Fabry Disease

THE CHAMELEON AMONGST RARE CONDITIONS

Responses

to common questions

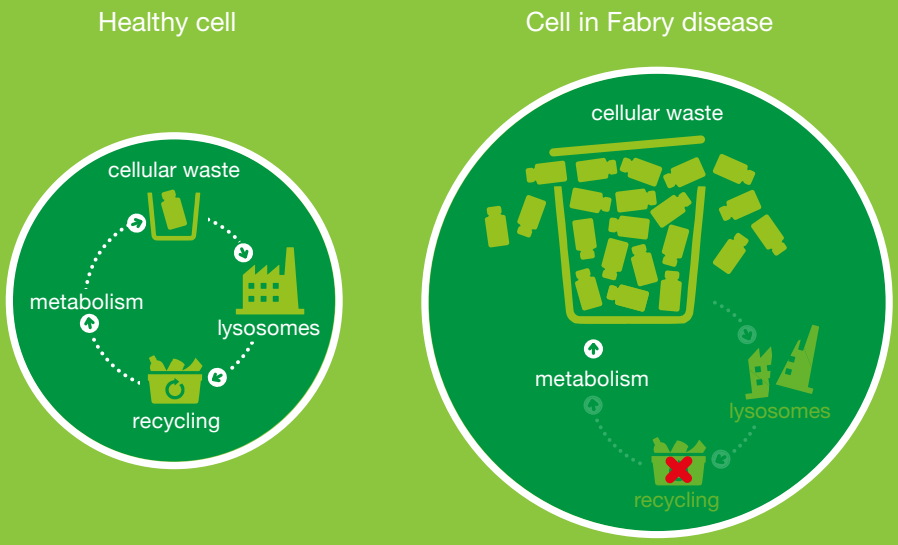
If you have just been diagnosed with Fabry disease it is likely that you have been suffering for some time. Fabry disease hides amongst its symptoms like a chameleon in the jungle. Even experienced doctors have difficulty recognising the condition.

This brochure answers some of the most commonly asked questions. It will support the conversation with your doctor, but will never replace it. Please contact your doctor if you have any concerns or want to know more.

WHAT IS FABRY DISEASE?

Fabry disease belongs to the lysosomal storage disorders. The disease is caused by a mutation (change) of the gene for the alpha-galactosidase enzyme (or α-Gal A). This change means that the enzyme can no longer function properly.

Enzymes are proteins that can run and speed up processes. Most cells in the body contain the enzyme α-Gal A, which helps the body break down nutrients and waste products. In healthy people with normal functioning α-Gal A, this enzyme cleaves a fatty substance called globotriaosylceramide (or Gb3) into smaller parts to allow it to be removed more easily. In people with Fabry disease, α-Gal A no longer works properly or does not work at all. Gb3 is, therefore, not broken down and instead accumulates in cells.



Lysosomes – the «recycling machines» of the cell

Lysosomes are small cell components that are responsible for the breakdown of nutrients and the recycling of waste products.

They prevent excess material from accumulating in cells. They are supported in this task by «molecular tools», enzymes. The enzymes – in the case of Fabry disease, the enzyme is α-Gal A – break down endogenous fatty substances into small building blocks that can be recycled. This breaks down cellular waste and reuses the raw material.

If the tools for «waste breakdown» are not functioning, the «waste» accumulates in the cells. This can result in dysfunction in various organs and parts of the body.

WHAT ARE THE SYMPTOMS OF FABRY DISEASE?

Fabry disease can appear with a wide range of different signs of illness. However, sufferers don‘t necessarily develop all symptoms, and the severity of symptoms varies from person to person. Therefore, it is particularly difficult to detect and diagnose Fabry disease. Symptoms can begin in childhood and change over time.

The most common symptoms of Fabry disease include:

- ➔ Burning pain in hands and feet
- ➔ Small, dark red skin changes that are slightly raised (called angiokeratomas)
- ➔ Gastrointestinal complaints such as abdominal cramps, diarrhoea and early bloating when eating
- ➔ Reduced or absent sweating

Fabry disease can also worsen kidney function, but this is not always noticed by the patient. Your doctor will therefore check your kidneys regularly (typically using urine and blood tests). Fabry disease can also cause thickening of the heart. This can lead to shortness of breath, but can also proceed without symptoms. Your doctor will, therefore, also check your heart regularly for relevant signs.

