A VISUAL GUIDE TO UNDERSTANDING FABRY DISEASE

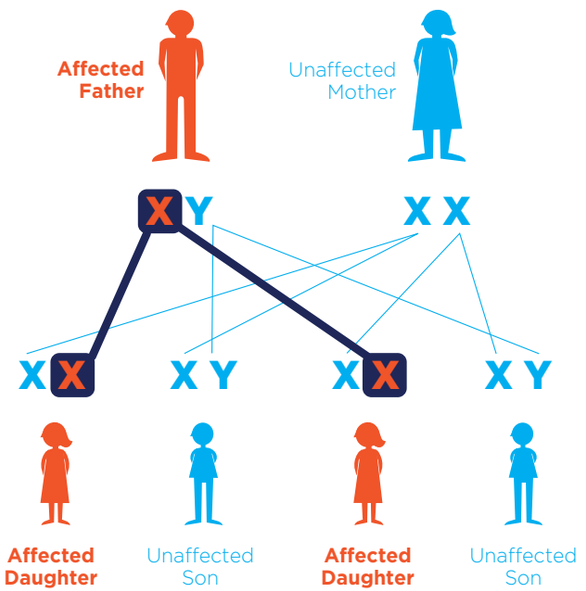
INFORMATION FOR FAMILIES LIVING WITH FABRY DISEASE

Amicus Therapeutics

Amicus Therapeutics has developed this educational resource in collaboration with the rare disease community and thought leaders.

How does Fabry disease affect families?[7]

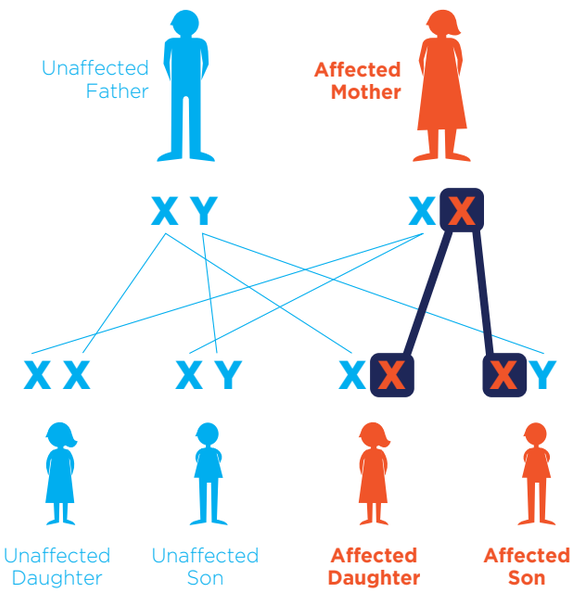
Fabry disease is an **X-linked disorder**. It is caused by a disease-causing variant of a gene (called the *GLA* gene) that is located on the X **chromosome**. This gene variant can be passed down by either parent. In rare cases, Fabry disease can be caused by a gene variant that occurs spontaneously in a child and is not present in either parent (called a ***de novo*** variant or *de novo* mutation).



HOW FATHERS PASS DOWN FABRY DISEASE

Men have one X chromosome and one Y chromosome. A father with Fabry disease passes his disease-causing variant of the *GLA* gene to all of his daughters, because daughters inherit their father's only X chromosome. An affected father cannot pass the gene variant to his sons, because sons inherit a Y chromosome from their fathers.

X = chromosome with disease-causing gene variant
X = chromsome without disease-causing gene variant
Affected = person with Fabry disease
Unaffected = person without Fabry disease



HOW MOTHERS PASS DOWN FABRY DISEASE

Women have two X chromosomes. A mother who has a disease-causing variant of the *GLA* gene on one of her two X chromosomes has a 50% chance of passing down Fabry disease to each of her children. Since males have only one X chromosome, if they inherit the disease-causing gene variant, they will develop Fabry disease. Because females have two X chromosomes, a daughter who inherits one copy of the disease-causing gene variant may have a normal copy of the *GLA* gene on her other X chromosome. This may allow her body to produce some normal α-Gal A. Affected daughters may have more variable symptoms than affected sons for this reason.[5]

What do these words mean?

