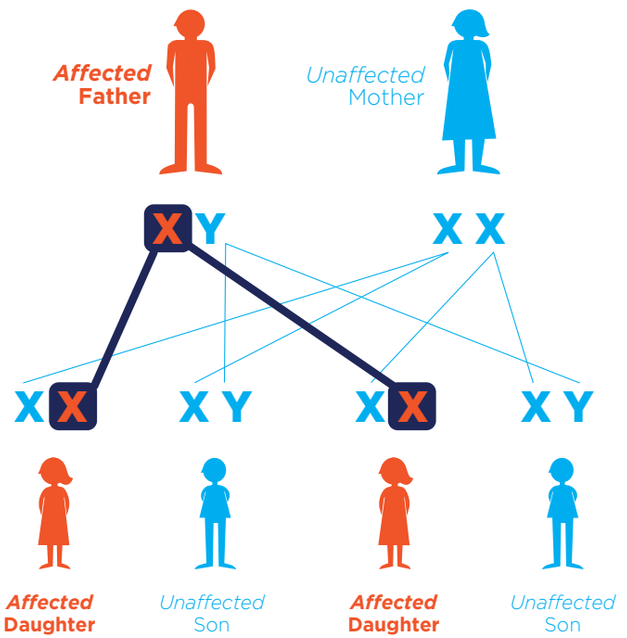
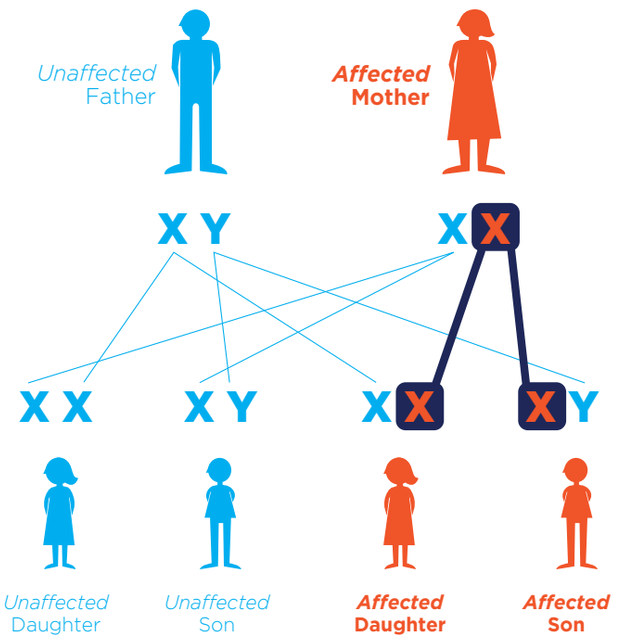
A VISUAL GUIDE TO UNDERSTANDING FABRY DISEASE

INFORMATION FOR PEOPLE LIVING WITH FABRY DISEASE—AND THEIR FAMILIES

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[1]

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[1]

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 can occur randomly in some cells and not others, so daughters may have a broader range of 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

Deoxyribonucleic acid (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

For additonal information, talk to your healthcare provider

Fabry is a rare, progressive, genetic disease affecting 1 in 117,000 people, although it may be more common than this[1,2]

LSD

It's a type of disease called a *lysosomal storage disorder*, or LSD[1]

People with LSDs have problems making specific lysosomal enzymes[1]

α

In Fabry disease, the affected enzyme is α-galactosidase A, or just α-Gal A[1]

GL-3

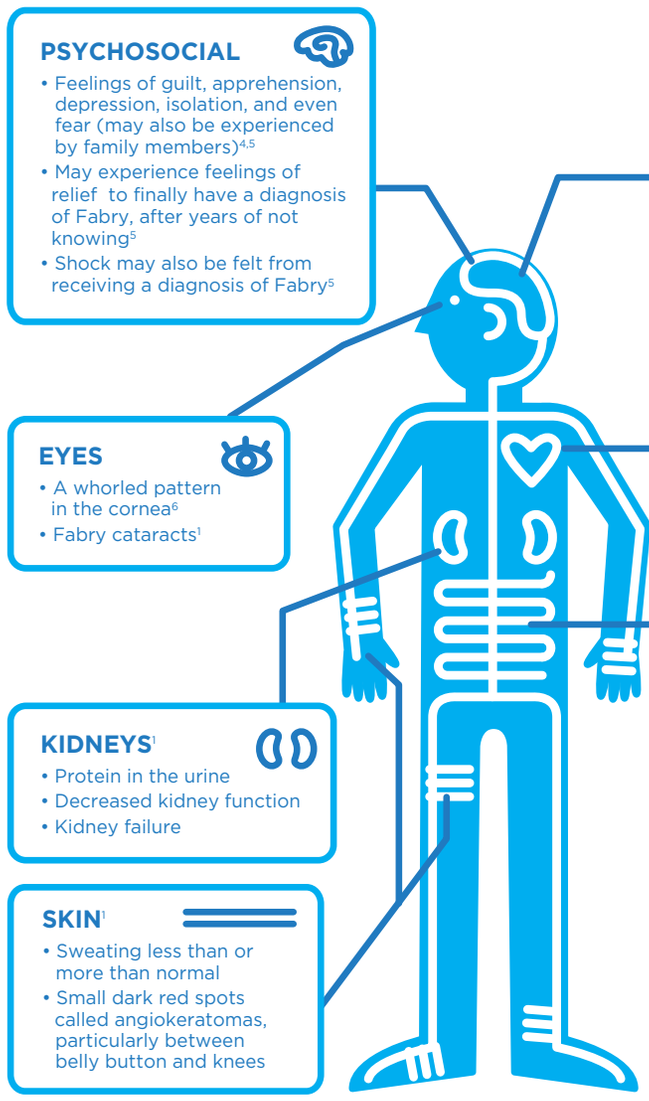
Usually, α-Gal A breaks down substances in the cell called globotriaosylceramide (GL-3) and plasma globotriaosylsphingosine (lyso-Gb_3)[3]