The risk of stroke may also increase with Fabry disease. Your doctor will advise you how to reduce this risk.

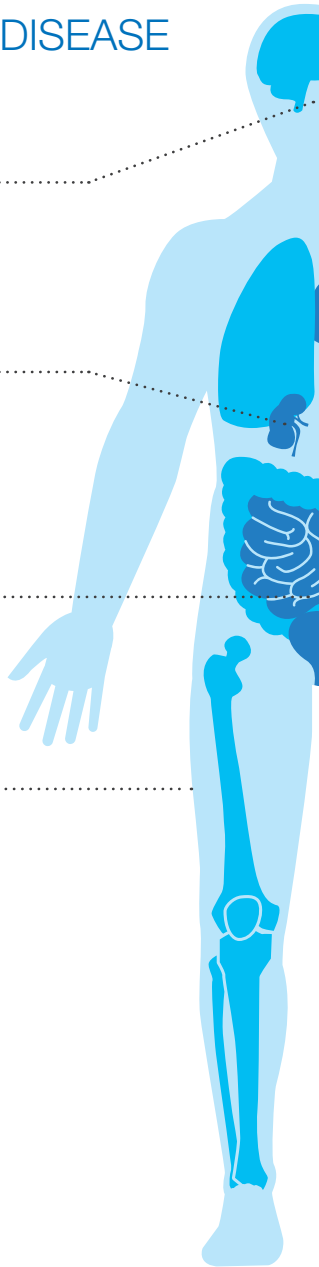
The chameleon amongst rare conditions

The symptoms may appear very varied in Fabry disease – the course of the disease is difficult to predict in individual patients. You may only be experiencing some of these symptoms or your symptoms may only be mild. Men almost always show signs of the disease. Women may also show symptoms: These are then of similar severity, but often have a later onset.

Why do I have different symptoms to other people with Fabry disease, even within my family?

Patients with Fabry disease often have similar symptoms. The severity and age at which symptoms occur can vary widely, even within a family. This is because, apart from the gene mutation itself, many other factors have an impact on symptoms, including environmental factors and other genes.

POSSIBLE SYMPTOMS OF FABRY DISEASE



Ears

- Hearing impairment

Kidneys

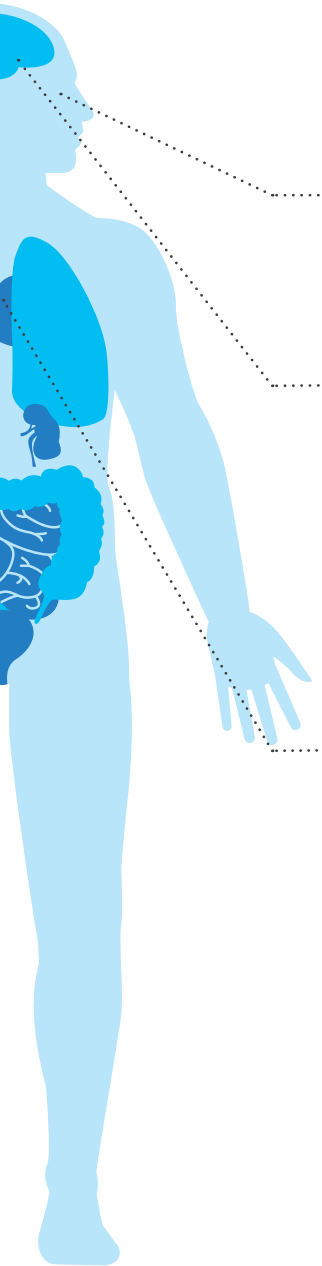
- Loss of function
  (often without noticeable symptoms)

Digestive tract (bowel)

- Pain, diarrhoea

Skin

- Small, dark red, raised skin patches
  (angiokeratomas)
- Inability to sweat
- Hypersensitivity to cold and heat