A glossary of important terms when discussing Fabry disease

- **Cell:** basic building block of all living things
- **Chaperone therapy:** a type of therapy that interacts with enzymes to improve their function and stability
- **Chromosome:** structure that contains genes
- **Computed tomography (CT) scans:** a special kind of x-ray
- ***De novo* variant or mutation:** an alteration in a gene that is present for the first time in one family member and can be passed to future generations
- **Deoxyribonucleic acid (DNA):** substance within genes that contains instructions, or code, for making proteins, including enzymes
- **Enzyme:** a special type of protein that speeds up chemical reactions that take place within a cell
- **Enzyme replacement therapy (ERT):** a treatment that replaces missing or nonfunctioning enzymes
- **Gene:** the basic unit of heredity contained within each cell, made up of DNA, that is passed from parent to child
- **Gene variant:** (also known as mutation) a change to the structure of a gene that can alter the gene's function, sometimes resulting in diseases or conditions
- **Lysosomal disorders:** (also known as lysosomal storage disorders) a group of more than 70 diseases that result from accumulation of waste products in lysosomes[4]
- **Lysosome:** a sac found in cells that contains enzymes that digest cell waste
- **Sign:** objective evidence of a disease or condition that can be recognized by the patient as well as others
- **Stroke:** damage to the brain resulting from blockage of blood flow or rupture of a blood vessel
- **Symptom:** subjective evidence of a disease or condition that can only be perceived by the person who has the disease
- **Transient ischemic attack (TIA):** a brief period of nerve or brain dysfunction (without tissue damage) caused by loss of blood flow in the brain
- **X-linked disorder:** an inherited disorder caused by variants in a gene located on the X chromosome

What is Fabry disease?

For additonal information, talk to your health-care provider.
(Note: some words that may be unfamiliar are **highlighted** and are defined in the glossary at the end of this brochure)

Fabry disease is a rare genetic disorder.[1]

Estimates of how many people have Fabry disease vary, but researchers believe it may affect as many as 1 in every 1400 to 9000 people in some parts of the world.[2]

It's a type of disease called a **lysosomal disorder.**[3]

People who have lysosomal disorders have problems making specific lysosomal **enzymes** or other proteins.[4]

In Fabry disease, the affected enzyme is called α-galactosidase A, or just α-Gal A.[3]

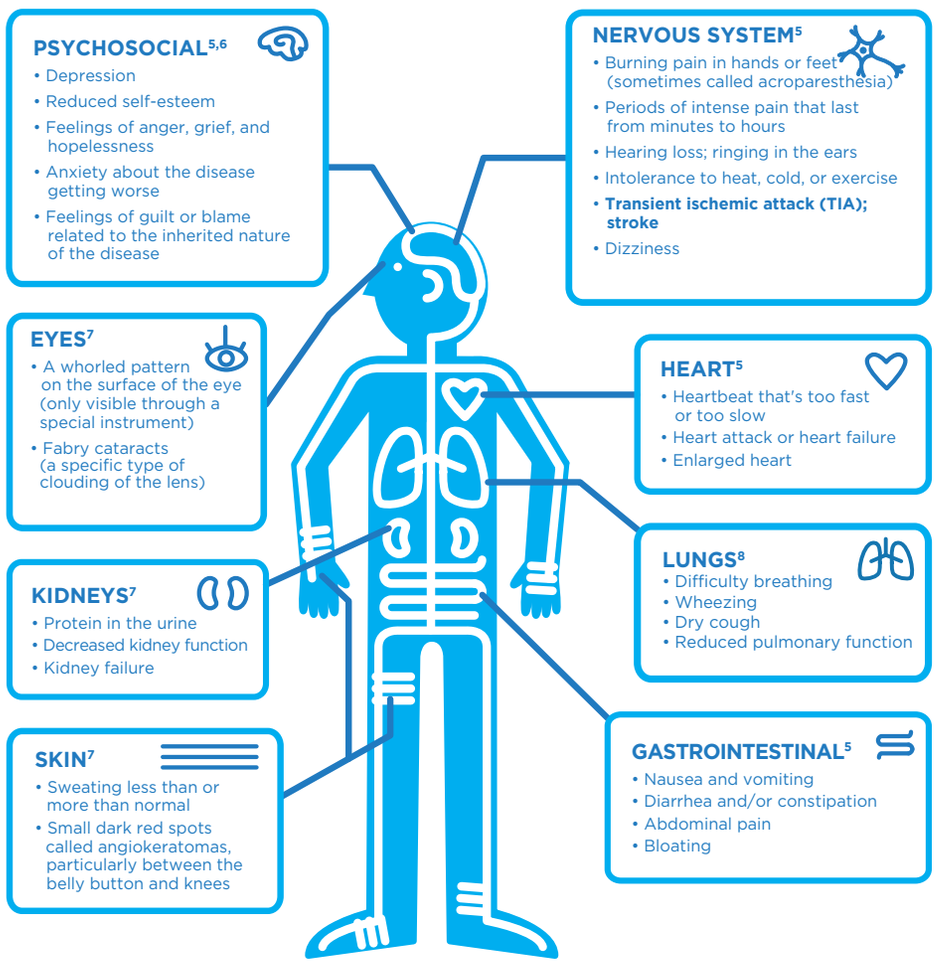
Usually, α-Gal A breaks down certain fatty materials in the **cells**, primarily a substance called globotriaosylceramide (GL-3).[5]

