Fabry disease is a rare, serious, but treatable condition.

This leaflet aims to answer some of the questions you may have about the causes, inheritance and treatment of Fabry disease, and offers recommendations on what to do if you and/or a member of your family has been diagnosed with the condition.
WHAT IS FABRY DISEASE?

Fabry disease (or Anderson-Fabry disease) is an uncommon inherited disorder caused by the lack of activity of an enzyme called alpha-galactosidase A, as the result of a genetic change (mutation). This enzyme is responsible for breaking down a fatty substance, known as globotriaosylceramide (Gb₃), in the cells of the body. The build-up of Gb₃ deposits in the cells interferes with their normal functions, leading to progressive damage to the major organs in the body and resulting in a wide range of symptoms and complications.

HOW IS FABRY DISEASE DIAGNOSED?

Fabry disease can be very difficult to distinguish from more common conditions, and sufferers can stay without a correct diagnosis for years. However, once it is recognised that a patient may have Fabry disease, the actual diagnosis to confirm the condition can be accurately done with a simple blood test in most cases, and in other cases further analyses may be needed. Therefore, if you suspect that you or someone you know might have Fabry disease, it is important to speak to your family doctor about further referral and assessment with a specialist in genetic diseases.

WHAT IS THE TREATMENT FOR FABRY DISEASE?

Treatment of Fabry disease consists of the replacement of the deficient enzyme with enzyme replacement therapy (ERT). This is given as an infusion into a vein. In most cases, ERT is used in conjunction with treatments for the management of specific symptoms, which are tailored to the individual.
WHAT ARE THE SYMPTOMS?

Each person can be affected by Fabry disease in a different way, and can therefore experience varying degrees and combinations of symptoms. The most common signs and symptoms include:

- Depression and fatigue
- Hearing problems such as ringing in the ear or hearing loss
- Impaired ability to sweat, which in turn causes frequent fevers and a low tolerance to heat or exercise
- Stomach problems such as pain, nausea, vomiting or diarrhoea
- Changes in the eye
- More serious problems affecting the heart, kidney and nervous system can typically be seen in older patients as the disease advances
- Small raised dark red spots (called angiokeratomas) on your skin
- Pain and burning sensation in hands and feet
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Fabry disease is not contagious, but it is a hereditary condition that can be genetically inherited from parents to children, in a pattern illustrated below.

Every cell in the human body contains chromosomes, which are thread-like structures carrying genetic information. Females have two X chromosomes in each cell (an X from each parent), and males have one X and one Y chromosome (an X from their mother and a Y from their father).

The gene that is altered in Fabry disease is located on the X chromosome. This means that men are always affected by the disease, whereas women (called ‘carriers’) may not have symptoms, or their symptoms may be less severe or appear later in life.

On average, a carrier mother will have a 50/50 chance of passing the gene change to her children (whether a boy or a girl), whereas an affected father will pass on the changed gene to his daughters but not his sons. This results in the two scenarios represented here:

Although Fabry disease is usually passed on through the X chromosome, there are other genetic mutations that can happen in families with no family history too. Consult your doctor if you want more information about the genetic nature of the disease.
**WHAT IS PEDIGREE ANALYSIS?**

In a pedigree family tree, squares represent males, circles females, and the shaded shapes are individuals who may be affected with the condition. This simple depiction allows a large amount of information to be condensed into a straightforward diagram, which doctors can then use to visualise inheritance patterns, calculate the risk for each family member, and identify those who should be tested to establish a diagnosis.

**HOW DO I FIND OUT IF ANY OF MY RELATIVES MAY HAVE INHERITED FABRY DISEASE?**

The gene responsible for Fabry disease can be passed on for several generations, thereby potentially affecting many close and distant relatives. To work out the risk of inheriting Fabry disease for your relatives, a doctor will ask for your family’s medical history, and map out a family tree using symbols to represent genetic relationships; this is called **pedigree analysis**. Note that you are likely to need your family’s consent before disclosing their medical history, therefore always seek advice from your doctor if you are unsure about talking to your family.

**WHAT SHOULD I DO IF I HAVE BEEN DIAGNOSED WITH FABRY DISEASE?**

Fabry disease is a complex condition that is often missed or misdiagnosed. As such, an accurate diagnosis means that treatment can be started in a timely manner.

Due to the hereditary nature of this disorder, a diagnosis not only has important health consequences for you, but may also have implications for your family. For each newly identified Fabry disease patient (called the ‘**proband**’) several additional cases may be identified in the extended family through pedigree analysis. It is therefore important that you speak to your doctor or a genetic counsellor about drawing a pedigree family tree to work out if testing should be offered to any of your relatives.
**HOW SHOULD I TELL MY FAMILY ABOUT MY CONDITION?**

Telling your family members that they might be at risk of Fabry disease can seem like a daunting task. However, there is plenty of help on offer from your doctor, genetic nurse, or genetic counsellor on how best to communicate with your relatives. Do seek the advice of these medical professionals before you speak to your family, so that you are prepared for a frank and considered discussion, which will facilitate the early diagnosis of those at risk.

There are also a number of patient organizations that can provide further information and support, their details may be found below.

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Fabry International Network

[www.fabrynetwork.org](http://www.fabrynetwork.org)