What is Friedreich’s Ataxia?

Friedreich’s Ataxia is a rare genetic neuro-muscular disorder first described in a series of papers published from 1863 to 1877 [1-5] by neuropathologist Nikolaus Friedreich. As the name implies, the most common symptom is ataxia, which is a Greek word meaning “without order” and refers to an affected person’s inability to maintain proper voluntary control and co-ordination of their muscles. This often results in a difficulty walking, which gradually worsens over time and usually results in the need for a wheelchair, but can also affect other parts of the body including the arms, feet and trunk. Other symptoms of Friedreich’s Ataxia include speech problems, unresponsive lower limb reflexes, abnormal curvature of the spine, swallowing and sphincter abnormalities, vision and hearing impairments, deterioration of the heart muscle and diabetes [6-9]. Symptoms usually manifest around puberty, but can also be exhibited as early as 2 years of age or as late as 25 years or older. Disease progression can be variable depending on the severity of the genetic abnormality present and if the genetic abnormality is severe enough it can drastically reduce life expectancy. An affected person’s average life expectancy is significantly reduced to 35 - 40 years of age [10]. The symptoms of Friedreich’s Ataxia have a devastating influence not only on the affected person’s quality of life but also on family members who are left helpless to do anything about it, as there is currently no known cure for this disorder.

What causes Friedreich’s Ataxia?

Although Friedreich’s Ataxia is rare, it is the most common hereditary ataxia, affecting an estimated 3-4 people per 100,000 [11]. Friedreich’s Ataxia is an autosomal recessive disorder [12], meaning that both parents must pass on the genetic abnormality to the offspring. The parents themselves may not display the symptoms of the disorder if they only carry one copy of the affected gene.

How does this genetic abnormality lead to the symptoms of Friedreich’s Ataxia?

The genetic abnormality for Friedreich’s Ataxia, which was discovered in 1996, is found on chromosome 9 [13] in a region that encodes for a protein called frataxin. This genetic abnormality results in this specific part of the code being incorrectly read, which results in low amounts of the frataxin protein being produced. The precise function of frataxin is not fully understood however it is believed to be important in regulating iron within a part of the cell called the mitochondria [14]. Mitochondria are the energy producing centres of cells and are therefore extremely important. It has been speculated that the low levels of frataxin allow for a toxic build up of iron and other metals in the mitochondria, which in turn causes the tissues (nerves, muscles, glands) commonly affected in Friedreich’s Ataxia to become vulnerable. Why some tissues are more vulnerable than others is not fully known yet, but promising research is being conducted into preventing and/or slowing down the disorders progression in those who are affected.
What does Friedreich’s Ataxia look like in the brain and spinal cord?

To the naked eye, the brains of those affected by Friedreich’s Ataxia usually look quite normal, the main difference seen at this level is a noticeable deterioration of the spinal cord and in some cases a region of the brain (the cerebellum) that is crucial for executing the smooth co-ordination of different movements [10].

Under the microscope, the deterioration in the spinal cord and the cerebellum is usually due to a severe loss of brain cells, so called neurons [12]. A build up of supporting cells called glia usually accompanies this neuronal loss. The increased presence of these cells is indicative of neuronal damage or ‘trauma’ to the area.

These changes affect the signals that are sent from the body to the brain, such as touch and pressure information, but also the signals that the brain sends to the body, such as information concerning muscle movement. This, combined with damage to the cerebellum, that is responsible for co-ordination, helps to explain the debilitating ataxia symptoms seen in people who are affected with Friedreich’s Ataxia.

Can Friedreich’s Ataxia be treated?

Unfortunately there is currently no known cure for Friedreich’s Ataxia and so current treatments are directed toward alleviating and managing symptoms. Other avenues for potential treatments [15] that are currently being undertaken by scientist worldwide include a number of promising investigations such as:

- Helping the mitochondria perform and function better
- Reducing the stresses placed on the mitochondria
- Seeing if the functions that frataxin normally perform can be replaced by something else or regulated differently
- Seeing if frataxin can be boosted in the mitochondria by other means
- Help the affected genes make more frataxin
- And/or administer new genes to make more frataxin

Many of these therapies are currently in clinical trials and although there is still plenty of work to be done, the advancements seen so far in the knowledge of this debilitating disorder coupled with the extremely active worldwide collaborative effort by scientists, clinicians and the public give hope to those affected by Friedreich’s Ataxia and their families.
References:

15. FA Treatment Pipeline Dec 2013 [http://www.curefa.org/pipeline.html]