involuntary movements of the eye (nystagmus) can also be common.

Scoliosis, an abnormal curvature of the spine, can become an issue and can impair respiration. Spinal bracing may be required, and in more severe cases spinal fusion surgery. An

orthopedic specialist is essential in monitoring the scoliosis.

Conditions associated with Friedreich Ataxia

There are conditions associated with FA that do not result from the degeneration of nerves.

Cardiac problems are common and are present in approximately 80 percent of FA individuals and arise from various forms of heart disease that often accompany FA. These include cardiomyopathy (enlargement of the heart), myocardial fibrosis (formation of scar tissue in heart muscle) and heart failure.

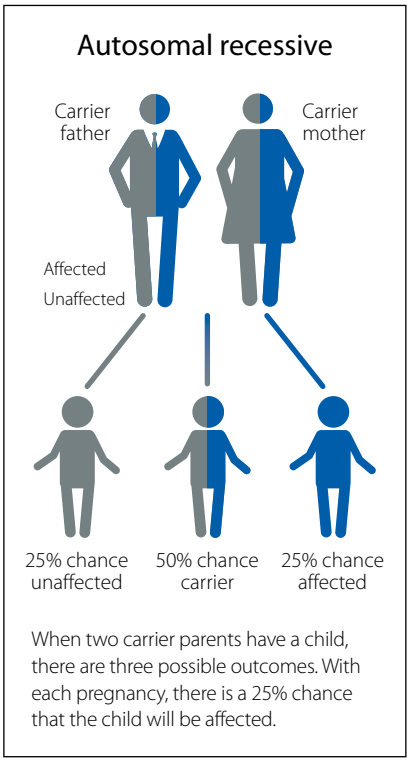
Symptoms can include chest pain, shortness of breath, and heart palpitations. Other heart rhythm abnormalities may be present, such as a fast heart rate (tachycardia) or a heart block, which is the impaired conduction of electrical impulses, necessary for the contraction of the heart. Cardiac problems can be treated with medication, though severe forms of heart disease can be fatal.

Diabetes mellitus is a condition characterised by abnormally high blood and urinary sugar levels. About 10 percent of individuals will develop this and will experience increased thirst, hunger and urination. This can be managed with diet and medication, such as insulin.

What causes Friedreich Ataxia?

FA is an autosomal recessive disorder.

Humans have 46 chromosomes made up of genes. Each chromosome, which is a tightly coiled chain of DNA (deoxyribose nucleic acid) contains millions of chemicals called bases. The four bases are adenine, thymine, cytosine and guanine (A, T, C and G), which pair together in sets of three to form coded messages. These messages are instructions for producing proteins that make the body function.



When two carrier parents have a child, there are three possible outcomes. With each pregnancy, there is a 25% chance that the child will be affected.

In FA, there is a defect in a gene on chromosome 9. In 98 percent of cases there is a triplet repeat expansion of the GAA sequence of bases. A greater number of repetitions is related to earlier onset and faster progression of the disorder.

The corresponding protein that is altered due to this repeat is called frataxin and is produced in diminished amounts. Frataxin is found in energy-producing parts of cells called mitochondria. When frataxin levels are low, cells (particularly in the brain, spinal cord, and muscle cells) cannot produce energy properly and the build-up of toxic by-products leads to "oxidative stress", which has the potential to destroy cells.

In FA, this "oxidative stress" affects nerve cells in the spinal cord and the peripheral nerves, which connect the spinal cord to muscles and sensory organs. This results in failure to stimulate some muscles, which will eventually weaken and waste away (atrophy).

There is also damage to the cerebellum, which is a small structure at the back of the brain which helps to plan and co-ordinate movements. Combined, these problems lead to the progressive losses of muscle strength, sensation, balance and coordination that characterise FA.

Diagnosis of Friedreich Ataxia

Diagnosis usually commences after the identification of key characteristics of FA. Several tests are available to confirm diagnosis of FA and associated conditions:

- Physical examination – test of reflex and sensory responses.
- Electromyography (EMG) – observes the electrical activity of muscles and its consistency with activity typical of individuals with FA.
- DNA testing – can identify the presence of the abnormal gene in the individual with FA as well as carriers.
- Nerve or muscle biopsy – can confirm diagnosis.
- Nerve conduction studies – measure the speed with which nerves transmit impulses.
- MRI (magnetic resonance imaging) or CT (computed tomography) scan, which maps the brain and the spinal cord. ®