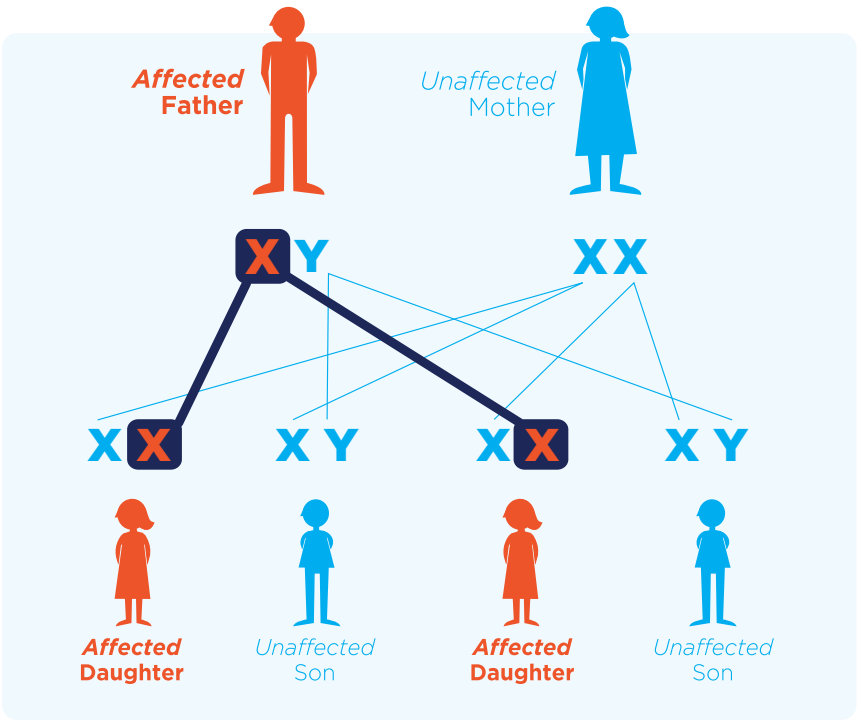
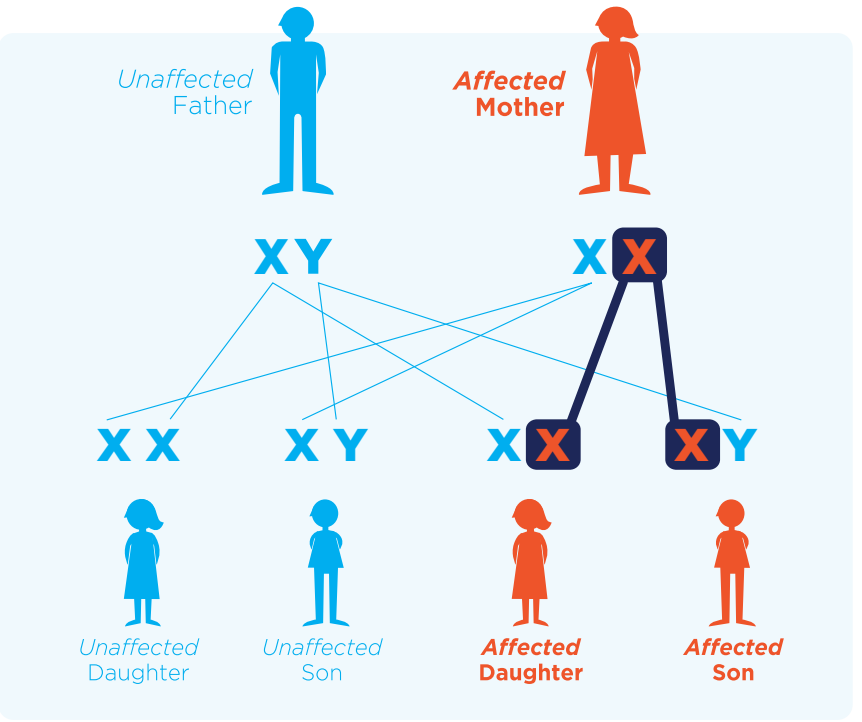
A VISUAL GUIDE TO UNDERSTANDING FABRY DISEASE

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	*Chromosomes*	*De novo mutation*	*Deoxyribonucleic acid (DNA)*	*Enzyme*	*Lysosome*	*Lysosomal disorder (LD)*	*Mutation*	*X-linked disorder*
Basic building block of all living things	Structures that contain DNA and a person's genetic code	An alteration in a gene that is not inherited but is present for the first time	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	A special type of protein that speeds up a reaction that takes place within a cell	A specialised fluid-filled sac found in cells that contains enzymes	A group of over 50 diseases resulting from the accumulation of waste products in lysosomes	A permanent error in the DNA code	Inherited disorder caused by a mutation in a gene on the X chromosome

Breaking down Fabry: facts about the disease

For additional 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]

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

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

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

Usually, α-Gal A breaks down substances in the cell called globotriaosylceramide (GL-3) and globotriaosylsphingosine (lyso-Gb3) [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 build-up damages tissues and organs, leading to the symptoms of Fabry disease [1]

What causes Fabry disease?

