What is Fabry?

Fabry International Network

Fabry disease is a rare, genetic condition which is estimated to affect around 1 in 100,000 people. [1]

In Fabry, an absence or reduced level of an enzyme called α-galactosidase A (α-Gal A), means that the body cannot break down certain types of fats, called globotriaosylceramide (GL-3) and plasma globotriaosyl-sphingosine (lyso-Gb3), and GL-3 builds up in a variety of cells in the body. [1]

This build-up causes damage to tissues and organs and leads to a range of symptoms and complications, which vary from one person to another. [1]

Disease progression is influenced by the sex of the individual (male or female) and how the disease presents, called its phenotype, which is classified as either non-classical (mild form) or classical (severe form).

Symptoms and complications vary from one person to another [1]

SKIN
- Sweating less than normal
- Small dark red/purple spots located between the belly button and the knees

KIDNEYS
- Protein in urine
- Decreased kidney function
- Kidney failure

EYES AND EARS
- Hearing loss (in children)
- Ringing in ears
- Cloudy vision (cataracts)

BRAIN AND NERVES
- Burning in the hands and feet
- Intolerance to heat/cold
- Vertigo/feeling dizzy
- Pain
- White matter lesions
- Depression
- Mini stroke (TIA)
- Stroke

STOMACH & BOWELS
- Feeling sick/being sick
- Diarrhoea
- Pain/bloating after eating
- Difficulty managing weight
- Feeling full after eating a small amount of food

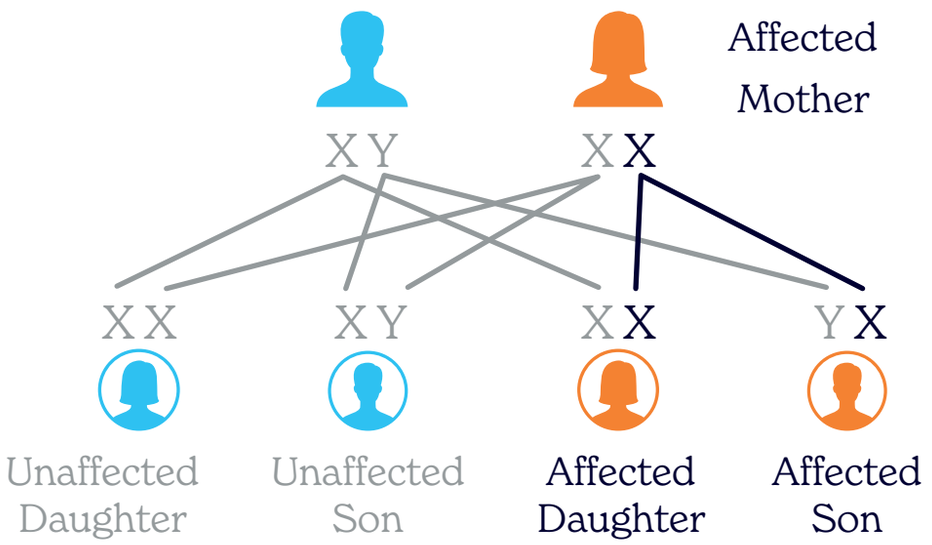
HEART
- Irregular heart beat
- Enlarged heart
- Heart attack
- Heart failure

OTHER
- Tiredness that is not relieved
- by rest or sleep
- Shortness of breath
- Cough/wheezing

As Fabry disease is an X-linked disorder it can be passed to children by either parent

