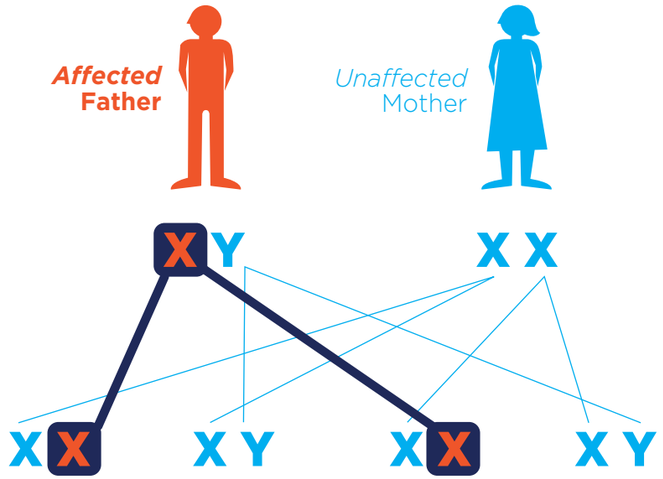
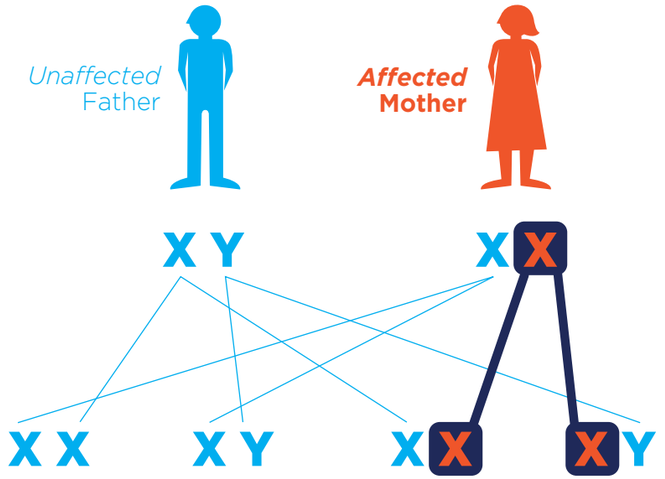
A VISUAL GUIDE TO UNDERSTANDING FABRY DISEASE

WHAT PEOPLE LIVING WITH FABRY DISEASE— AND THEIR FAMILIES— NEED TO KNOW

How does Fabry disease affect families?

Fabry disease is an X-linked disorder. It is caused by a mutation in a gene on the X chromosome and can be passed down by either parent.





HOW *FATHERS* PASS ALONG FABRY DISEASE

Men have one X chromosome and one Y chromosome. Women have two X chromosomes. A father with Fabry disease passes his mutation to all of his daughters, because daughters inherit their father's only X chromosome. An affected father never passes the mutation to his sons, because sons inherit a Y chromosome from their fathers.

HOW *MOTHERS* PASS ALONG FABRY DISEASE

A mother who has the mutation on one of her two X chromosomes has a 50% chance of passing down Fabry disease to each of her children. Since men only have one X chromosome, if they inherit the mutation, they will develop Fabry disease. In affected daughters, the α-Gal A mutation will occur randomly in some cells and not others, so daughters may have less severe or more variable symptoms than sons.

What do these words mean?

A glossary of important terms when discussing Fabry disease

Cell
Basic building block of all living things

Chromosomes
Structures that contain DNA and a person's genetic code

De novo mutation
An alteration in a gene that is not inherited but is present for the first time

DNA
Basic unit that allows for the transmission of genetic information from one generation to the next and contains instructions, or code, for making proteins and enzymes

Enzyme
A special type of protein that speeds up a reaction that takes place within a cell

Lysosome
A specialized fluid-filled sac found in cells that contains enzymes

Lysosomal storage disorder (LSD)
A group of over 50 diseases resulting from the accumulation of waste products in lysosomes

Mutation
A permanent error in the DNA code

X-linked disorder
Inherited disorder caused by a mutation in a gene on the X chromosome

Breaking down Fabry: facts about the disease

Fabry is a rare, progressive, genetic disease affecting 1 in 40,000 to 60,000 males, although it may be more common than this