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

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

CAR
CAT

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

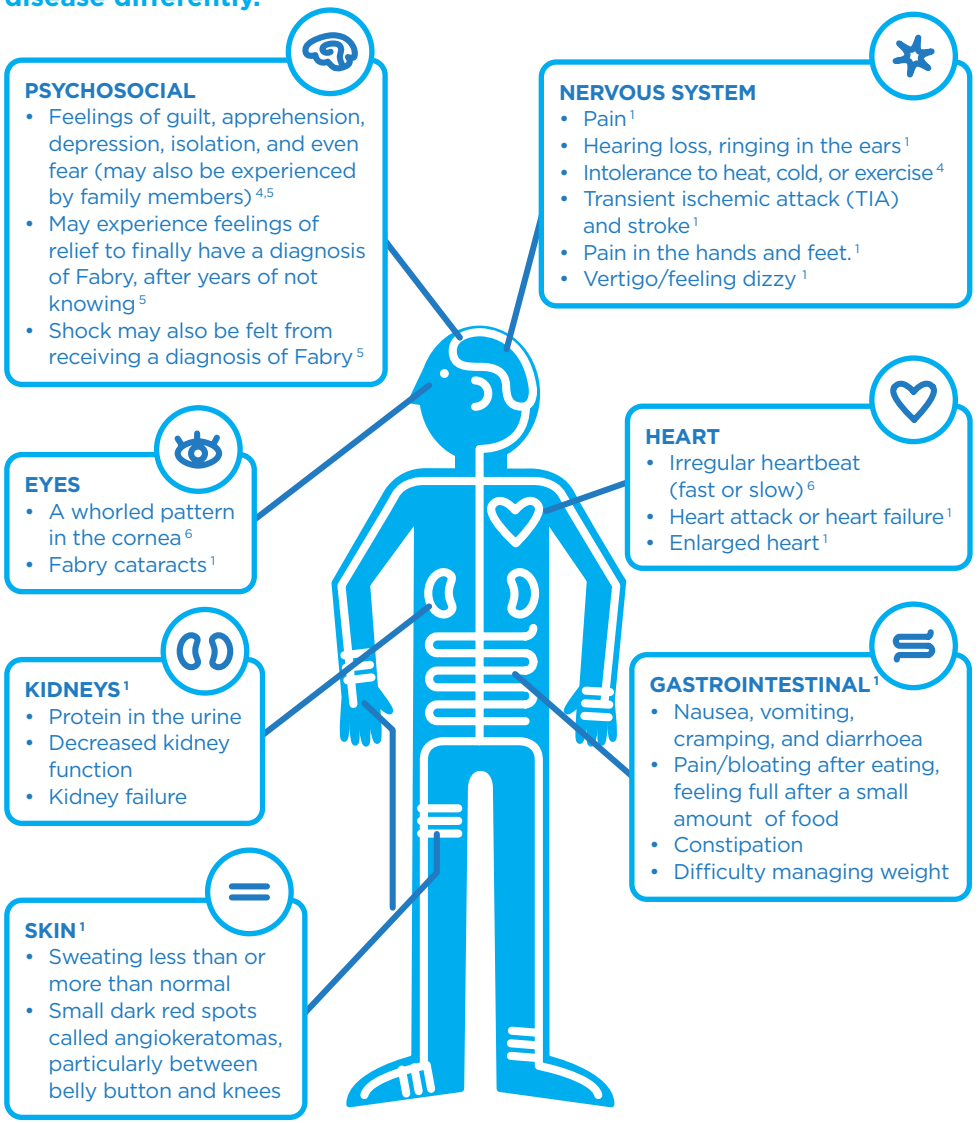
People with some mutations make very little or no α-Gal A [7]

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

EVERY PATIENT IS **UNIQUE**

How Fabry disease could affect you

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



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

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

IF YOU'RE MALE, YOU GET A BLOOD TEST THAT CHECKS YOUR α-GAL A ***ENZYME*** ACTIVITY IN PLASMA OR LEUKOCYTES[1]

\+ → THE TEST IS ***POSITIVE*** OR ***UNCERTAIN***

\+ → IF YOU'RE FEMALE OR A MALE MOVING ON FROM THE ENZYME TEST, YOU GET A BLOOD TEST THAT CHECKS THE α-GAL A ***DNA CODE***[1]

\+ → A FABRY DISEASE MUTATION IS FOUND

\+ → YOU HAVE FABRY DISEASE

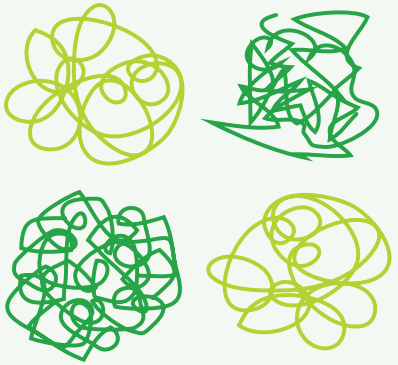
- YOUR DOCTOR MAY SUGGEST ***GENETIC COUNSELLING***
- YOUR DOCTOR BEGINS TO CREATE A ***PERSONALISED APPROACH*** TO YOUR MONITORING AND TREATMENT
- YOUR ***FAMILY HISTORY*** IS TAKEN
- YOUR DOCTOR MAY SUGGEST GENETIC TESTING FOR ***OTHER FAMILY MEMBERS*** AT RISK OF HAVING A FABRY DISEASE MUTATION[1]

\- → THE TEST IS ***NEGATIVE*** → YOU DO NOT HAVE FABRY DISEASE

\- → NO MUTATION IS FOUND → YOU DO NOT HAVE FABRY DISEASE

Why do mutations matter?

More than 1000 mutations have been identified in the gene linked to 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]

For those looking to learn as much as possible about Fabry and its effects, please refer to your local patient organisation or talk to your healthcare professional.

REFERENCES:

1. Germain DP. Fabry disease. *Orphanet J Rare Dis*. 2010;5:30.
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.
4. Desnick RJ, Brady R, Barranger J, et al. Fabry disease, an under-recognized multisystemic disorder: expert recommendations for diagnosis, management, and enzyme replacement therapy. *Ann Intern Med*. 2003;138(4):338-346.
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 March 2019.
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 -galactosidase A activity and genetic mutations on clinical course. *Medicine* (Baltimore). 2002;81(2):122-138.

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