Mother

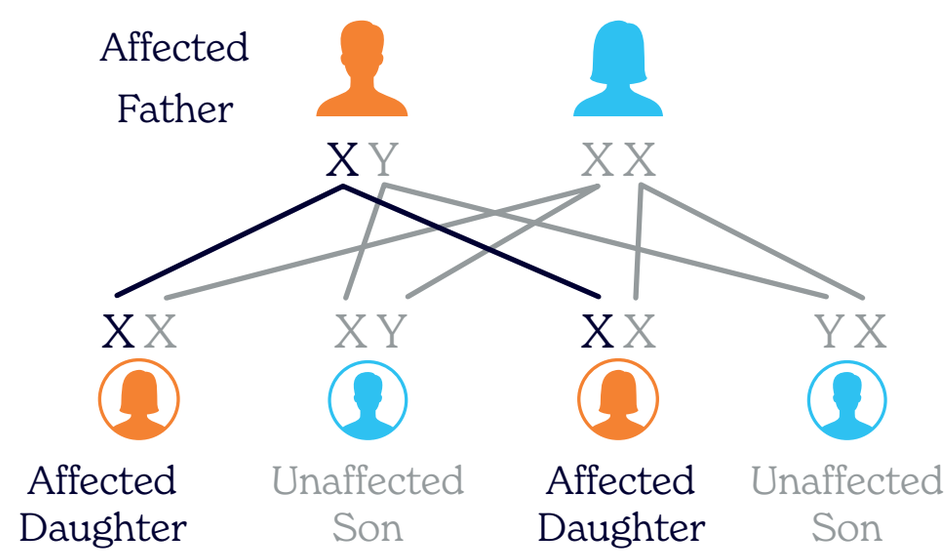
A mother with Fabry has a 50% chance of passing her X mutation to any of her children



- Fabry is caused by a mutation in the α-galactosidase A gene (GLA) on the X chromosome
- More than 1000 different mutations which cause Fabry disease have been identified [2]
- The mutation type may indicate what symptoms an individual will have, when they will appear and how bad they will be or will become

Father

A father with Fabry passes his X mutation to all of his daughters. His son's do not inherit Fabry because they inherit his Y chromosome



A woman has heterozygous disease
She has the Fabry gene on at least one of her two X chromosomes (XX), one inherited from her mother, one inherited from her father

Planning a family

When considering starting a family, individuals with Fabry may wish to consider genetic counselling.

Genetic counselling helps individuals and families understand the medical, psychological, social and reproductive implications of having a genetic condition

Fabry and fertility

There is limited information on fertility in individuals with Fabry disease.
One study reported normal hormone levels and fertility in both males and females with Fabry when compared with the general population. [3]
A recent study of males reported that Fabry disease may affect sperm characteristics (e.g. count, shape and movement), but it does not impact hormone function and only slightly reduces fertility rates. [4]

Pregnancy Testing for Fabry

A number of tests are available to check for Fabry before a child is born:

- Before pregnancy – pre-implantation diagnosis of embryos - similar to in vitro fertilisation (IVF)
- Week 5 onwards – free-foetal DNA testing
- Weeks 10–12 – chorionic villous sampling (CVS)
- Weeks 16–17 – amniocentesis

Pre-implantation diagnosis is used to check embryos for a known condition in the family before unaffected embryos are implanted into the mother

CVS involves removing and testing a small sample of cells from the placenta

Amniocentesis involves removing and testing a small sample of cells from the amniotic fluid, the fluid that surrounds the unborn baby in the womb

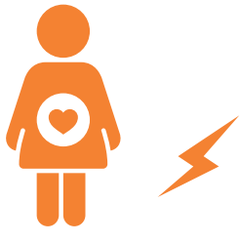
Cells from the baby (free foetal DNA) can be detected in the mother's blood from around five weeks of pregnancy
These cells can be analysed to find out the sex of the foetus

Not everyone chooses to find out if their unborn child has Fabry disease before they are born, instead testing can be carried out at a later stage.

Pregnancy

The effect of pregnancy on Fabry symptoms

A retrospective study looking at the impact of Fabry disease on pregnancy found several Fabry-related symptoms worsened during pregnancy. These included: gastrointestinal symptoms, a sensation or burning/pricking/tingling in hands and feet, protein in the urine, headaches and post-partum depression.[5]



A retrospective study is one which looks at information or events that have taken place in the past

Post-partum is the period of time after giving birth

Notes

Psychological problems Depression in Fabry

Around **10–25%** of the general population experience **depression** or **anxiety** at least once over their lifetime.[6]
The numbers are much higher in those with Fabry disease. [7]
More Fabry males report severe depression than Fabry females (36% vs 22%). [8]
Men with Fabry are more likely to have higher scores for symptoms of anxiety and depression than women with Fabry, or those without Fabry.[9]
Higher scores for anxiety and depression are also reported in adolescents with Fabry compared with those without the disease. [10]