Eyes

- Corneal opacities (cornea verticillata)

Nervous system

- Burning pain in hands and feet
- Pain radiating into other parts of the body

Note:
Pain may subside later in the disease

Heart

- May become enlarged (with possible shortness of breath, but poss. also without noticeable symptoms)
- Irregular heartbeat

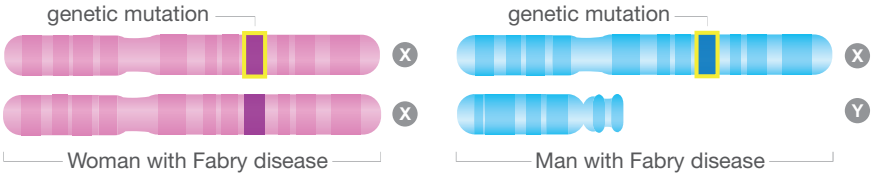
→ Not all patients with Fabry disease develop all of the symptoms described

→ The listed symptoms are not necessarily associated with Fabry disease

WHAT IS THE CAUSE OF FABRY DISEASE?

Fabry disease is a genetic disease that occurs only when one or both parents are affected.

The **genetic mutation** that causes Fabry disease is on the X-chromosome. Therefore, this is also called X-linked inheritance.



Men have one X and one Y chromosome, whilst women have two X chromosomes.

It is very rare that women have the genetic mutation which results in Fabry disease on both X chromosomes. Most women with Fabry disease have a change on one X chromosome and a healthy gene on the other. In women, symptoms of Fabry disease typically develop more slowly than in men, but not in all cases. Since men have only one X chromosome, a mutation of the Fabry gene has a stronger effect in men than in women.

Genetic mutation: Genes are made up of DNA, a type of instruction that tells the cells in the body how to assemble proteins.

A mutation results in a change in the gene, meaning that the assembly instructions for the protein are no longer correct. More than 900 different errors (mutations) in the assembly instructions can result in Fabry disease. With this change, an enzyme (alpha galactosidase A, abbreviated to α-Gal A), is less active or loses its activity altogether.

How common is Fabry disease?

Fabry disease is a rare disease, but is one of the most common lysosomal storage disorders.

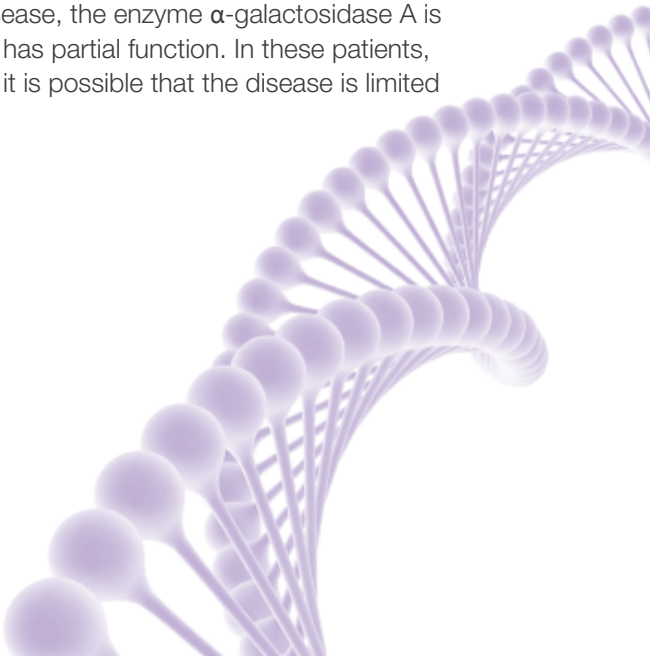
Globally, the frequency varies widely by region. In Switzerland, approximately 100 men are expected to have the disease; there are no reliable numbers available for women.

Are there different types of Fabry disease?

Two types of Fabry disease are distinguished: the «classical» and the «non-classical» or «atypical» form.

In patients with «classical» Fabry disease, the defective enzyme, α-galactosidase A, has no or has only very little activity. These patients tend to have symptoms in multiple organs.

