FABRY DISEASE

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What is Fabry disease?

Fabry disease is an inherited disorder. A chemical in the body which would normally be broken down builds up and causes damage, mainly to the heart, kidneys and brain. This chemical that builds up is called ‘GL-3’.

Why is it called Fabry disease?

In 1898, two Doctors - Dr Johann Fabry in Germany, and Dr William Anderson in England - independently published articles describing patients who had the disease. Dr Johann Fabry continued to work in this specialised area, and the disease was subsequently named after him. Much more work was conducted from that time to this, which has led toward developing a treatment for Fabry disease.

What causes Fabry disease?

A chemical called ‘GL-3’ builds up in the body in Fabry disease, because it is not broken down by the body.

An enzyme should break GL-3 down, but is missing or defective in Fabry disease. Chemical changes in the body need the help of enzymes to take place. There is a different enzyme for each type of chemical reaction in the body, so that thousands of enzymes make the body work. It is a bit like a production line in a factory, where a series of different machines make a series of changes to produce an end product, or to break down waste. If one machine on a factory production line were to break down, there would be a build up of half finished goods by the machine. This is what can happen if an enzyme in the human body is missing or defective.

In Fabry disease the missing enzyme is called alpha-galactosidase, and GL-3 is the chemical on which alpha-galactosidase should be acting.

What are the Symptoms of Fabry Disease?

Fabry disease can cause problems all over the body, because GL-3 builds up in the walls of blood vessels all over the body. The heart, kidneys and brain are mainly affected, and pain in the arms or legs is a common problem. Fabry disease is a serious condition. The disease can have variable effects, but often affected people develop complete kidney failure in their 20’s, and die of heart disease or stroke in their 30’s or 40’s. However, the new treatment with enzyme replacement (see below) may dramatically improve the outcome of this disease.
Pain
Pain is common in the hands and feet, and occurs in childhood onwards. This pain can be brought on by changes in temperature, stress or fatigue. The pain may be shooting or 'bony', as though it is coming from deep within the arm or leg. The medical term for this pain is acroparathesia.

Pain may also occur in the tummy, particularly after meals, and frequent bowel movements are quite common in patients with the disease.

Skin
Patients with Fabry disease are less inclined to sweat, which makes the control of their body temperature very difficult. The medical term for this is hypohidrosis.

Many patients have small reddish purplish dots on their skin around the bellybutton and the bathing suit area. The spots do not cause pain and are not usually very prominent, but the particular shade and distribution of the spots is unique to Fabry disease. Thus people with Fabry disease may be favourites as invited subjects to test young doctors in medical examinations!

Eye
Changes in the cornea of the eye with the appearance of a “starburst” can be seen in some patients, by an eye specialist using special equipment. They do not usually cause serious visual disturbance or blindness.

Kidney
Kidney function is usually normal in childhood, but the slow build up of GL-3 in the kidney causes progressive damage. Most people with Fabry disease slowly develop kidney failure, and need dialysis or a kidney transplant in their 20’s. A kidney transplant does not get affected by Fabry disease because it contains small amounts of the enzyme alpha-galactosidase from the donor, which protects the kidney (but unfortunately cannot help Fabry disease in the rest of the body).

Treatment with enzyme replacement may, in the future, be able to prevent the development of Fabry disease in many people.

Heart
The storage of the GL-3 in the heart begins to affect function in some patients, and the most common signs are enlargement of the heart, irregular heartbeat, heart valves not functioning as normal, and in the more severe cases, heart attack. Heart disease is one of the main causes of premature death in Fabry disease, but it is hoped that enzyme treatment will prevent many such deaths.
Brain
Patients with Fabry disease are more vulnerable to stroke, as small arteries in the brain become narrowed by GL-3. If a blood vessel in the brain blocks completely, part of the brain may be starved of blood and damaged, causing a stroke. This may be weakness down one side of the body, or more subtle effects on thought processes and co-ordination.

How is Fabry disease passed on?

Fabry disease affects only males, but females can be carriers, and pass it onto their sons, or onto their daughters as carriers. Someone with Fabry disease should consult a specialist in genetic diseases. It should be possible to diagnose Fabry disease with a blood test. Modern techniques may enable someone with Fabry disease to have test-tube babies and guarantee that a child will not have the disease, or be a carrier.

Occasionally women can also suffer from Fabry disease, and if this is the case, a specialist in genetic diseases should explain the inheritance pattern that would occur in that family.