Symptomatic treatment refers to a treatment or therapy (e.g. heat) that eases the symptoms of a disease (e.g. pain) without having any effect on the disease itself

A vicious cycle is when one problem causes another problem, which then makes the first problem worse

Psychological – relates to the mind and feelings

Physical symptoms vary over time and do not always respond to **symptomatic treatment** which can, in turn, lead to **psychological problems**, such as depression and anxiety.

Psychological symptoms can cause individuals to experience physical symptoms such as fatigue and- Post-partum is the period of gastrointe time after giving birthstinal problems and so a **vicious cycle** develops.

Nobody knows why there are high rates of depression in Fabry

Depression is often undiagnosed; **88% of mild-to-moderate** and **72%** cases of **severe depression** went undiagnosed in Fabry patients.[8]

Almost half of individuals with Fabry who **self-reported** depression had not received treatment for their depression.[11]

It is important to be aware of the potential warning signs of depression and to seek medical help

Signs of depression are complex and, like the physical symptoms associated with Fabry, can vary widely from one person to another.
An individual can have and show a mixture of **psychological, physical** and **social** signs that they are depressed.

Self-reported is when someone provides information about their own symptoms

Morbidity refers to having a disease or symptom of a disease

Mortality refers to the number of deaths caused by a disease

Signs of depression

Psychological	Psychological	Psychological
Low mood or sadness that does not go away	Moving or speaking more slowly than usual	Avoiding contact with friends and taking part in fewer social activities
Feeling hopeless and helpless	Decrease in physical activity	Neglecting hobbies and interests
Having low self-esteem	Changes in appetite or weight (increased or decreased)	Having di culties in your home, work or family life
Feeling tearful	Constipation	
Feelings of guilt	Unexplained aches and pains (e.g. headache/ stomach ache)	
Feeling irritable and intolerant of others	Lack of energy or enthusiasm	
Having no motivation or lost interest in doing things they used to enjoy doing	Low sex drive	
Finding it di cult to make decisions	Menstrual cycle changes	
Not getting any enjoyment from life	Sleep disorders (e.g. lack of sleep, too much sleep, early morning waking)	
Feeling anxious or worried		
Thoughts of self-harm		
Suicidal thoughts or attempts		

Treatment for depression

Treatment for depression usually involves a combination of **self-help,** talking therapies (e.g. counselling) and medicines.

Treatment recommendations

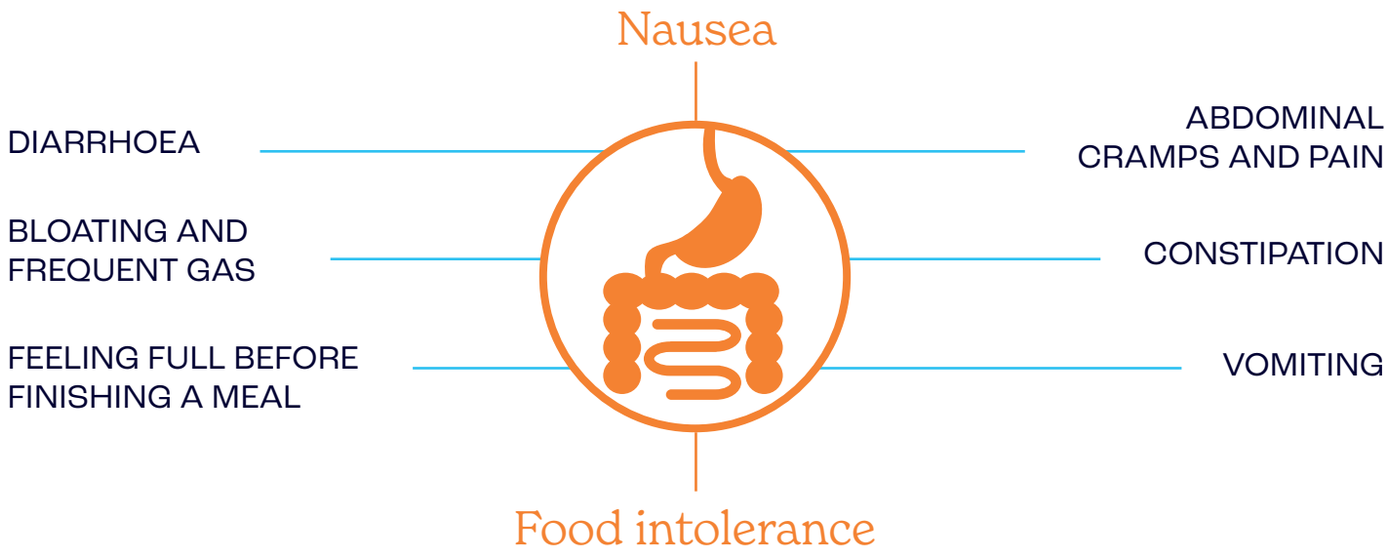
Treatment recommendations are based on whether the person has mild, moderate or severe depression.