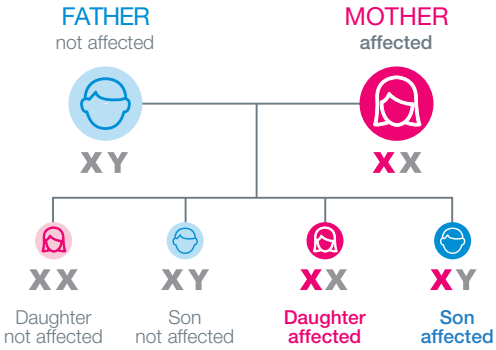
In patients with atypical Fabry disease, the enzyme α-galactosidase A is not completely defective, but still has partial function. In these patients, the disease is usually slower and it is possible that the disease is limited only to the heart or kidneys.



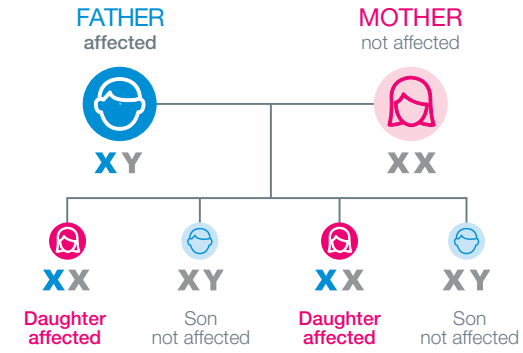
WILL I PASS FABRY DISEASE ON TO MY CHILDREN?

Since the altered gene is located on the X chromosome, it is also said that the inheritance of **Fabry disease from parents to children is X-linked**. Boys receive one X chromosome from the mother and one Y chromosome from the father. Girls have two X chromosomes, one from the mother and one from the father.

Women with a genetic mutation can pass this onto their sons and daughters via the X chromosome. **Affected women** pass the X chromosome with the defective gene on to daughters and sons with a probability of 50%



Affected men pass the X chromosome with the defective gene on to all daughters. Daughters from fathers with Fabry disease always inherit the genetic mutation and also develop Fabry disease. Sons from affected fathers are always healthy because only the Y chromosome is passed from the father to the son.



Do I have to tell my family that I have Fabry disease?

It is important that your family knows about your Fabry disease because it is an **inherited disease** that may also affect other family members. If your loved ones know about your diagnosis, they can themselves make important decisions about their health.

Your loved ones should be aware of your diagnosis and its importance. Tell them that you are informing them of your diagnosis so that they can also receive appropriate help. Ask your relatives about their health and tell them about your own.

You should discuss the following topics with your family:

- ➔ Impact of Fabry disease on your own health (refer to «What are the symptoms of Fabry disease?»)
- ➔ Inheritance of Fabry disease by the next generation
- ➔ Your family history to find out if other family members have or have had Fabry disease or if there have been and are other health problems tha «run in the family»

Provide your family members with information that you have received from your doctor or other sources. You will also find useful information on the Internet.

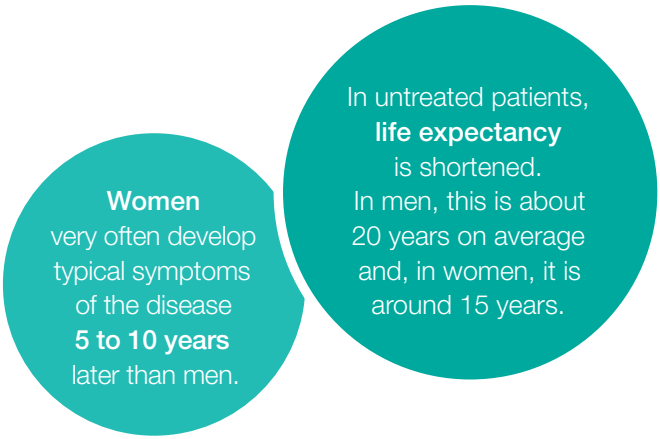
Is Fabry disease different in men and women?

Fabry disease is linked to the X chromosome. This means that symptoms in men typically appear earlier than in women.