LSD

It's a type of disease called a *lysosomal storage disorder*, or LSD

People with LSDs have problems making specific lysosomal enzymes

α

In Fabry disease, the affected enzyme is α-galactosidase A, or just α-Gal A

GL-3

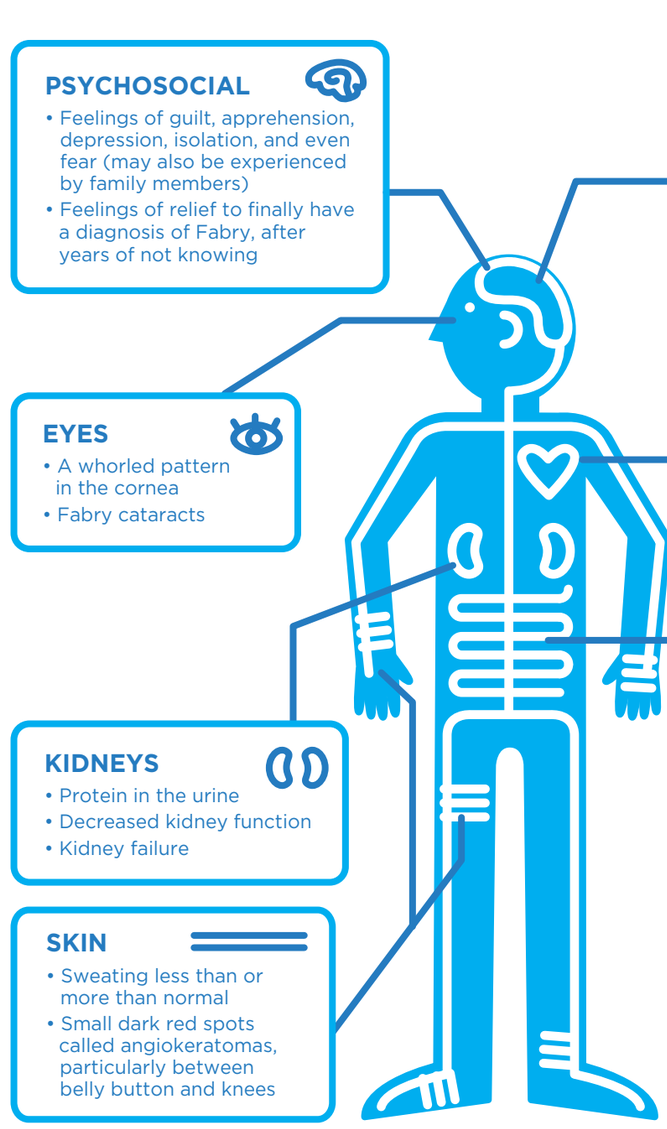
Usually, α-Gal A breaks down substances in the cell called globotriaosylceramide (GL-3) and plasma globotriaosylsphingosine (lyso-Gb_3)

In people with Fabry disease, α-Gal A does not break down GL-3; instead, GL-3 builds up, particularly in cells lining blood vessels

This build-up damages tissues and organs, leading to the symptoms of Fabry disease

How does Fabry disease affect the body?

From one person to another, everyone experiences Fabry disease differently.



PSYCHOSOCIAL
- Feelings of guilt, apprehension, depression, isolation, and even fear (may also be experienced by family members)
- Feelings of relief to finally have a diagnosis of Fabry, after years of not knowing

NERVOUS SYSTEM
- Pain
- Hearing loss, ringing in the ears
- Intolerance to heat, cold, or exercise
- Transient ischemic attack (TIA) and stroke
- Burning in the hands and feet, also called acroparesthesia
- Vertigo/feeling dizzy

EYES
- A whorled pattern in the cornea
- Fabry cataracts

HEART
- Irregular heartbeat (fast or slow)
- Heart attack or heart failure
- Enlarged heart

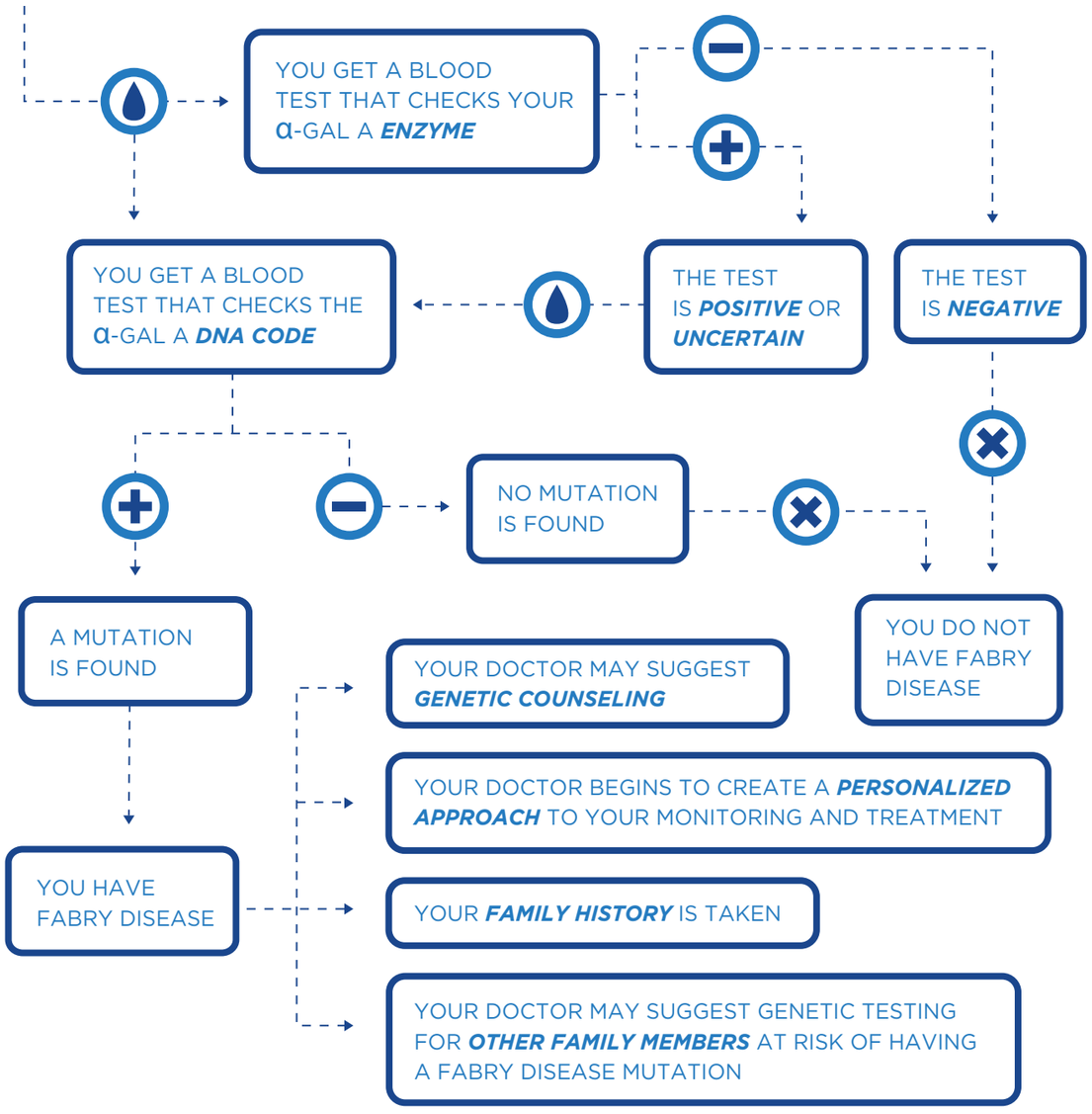
GASTROINTESTINAL
- Nausea, vomiting, cramping, and diarrhea
- Pain/bloating after eating, feeling full after a small amount of food
- Constipation
- Difficulty managing weight