Self-help for depression includes talking to a friend or relative, books, apps and online tools

Treatment depends on whether the depression is mild, moderate or severe

GI symptoms

Approximately 52–66% of Fabry patients report GI symptoms.[12,13] GI symptoms in Fabry vary from one person to another but often include:[14,15,16]



Abdominal pain and diarrhoea are the most common GI symptoms, affecting around half of the adults with classic Fabry and 60% of children.[12]

In a study of 25 adult patients, 14 reported feeling full before finishing a regular size meal and 12 feeling bloated.[13]

Both males and females experience abdominal pain with the same frequency, while diarrhoea affects more males than females.[12,13,17]

Constipation is also common and it can be twice as frequent in females than in males.[12,17]

Overall GI symptoms are experienced by more females than males.[12]

When do symptoms start?

Classic Fabry

Symptoms of classic Fabry become apparent early in childhood and adolescence with GI symptoms being one of the earliest to appear.[13,18] The average age at which GI symptoms become evident is 5 years in boys and 9.5 years in girls.[18] GI issues have been reported in children as young as one year old.[19]

Late-onset Fabry

Individuals with late-onset Fabry do not show any overall symptoms during childhood or adolescence, usually developing kidney and heart issues between 30 to 70 years of age.[20]

What causes GI symptoms?

GI symptoms are thought to be caused by two different processes:[15]

Nerve damage, which affects the messages the brain sends to the GI tract to control movement of food during digestion.

Accumulation of fats in the GI tract cells.

GI disturbances can have a significant impact on people with Fabry and their quality of life.[18]

Three key approaches can help improve GI symptoms

1. early diagnosis

- A Fabry diagnosis is often delayed and can take an average of 14 years in males and 16 years in females from when symptoms first appear.[21]
- If Fabry disease signs and symptoms are recognised promptly, then treatments can start earlier and possibly help delay more serious complications.
- Many people with Fabry who experience GI symptoms are incorrectly diagnosed with Crohn's disease, celiac disease, or irritable bowel syndrome (IBS).[14]

People with Fabry have to manage their diets to help improve GI symptoms. Some changes may include: [22]

- Adjusting meal sizes and patterns towards smaller, more frequent meals.
- Timing of meals, such as avoiding late night eating.
- Eliminating foods from the diet that are not tolerated such as spicy, lactose containing or greasy foods.

2. Diet and lifestyle

3. Treatment

There is no cure for Fabry disease but current treatments may prevent organ damage and greatly improve the quality of life of patients.