Whilst women can develop symptoms which are as serious as those which are seen in men, it is nevertheless the case that the onset of complaints is usually later. Heart and kidney injury caused by Fabry disease tends to have an earlier onset in men than in women. The progression of Fabry disease is also usually slower in women than in men.

What is the impact of Fabry disease on life expectancy?

Since the course of the disease is different in each patient, the effects on life expectancy are difficult to predict. It is, therefore, very important that patients with Fabry disease attend for regular check-ups. With good monitoring and treatment, life expectancy can be entirely within the normal range.



HOW IS FABRY DISEASE DIAGNOSED?

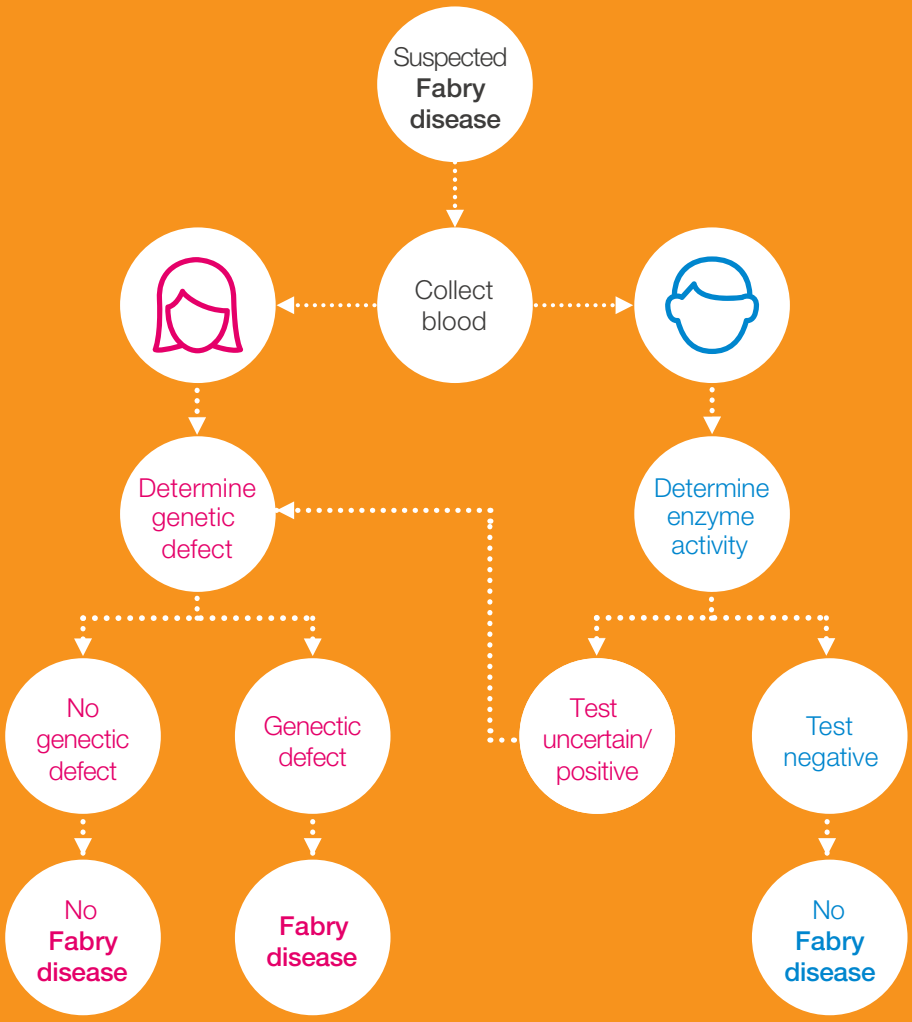
Fabry disease is usually diagnosed by a specialist. It is initially based on your symptoms, your family history and the results of blood and urine tests.

A low concentration of the enzyme α-Gal A in the blood indicates the presence of Fabry disease in boys/men. In girls/women, however, the enzyme level can normally be high. A genetic mutation for the Fabry gene must be confirmed by means of analysis to confirm Fabry disease. This also requires a small blood sample to be collected and sent for analysis.

The sooner Fabry disease is detected and treatment is initiated, the more likely it is that consequential adverse effects are prevented or delayed.