But, in people who have Fabry disease, α-Gal A does not break down GL-3; instead, GL-3 builds up in cells throughout the body, particularly in cells lining the blood vessels.[6]

This buildup causes damage to organs and tissues that gradually worsens over time, leading to the **signs** and **symptoms** of Fabry disease.[6]

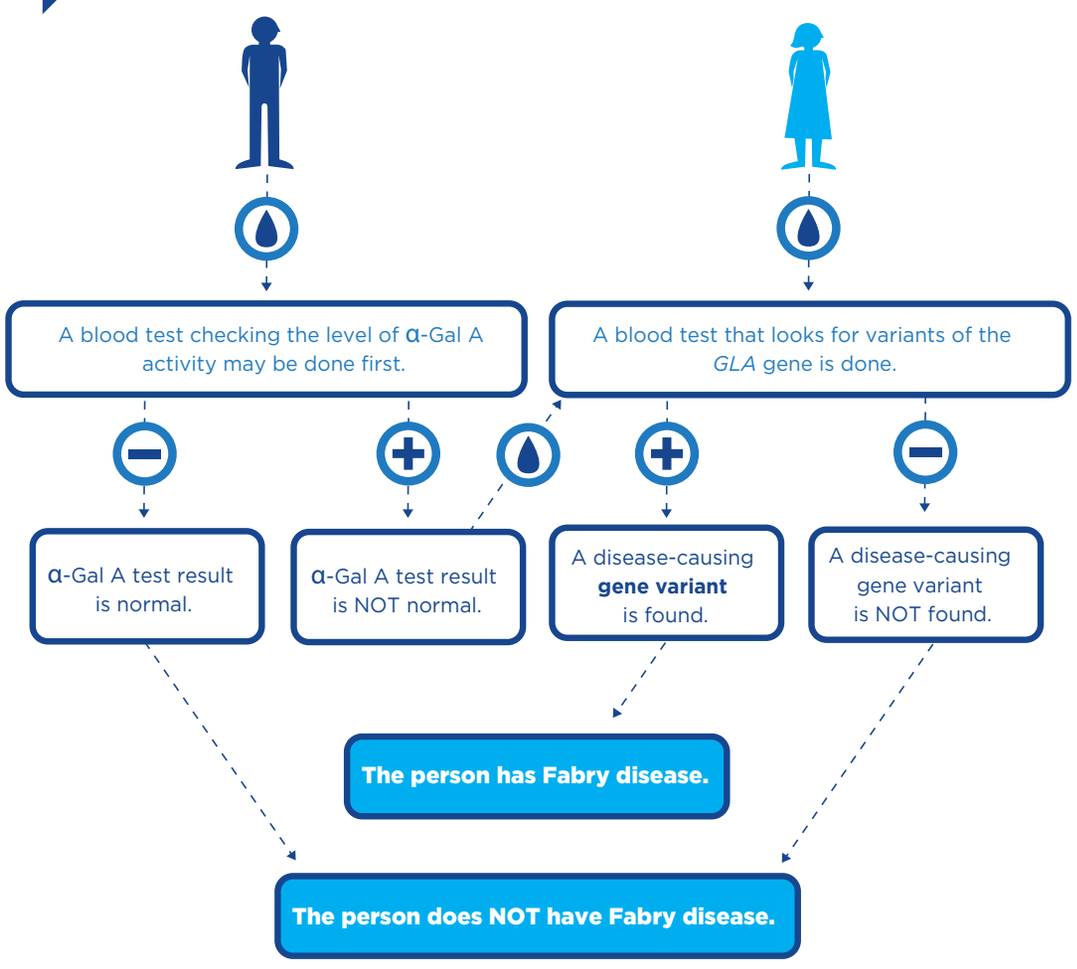
How does Fabry disease affect the body?