Oral chaperone therapy

Chaperones are small molecules that assist enzymes in becoming functional by helping them take the correct shape and stay stable. Chaperone therapy is only suitable for people with amenable mutations of the α-GaL A enzyme. Treatment has shown meaningful reduction in diarrhoea in patients with Fabry disease and amenable mutations.[23]

Intravenous enzyme replacement therapy (ert)

For people with Fabry, ERT is a long-term therapy whereby the missing or deficient enzyme is given via an intravenous infusion. Recent studies looking at improvements of GI symptoms for patients on ERT have shown a reduction in abdominal pain and diarrhoea in females15 and a reduction in abdominal pain or diarrhoea from weekly occurrences to only occasionally in males who had been on ERT for 6–7 months.[24]

Notes

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Connect with other patients

Support groups can be empowering by helping you feel less isolated or learn how to advocate for your condition. Find more information on Disease on the Fabry International Network website!

FABRYNETWORK.ORG

Why should you join a patient organisation?

- Connect with other patients, caregivers, and stakeholders, within your region through calls, webinars, and in-person meetings
- Participate in regional and local events to connect, learn and address the nation's leading issues
- Develop relationships with key decision-makers and opinion leaders
- Share your story to help other patients by raising awareness
- Receive news and information on what the organisation is taking action on and participate in events
- Patient organisations often have access to breaking news before it is generally known. They have opportunities to participate in advocacy efforts

What can a patient organisations offer you

Support: Most organisations help people connect with each other. They may provide opportunities to meet in person at yearly conferences, summer camps, or local meetings. Whether in person or online, support from others can empower you to take charge of your health. Medical Information: Most organisations provide medical information in easy-to-understand terms to help you learn more about your medical condition, available treatment options, and current research. Information is often on the group's website, but may also be available by mail, phone, or e-mail.

Resources: Patient organisations often have a list of helpful resources, such as related non-profit advocacy groups, financial assistance resources, and sources for special medical equipment. They may also be able to give advice on dealing with school or health insurance issues.

List of doctors or clinics: Many organisations have a list of medical care professionals and clinics to help you find specialists with experience in diagnosing or treating a rare medical condition. They may work closely with clinical centers, sometimes called Centers of Excellence, or be involved in the training of specialists. Other groups may have a list of doctors recommended by their members. Many groups also have a medical advisory board made up of experts in the field. If you can't find this information on the group's website, call or e-mail the group to see if they can provide you with a list of doctors or clinics.

Registry: A registry is a collection of information about individuals, usually focused around a specific diagnosis or medical condition. Many rare disease registries are maintained by advocacy groups to help advance medical research for a particular medical condition. If the group does not have its own disease registry, it may know of an appropriate registry for your medical condition.

Research and Clinical Trials: Clinical trials are medical research studies in which people participate as volunteers. These studies may be evaluating new treatments or medications, searching for the cause(s) of a medical condition, or researching how the symptoms of the condition change over a person's lifetime. Whether you are interested in enrolling in a clinical trial or aim to stay aware of potential new treatments and advances, you may want to find a non-profit advocacy group that provides information about the latest medical research. Some groups raise money to offer grants to medical researchers or pharmaceutical companies who are developing new treatments. Often these groups will keep information on their website about the progress of supported research.

Advocacy: Advocacy for Fabry disease may involve educating the public or medical community about the condition. A group may also take issues to local, state and federal governments in an effort to pass legislation that will improve the lives of those affected by rare and genetic conditions.

What should you look for in a support

Evaluating a group is not always easy. When you are looking for a patient organisation, you want to make certain that the group offers helpful and up-to-date information. The mission statement of the group can help you understand the focus of the group's activities. Also look at who is involved in running the group. The group's staff members may have the medical condition themselves or have an affected family member. Other staff members may have a degree in a related field, such as social work, public health, education, communication, or medicine.

Connect with your patient organisation!

Click on the link to visit the FIN website to find an overview of our member organisations.

For more information, please reach out to coordinator@fabrynetwork.org

FABRYNETWORK.ORG

Fabry International Network is an international non profit organization. The primary aim of Fabry International Network is to facilitate collaboration between patient organisations to support those affected by Fabry disease. FIN is connected to over 52 countries and 64 patient associations around the world. Membership is free and open to any national patient organisation in which Fabry patients are represented.

FIN's vision is of a world where every single person affected by Fabry disease has the best quality of life possible through early diagnosis, treatment and cure.

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