After the diagnosis of Fabry disease, the doctor will perform what is known as family-tree analysis to determine whether there may be other affected family members. Fabry disease is a genetic disease that is inherited by the children from the parents (please also refer to «Will I pass Fabry disease on to my children?»). It is important that other family members know whether or not they have Fabry disease. Family-tree analysis determines which family members are affected.

The process of diagnosing Fabry disease



WHAT ARE THE TREATMENT OPTIONS?

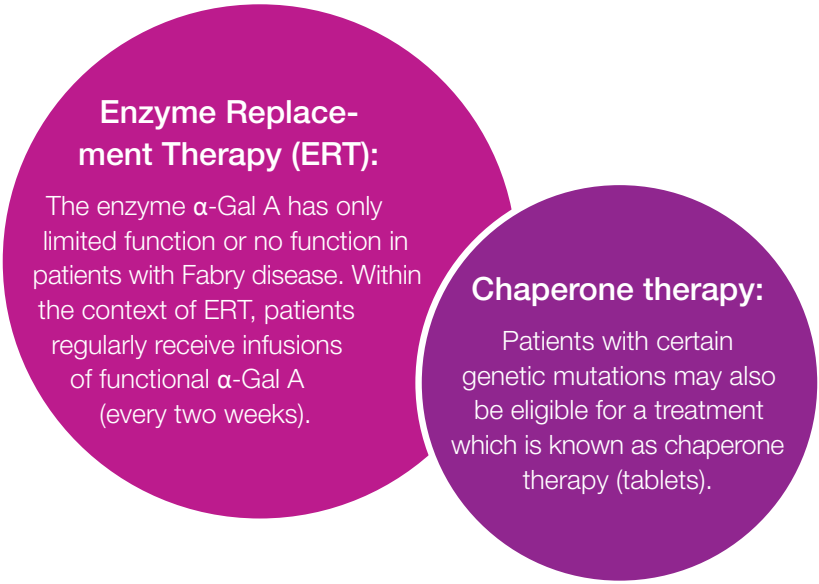
There are options for the treatment of the symptoms of Fabry disease as well as the treatment of the disease itself.

Treatment options for Fabry disease:

- Drugs, for example for the treatment of pain, digestive problems, high blood pressure (hypertension), kidney problems and drugs to reduce the risk of stroke
- Hearing aids for hearing disorders, possibly pacemakers in the case of some heart diseases

Symptoms should be treated because vital organs could be damaged. This can lead to severe, sometimes even life-threatening complications.

Treatments for Fabry disease itself:



What are the side effects of enzyme replacement therapy or chaperone therapy?

Enzyme replacement therapy is given directly into the vein; this may sometimes cause an infusion reaction. However, this is commonly only a mild reaction that occurs in most cases only at the beginning of the treatment programme. If you feel unwell during or after the infusion, tell your doctor or nurse immediately.

In chaperone therapy, the most common side effect is headache, which occurs in one in 10 patients.

Do I have to be treated even if I do not have any symptoms?

Fabry disease is a progressive disease. Signs of progression can often be detected only in the laboratory or as a result of analyses, as symptoms often only occur with advanced loss of organ function. Your doctor will tell you what the appropriate start date for your treatment is. Regular check-ups in a centre specialising in Fabry disease are important for the early detection of a possible progression of the disease so that you can be treated promptly. Please contact your doctor if you are not scheduled for regular check-ups.

Do women and children with Fabry disease need to be treated?

Whether women and children with Fabry disease require treatment depends on whether they have symptoms and how the disease affects the organs. Your Fabry disease specialist will tell you when the right time for the start of treatment is.

How will I know that the treatment works?

Fabry disease tends to develop slowly in most cases and successful treatment is often not detectable immediately. Therefore, you may not notice any immediate change after starting treatment. Regular check-ups are important both before and during treatment, so that your doctor can assess how the treatment is working in your case.

LIVING WITH FABRY DISEASE

What is the cause of pain with Fabry disease?