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

SKIN
- Sweating less than or more than normal
- Small dark red spots called angiokeratomas, particularly between belly button and knees

Bottom line: Talk to others with Fabry disease and share your experiences. It may help!

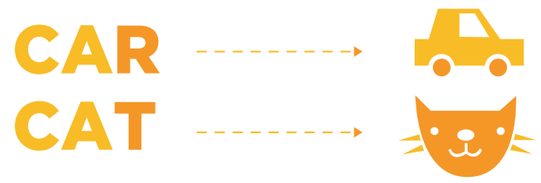
A doctor suspects Fabry disease—what happens next?



What causes Fabry disease?

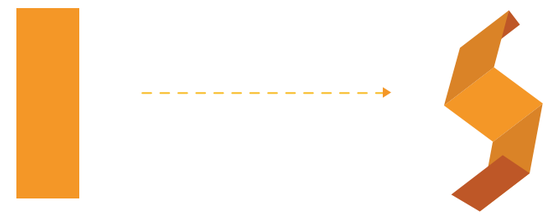
Everyone has information coded into their cells called DNA—which is inherited from one's parents

Sometimes, mutations occur in the DNA code that makes up a particular gene



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

People with some mutations make very little or no α-Gal A



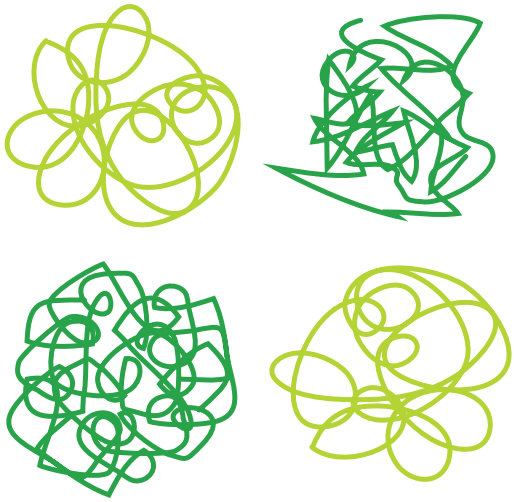
People with certain types of mutations may make α-Gal A, but it doesn't function correctly

Other resources that may be helpful include:

- **The Fabry International Network** *fabrynetwork.org*
- **Fabry Support & Information Group** *fabry.org*
- **The National Fabry Disease Foundation** *fabrydisease.org*
- **The Society for Mucopolysaccharide Diseases (UK)** *mpssociety.org.uk*
- **Canadian Fabry Association** *fabrycanada.com*
- **Fabry Australia** *fabry.com.au*
- **National Institutes of Health NINDS Fabry Disease Information Page** *ninds.nih.gov/disorders/fabrys*
- **The National Organization for Rare Disorders** *rarediseases.org*
- **EURORDIS – Rare Diseases Europe** *eurordis.org*

Why do mutations matter?

At least 800 different gene mutations have been identified that can cause Fabry disease



The type of mutation can affect ***when*** symptoms appear, ***what kind*** of symptoms appear, and ***how bad*** the symptoms are or may become

It's important for individuals or families with Fabry to know ***which mutation*** they have