Men get full Fabry disease, and affected women are generally completely healthy but are carriers. This type of inheritance is called ‘sex linked inheritance’.

Sex linked Inheritance

Diseases which are transmitted by sex linked inheritance have the gene for the condition on the X chromosome.

The human body is made up of cells. Within each cell are threads of DNA which carry our genetic information in the form of genes. The human body has two copies of each chromosome, one from each parent. There are 23 pairs of chromosomes, so there are 46 chromosomes in total. One pair determines whether a person is male or female. This pair is made up of ‘X’ and ‘Y’ chromosomes. If someone has 2 ‘X’ chromosomes, ‘XX’. they are female. The ‘Y’ chromosome is smaller than the ‘X’ chromosome. The alpha-galactosidase gene is carried on the chromosomes which determine sex and is missing from the ‘Y’ chromosome. Therefore, if a male has a defective alpha-galactosidase gene, there is no normal copy to produce normal enzyme.

A woman has two ‘X’ chromosomes. If one is abnormal, there is a second copy which produces effective levels of alpha-galactosidase.

The inheritance will be described from the point of view of a man with Fabry disease, and then from the point of view of a woman who is a carrier for Fabry disease.
A man with Fabry disease

His parents
Fabry disease should have been inherited from his mother. If she has other children, or is considering having more children in the future, she should see a genetic specialist for advice. Each of her sons has a 50:50 chance of having Fabry disease, each daughter a 50:50 chance of being a carrier.

His brothers
There is a 50:50 chance that a brother will have Fabry disease. Brothers should have a blood test for diagnosis. If a brother does not have Fabry disease, his own children will not get the disease or be carriers.

His sisters
There is a 50:50 chance that each sister will be a carrier for Fabry disease, and should have a blood test. If the sister is clear, she cannot pass Fabry disease on to her children. If she is a carrier, read the inheritance rules for a carrier below.

His sons
A man with Fabry disease cannot pass the condition onto his sons. This is because the abnormal gene is on the ‘X’ chromosome, and in order to have a son, a man has to pass on his ‘Y’ chromosome to the child, and this does not carry Fabry disease.

His daughters
Each daughter will be a carrier for Fabry disease, though this should be confirmed by a specialist. This is because for the man to have a daughter, he has to pass on an X chromosome. A man only has one X chromosome, which must be abnormal if he has

Who to test if a woman is a carrier for Fabry Disease

Her parents
Fabry disease could have been inherited from her mother or father. If it was her father, the diagnosis should be obvious by the time the man is old enough to have children. Therefore, the mother should be tested for carrier status if the father is fit and well.

Her brothers
If Fabry disease is inherited from the father, the male children should all be clear and cannot pass the condition onto their children. If Fabry disease is inherited from the mother’s side, there is a 50:50 chance that he will have Fabry disease.
Her sisters
If Fabry disease is inherited from the father, the female children should be carriers for Fabry disease. If Fabry disease is inherited from the mother’s side, there is a 50:50 chance that the sister will be a carrier.

Her sons
There is a 50:50 chance that each son would have Fabry disease. An unaffected son would not pass the disease on.

Her daughters
There is a 50:50 chance that a daughter will be a carrier for Fabry disease. An unaffected daughter would not pass the disease on.

Is there treatment for Fabry disease?

Until 2001, the only treatment for Fabry disease was to try and cope with the problems it caused - such as using dialysis or kidney transplantation for kidney failure. However, genetic engineering technology has enabled the production of large amounts of the enzyme, alpha-galactosidase, that is missing in people with Fabry disease.

The enzyme has to be given by injection. Trials have shown that the replacement enzyme removes GL-3 from the blood and from tissues where it has built up. These effects are very dramatic, and it is possible that people treated from childhood may never develop the serious consequences of Fabry disease, but lead normal lives. For people with established problems from Fabry disease, it is hoped that the disease will not progress. However, damage that has already been done to the brain, heart and kidneys would not be reversed.

The injections of enzyme need to be given every 2 weeks or so. There is a small risk of an allergic reaction, so for an initial phase the injections must be given in hospital. The allergic reaction means that some people cannot continue treatment with the enzyme.

Anyone with Fabry disease who has not already discussed enzyme treatment with their doctors should do so.
The National Kidney Federation cannot accept responsibility for information provided. The above is for guidance only. Patients are advised to seek further information from their own doctor.

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