CONDITION

Fabry disease

Fabry disease is an inherited condition that causes certain fatty substances to build up and damage organs over time.

WHAT IT IS
Inherited condition causing fatty waste buildup inside cells

BODY SYSTEM
Kidneys, heart and circulation, nervous system, skin, and digestion

MAIN SYMPTOMS
Burning limb pain, reduced sweating, digestive problems, fatigue

WHAT CAUSES IT
Inherited changes in the GLA gene

HOW IT IS DIAGNOSED
GLA gene testing and alpha-galactosidase A enzyme testing

MAIN TREATMENT
Enzyme replacement or eligible-variant chaperone therapy, plus organ care

CAN IT BE CURED?
No, treatment can slow organ damage

IS IT AN EMERGENCY?
Sometimes, with stroke, heart-attack, or dangerous-rhythm signs

LONG-TERM OUTLOOK
Often manageable, though heart, kidney, or brain disease may progress

Overview

Fabry disease is a rare, lifelong genetic condition affecting an enzyme called alpha-galactosidase A. Enzymes are proteins that help cells carry out chemical processes.

When this enzyme is missing or does not work well, certain fatty substances cannot be broken down normally. They collect inside cells, particularly in blood vessels, the kidneys, heart, nerves, skin, and digestive system. This buildup can gradually damage tissues and organs.

Fabry disease is a lysosomal storage condition. Lysosomes are structures inside cells that break down and recycle waste. In Fabry disease, part of this recycling system does not work properly.

Some people develop pain, reduced sweating, skin spots, or digestive symptoms during

childhood. Others have no noticeable problems until adulthood, when heart or kidney changes may be found. Symptoms vary greatly, even among relatives with the same genetic change.

Early recognition matters because treatment and monitoring may reduce symptoms and limit organ damage. Treatment cannot cure the underlying genetic change or reverse all established damage.

Symptoms

Classic Fabry disease usually begins in childhood or adolescence. Later-onset forms may mainly affect the heart, kidneys, or brain during adulthood.

Early symptoms can include:

Angiokeratomas often appear around the hips, groin, buttocks, or upper legs. They are usually harmless but may bleed if injured.

An eye examination may find a swirl-like pattern called cornea verticillata on the clear front surface of the eye. It usually does not affect vision.

As the condition progresses, some people develop protein in the urine, reduced kidney function, thickened heart muscle, irregular heartbeats, hearing loss, or stroke-like symptoms. Someone with a later-onset form may have few typical childhood symptoms.

Symptoms alone cannot confirm Fabry disease because other conditions can cause similar pain, fatigue, digestive problems, or organ changes.

- Burning, tingling, or severe pain in the hands and feet
- Pain attacks triggered by heat, fever, exercise, stress, or tiredness
- Reduced sweating or, less commonly, excessive sweating
- Difficulty coping with hot weather or strenuous exercise
- Stomach pain, nausea, diarrhoea, constipation, or feeling full quickly
- Tiredness, dizziness, headaches, or ringing in the ears
- Small, dark red or purple skin spots called angiokeratomas

Causes and risk factors

Fabry disease is caused by a harmful change in the GLA gene, which provides instructions for making alpha-galactosidase A.

The GLA gene is on the X chromosome, making Fabry disease an X-linked condition.

A person with one X chromosome and a harmful GLA variant will usually develop Fabry disease, although its severity and age of onset vary. A person with two X chromosomes may also have significant symptoms because cells switch off one X chromosome, and the pattern differs across the body.

A father with a GLA variant passes it to all his daughters and none of his sons. A mother with a GLA variant has a one-in-two chance of passing it on in each pregnancy. These probabilities do not predict disease severity.

The main risk factor is having a close biological relative with Fabry disease or a known GLA variant. Sometimes the variant is found after unexplained heart or kidney disease develops. Rarely, it is a new change not inherited from either parent.

Diagnosis

Diagnosis combines enzyme and genetic testing with medical history and organ assessment.

Alpha-galactosidase A activity can be measured using blood cells or a dried blood spot. Very low activity strongly supports the diagnosis in people with one X chromosome. People with two X chromosomes can have levels within the usual range, so a normal enzyme result does not rule out Fabry disease.

Genetic testing looks for a disease-causing GLA variant and is especially important for confirming the condition in women and girls. Some variants have uncertain effects and require review by a genetics or metabolic specialist.

A blood marker called lyso-Gb3 may support diagnosis and follow-up, but it is not interpreted alone. A positive newborn screening result also requires confirmatory testing.

Tests to assess organ involvement may include:

Testing biological relatives can identify affected people before major organ problems appear.

- Blood and urine tests for kidney function and urine protein
- An electrocardiogram and heart imaging
- Hearing and eye assessments
- A neurological examination and, when needed, brain imaging
- Review of pain, sweating, digestion, mood, and daily function

Treatment and management

Care is usually coordinated by a team familiar with inherited metabolic conditions. Kidney, heart, nerve, pain, hearing, genetics, and mental health specialists may also be involved.