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[1]

This buildup damages tissues and organs, leading to the symptoms of Fabry disease[1]

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)[4,5]
- May experience feelings of relief to finally have a diagnosis of Fabry, after years of not knowing[5]
- Shock may also be felt from receiving a diagnosis of Fabry[5]

NERVOUS SYSTEM

- Pain[1]
- Hearing loss, ringing in the ears[1]
- Intolerance to heat, cold, or exercise[4]
- Transient ischemic attack (TIA) and stroke[1]
- Burning in the hands and feet, also called acroparesthesia[1]
- Vertigo/feeling dizzy[1]

EYES

- A whorled pattern in the cornea[6]
- Fabry cataracts[1]

HEART

- Irregular heartbeat (fast or slow)[6]
- Heart attack or heart failure[1]
- Enlarged heart[1]

GASTROINTESTINAL[1]

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

KIDNEYS[1]

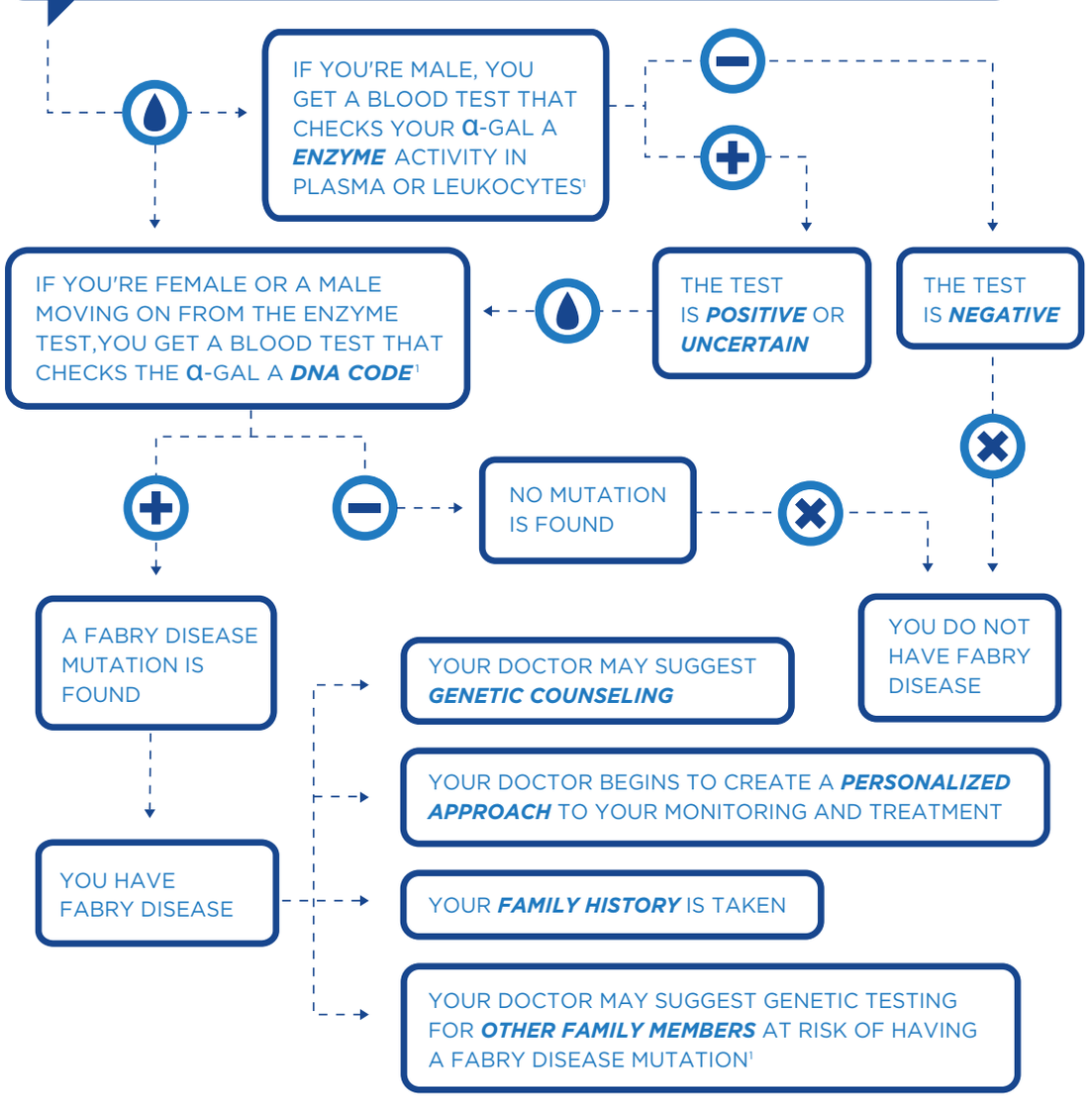
- Protein in the urine
- Decreased kidney function
- Kidney failure