Pain is the most noticeable and often the earliest detectable symptom. The disease is caused by damage to the nerve fibres, which is noticed in the form of pain (called neuropathic pain). Pain is at times very severe and is in many cases caused by changes in temperature, stress and physical exertion.

If you have sudden or persistent pain, pain therapy can help. You should also keep a pain diary in order to obtain a better understanding of the disease. Contact your Fabry disease specialists for more information about the targeted treatment of neuropathic pain.

Can I continue to work with Fabry disease?

Whilst Fabry disease is associated with symptoms (please refer to «What are the symptoms of Fabry disease?»), they are treatable. Physically strenuous occupations or working under extreme temperature conditions may be difficult for some patients with Fabry disease. After some adjustments to the work environment, however, many patients with Fabry disease can continue working.

How often should I have check-ups?

In general, you will need a check-up with a Fabry specialist at least once a year. Several things are examined on such occasions, for example:

- ➔ Your general state of health
- ➔ Your kidney function
- ➔ Your heart function
- ➔ Presence and severity of pain
- ➔ Blood and urine analyses

If you have any problems in one of these areas or if you have a new onset or a worsening of symptoms, more frequent monitoring may be required.

Recent evidence indicates that the timely starting of Fabry-specific therapy can help to with better control of disease progression. However, worsening of the disease often occurs without noticeable symptoms. The annual check-ups are therefore essential even if you do not have any or only minimal discomfort at that time.

➔ Don’t be afraid to ask if you don’t understand the purpose or result of an examination!

Can I exercise with Fabry disease?

In principle, the answer is: Yes, absolutely. Exercise improves physical health. Physically active people have a better baseline in preventing many diseases than their sedentary peers. Even a low level of regular physical activity has a positive impact on health.

In addition, it is proven by now that regular exercise and physical activity is an effective therapy for mild to moderate depression. Select the type of exercise or sport depending on your disease status and discuss it with your doctor.

Since temperature changes and physical exercise can trigger pain, you should observe the following tips:

- ➔ Dress in layers so that you can always add or remove a layer if you are too hot or too cold
- ➔ Avoid extreme heat or extreme cold
- ➔ Be careful to keep warm in the cold, especially your hands and feet

Does Fabry disease have an impact on pregnancy?

Effects on the course and outcome of pregnancy are unknown, but the symptoms of Fabry disease may worsen during pregnancy and some medications may need to be stopped. If you are pregnant or planning to become pregnant, please contact your doctor.

Do I need to change my diet?

In principle, you do not need to change anything, but you can generally influence your wellbeing with a healthy diet.

The following basic rules apply:

- ➔ «5 A day»: Each day, eat **5 servings of fruit and vegetables** (raw or cooked) in different colours
- ➔ Every day, eat fibre-rich cereals (such as whole wheat bread, whole grain pasta and muesli).
- ➔ Drink plenty of fluids, for example unsweetened tea or mineral water

Can I still go on holiday?

Absolutely. However, since the prescribed medications have different names in some countries, you should make a note of not only their names, but also the active ingredients. Your doctor may give you an appropriate certificate if you travel abroad. Where possible, you should arrange your trip in the intervals between the test and treatment visits.

What about smoking?

Smoking is harmful to all people. Smoking is known to increase the risk of kidney failure, stroke, heart attack, lung cancer and other respiratory disorders. Since people with Fabry disease have a higher risk of stroke and heart or kidney disease, smoking can significantly increase these risks! Please refer to www.lungenliga.ch/rauchstopp for information and help with stopping smoking.

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WHERE CAN I FIND FURTHER SUPPORT?

Reliable help and support are critical so that you do not feel as though you have to cope with everything on your own. Talk openly with your family and friends about the disease and help them to understand and support you.

For more information and support, please contact the patient organisation for Fabry disease in Switzerland:

fabrysuisse
CH-8000 Zürich
www.fabrysuisse.ch

Fabry disease specialists in Switzerland
In Switzerland, there are centers specialized in the treatment of patients with Fabry's disease. For a list of these Fabry specialists please contact: info@fabrysuisse.ch.

International patient organisation for Fabry Disease
www.fabrynetwork.org

For more questions,
please contact your
Fabry disease specialist

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