Enzyme replacement therapy provides manufactured alpha-galactosidase A through regular intravenous infusions. It can reduce fatty-substance buildup and may slow kidney, heart, and other organ damage. Established scarring may not reverse. Infusion reactions and immune responses can occur, so treatment is monitored.

Migalastat is an oral pharmacological chaperone that helps certain altered forms of the enzyme fold correctly and function better. It is only suitable for specific GLA variants described as amenable. Eligibility also depends on factors such as age, kidney function, and local approval.

Other care targets symptoms and complications. This may include treatment for nerve pain, digestive symptoms, high blood pressure, urine protein, irregular heart rhythms, heart failure, stroke risk, or kidney failure. Some people need a pacemaker, implanted defibrillator, dialysis, or kidney transplantation.

A kidney transplant can treat kidney failure but does not correct Fabry disease elsewhere in the body. Disease-specific treatment and heart monitoring may still be needed.

Regular follow-up is important even when you feel well. Monitoring can detect gradual kidney or heart changes before they cause clear symptoms. Gene-based treatments are being studied but are not an established cure.

Complications

Fabry disease can affect several organs. Risk is influenced by the genetic variant, biological sex, age, existing damage, and access to treatment.

Possible complications include:

Not everyone develops every complication. Later-onset forms may mainly involve one organ, but ongoing assessment is still needed because other effects can appear.

- Chronic kidney disease and kidney failure
- Thickened or scarred heart muscle
- Irregular heart rhythms, slow heartbeat, or sudden cardiac problems
- Heart failure
- Transient ischaemic attacks or strokes

- Progressive or sudden hearing loss
- Long-lasting nerve pain and reduced heat tolerance
- Anxiety, low mood, sleep problems, and limits on daily activities

Prevention

Fabry disease cannot be prevented through diet, exercise, vaccination, or lifestyle changes because it is caused by an inherited genetic variant.

Genetic counselling can explain inheritance, testing for relatives, and reproductive options. These steps cannot prevent disease in someone who already has the variant, but they can support informed decisions and earlier diagnosis.

Managing blood pressure, avoiding smoking, staying active within your limits, and following kidney and heart care advice may protect general health. These measures do not remove the underlying cause.

Living with it and what to expect

Fabry disease is lifelong, but its course varies. Some people have frequent pain and digestive symptoms from childhood. Others remain well for years or mainly develop heart or kidney changes later.

Organ damage usually develops gradually. Treatment may slow it, particularly when started before extensive scarring, but cannot guarantee that complications will not occur. Nerve pain may continue even when laboratory markers improve.

Follow-up may involve blood and urine tests, heart rhythm checks, heart scans, hearing assessments, and reviews of pain and daily function. Timing depends on age, symptoms, treatment, and organ involvement.

Many people with Fabry disease study, work, exercise, travel, and have families. Pain, fatigue, appointments, or infusion schedules can affect daily routines. Planning for hot weather, pacing activity, and arranging workplace or school adjustments may help.

Tell your care team about changes between visits, especially new palpitations, reduced exercise tolerance, swelling, hearing changes, or worsening pain. Treatment plans may need adjustment over time.

When to get medical help

Call emergency services for signs of a stroke or serious heart problem, including:

These symptoms need emergency assessment whether or not Fabry disease is the cause.

Seek urgent medical advice for sudden hearing loss, sustained palpitations, rapidly worsening breathlessness, new leg swelling, or a major reduction in urine. A severe or unusual pain episode that does not settle also needs prompt assessment.

Routine follow-up is appropriate for slowly changing symptoms, medication or infusion concerns, and questions about testing relatives or planning a pregnancy. Do not wait for a routine appointment if symptoms are new, sudden, or worsening quickly.

- Sudden facial drooping, arm weakness, or trouble speaking
- Sudden loss of vision, severe imbalance, or one-sided numbness
- New chest pressure or pain, especially with sweating or nausea
- Severe breathlessness, collapse, or fainting with a racing heartbeat

Common questions

Is Fabry disease fatal?

It can shorten life when it causes severe heart, kidney, or brain complications. Outlook has improved with earlier diagnosis, monitoring, disease-specific therapy, and treatment of complications. An individual's outlook cannot be predicted from the diagnosis alone.

Can women get Fabry disease?

Yes. Women and girls with a harmful GLA variant can have pain, kidney disease, heart disease, stroke, or other symptoms. Some are mildly affected, while others develop serious disease.

What age does Fabry disease start?

Classic Fabry disease can cause symptoms during childhood. Later-onset forms may not become apparent until middle or later adulthood. Age at diagnosis does not always show when organ changes began.

Is Fabry disease contagious or autoimmune?

No. It cannot be caught or passed through contact, and it is not caused by the immune system attacking healthy tissue. It results from a genetic change affecting a cell-recycling enzyme.

Can I have children if I have Fabry disease?

Yes, but the GLA variant may be inherited. Genetic counselling can explain the chance for each

pregnancy and available testing or reproductive options. Pregnancy may require coordinated heart, kidney, genetics, and obstetric care.

Can diet cure or control Fabry disease?

No diet can correct the missing or poorly functioning enzyme. Food choices may help digestive symptoms, kidney health, or cardiovascular health but do not replace disease-specific treatment.

Sources

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