SKIN[1]

- 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!

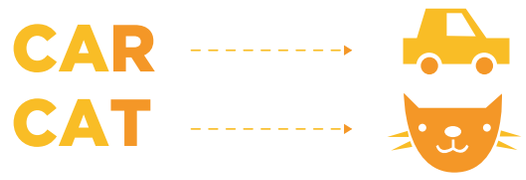
A doctor suspects Fabry disease—here's an example of what can happen



What causes Fabry disease?

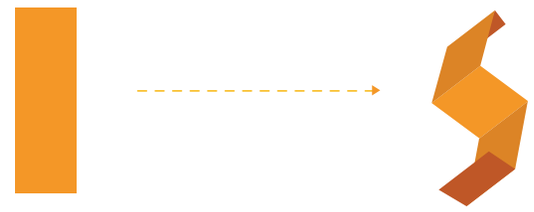
Everyone has information coded into his or her cells that's called DNA—which is inherited from his or her parents

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[7]



People with certain types of mutations may make α-Gal A, but it doesn't function correctly[8]

Other resources that may be helpful are below. Also, talk to your healthcare provider.

- **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
- **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/fabrys
- **NORD – National Organization for Rare Disorders**
  rarediseases.org
- **EURORDIS – Rare Diseases Europe**
  eurordis.org

Why do mutations matter?

At least 1000 different gene mutations have been identified that can cause Fabry disease[9]

The type of mutation may help predict ***when*** symptoms appear, ***what kind*** of symptoms appear, and ***how bad*** the symptoms are or may become[10]

It's important for individuals or families with Fabry to know ***which mutation*** they have[1]

References

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2. Meikle PJ, Hopwood JJ, Clague AE, Carey WF. Prevalence of lysosomal storage disorders. *JAMA*. 1999; 281(3):249-254.

3. Rombach SM, Dekker N, Bouwman MG, et al. Plasma globotriaosylsphingosine: diagnostic value and relation to clinical manifestations of Fabry disease. *Biochim Biophys Acta*. 2010;1802(9);741-748.

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5. Wehmann BA. Learning you have Fabry's disease: reactions and feelings. http://www.fabry.org/FSIG.nsf/Pages/Online. Dr. Wehmann – Article I. Accessed December 19, 2017.

6. Yousef Z, Elliott PM, Cecchi F, et al. Left ventricular hypertrophy in Fabry disease: a practical approach to diagnosis. *Eur Heart J*. 2013;34(11):802-808.

7. Schäfer E, Baron K, Widmer U, et al. Thirty-four novel mutations of the GLA gene in 121 patients with Fabry disease. *Hum Mutat*. 2005;25(4):412.

8. Gal A, Schäfer E, Rohard I. The genetic basis of Fabry disease. In: Mehta A. Beck M, Sunder-Plassmann G, eds. Fabry Disease: Perspectives From 5 Years of FOS. Oxford: Oxford PharmaGenesis; 2006: Chapter 33.

9. Cammarata G, Fatuzzo P, Rodolico MS, et al. High variability of Fabry disease manifestations in an extended Italian family. *Biomed Res Int*. 2015;2015:504784.

10. Branton MH, Schiffmann R, Sabnis SG, et al. Natural history of Fabry renal disease: influence of α-galactosidase A activity and genetic mutations on clinical course. *Medicine* (Baltimore). 2002;81(2):122-138.

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