The signs and symptoms of Fabry disease tend to gradually worsen over time. However, it's important to be aware that everyone experiences Fabry disease differently. Some signs and symptoms may be more or less severe in some people compared with others. Also, not everyone will experience all of the signs and symptoms listed below.



A doctor suspects Fabry disease—here's an example of what can happen.[5,6]

A doctor may suspect Fabry disease because of the signs and symptoms a person is having, and/or because others in the person's family have the condition. The process of diagnosing Fabry disease may be different in males and females.



What causes Fabry disease?

Everyone has information called **DNA** coded into his or her cells.

DNA is inherited through **genes** that are passed down from the person's mother and father.

Sometimes, gene variants (also called mutations) occur in the DNA code of a particular gene that can change the way the gene functions.

CAR
CAT

Think of it like spelling. One wrong letter can completely change the meaning of a word!

Some people with Fabry disease have variants of the galactosidase alpha *(GLA)* gene that cause their bodies to make very little or no α-Gal A.[9]

Others have different variants of the *GLA* gene that cause their bodies to make α-Gal A that doesn't function correctly.[10]

How is Fabry disease treated?[2,5]

People who are diagnosed with Fabry disease may be referred to a team of specialized health-care providers, such as nephrologists, cardiologists, genetic counselors, and other specialists.

Further testing may be done, including blood and urine tests, imaging tests such as **computed tomography** or CT, scans, and evaluations of sight and hearing

A personalized treatment plan is created, which may include:

- Treatments that help manage the specific signs, symptoms, and complications the person is experiencing
- **Enzyme replacement therapy (ERT)**
- For people who have certain gene variants, a type of treatment called **chaperone therapy**

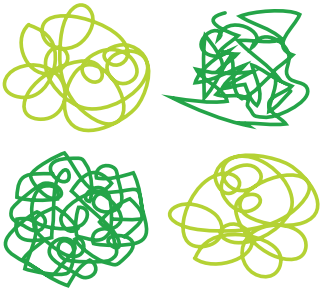
Research is currently being done on potential new treatments for Fabry disease. To find out more about ongoing research trials, search for Fabry disease on clinicaltrials.gov, or on clinicaltrialsregister.eu, or talk to your health-care provider.

Other resources that may be helpful are listed below.

- **Fabry International Network**
  fabrynetwork.org
- **Fabry Support & Information Group**
  fabry.org
- **The National Fabry Disease Foundation**
  fabrydisease.org
- **Society for Mucopolysaccharide Diseases (UK)**
  mpssociety.org.uk
- **Global Genes**
  globalgenes.org
- **Canadian Fabry Association**
  fabrycanada.com
- **Fabry Australia**
  fabry.com.au
- **National Institutes of Health (NIH) National Institute of Neurological Disorders and Stroke (NINDS) Fabry Disease Information Page**
  ninds.nih.gov/Disorders/All-Disorders/Fabry-Disease-Information-Page/2915/organizations/1022
- **NORD – National Organization for Rare Disorders**
  rarediseases.org
- **EURORDIS – Rare Diseases Europe**
  eurordis.org

Why are gene variants important?

More than 1000 different gene variants have been identified that can cause Fabry disease.[10]



The specific gene variant a person has may help predict when symptoms appear, what kind of symptoms appear, and how bad the symptoms may become.[5,7]

It's important for individuals and families with Fabry to know which gene variant they have.

References

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