

# Understanding Fabry Disease

## What is a Lysosome?

Millions of tiny units called cells make up the human body. Each cell has its own function that keeps the human body running. Within each cell, there are tiny structures that perform specific jobs to help our bodies function. One of these structures is called a **lysosome**. Lysosomes are the parts of our cells that store **enzymes**.

Lysosomal enzymes are needed by our bodies to help break down nutrients and waste products for our cells and body organs to work properly. Lysosomes are commonly referred to as the “garbage disposal” structure of our body.

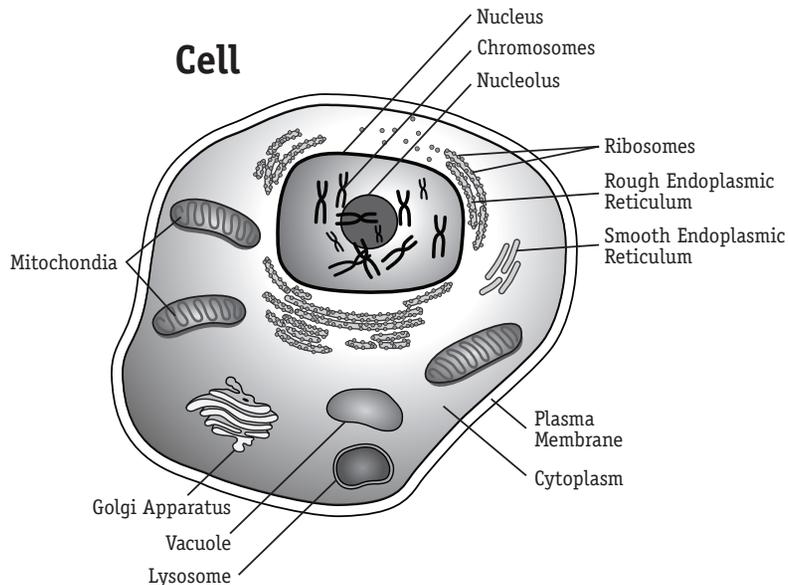
The enzymes then break down complex molecules, such as sugars, proteins, and fat. Therefore, in order for lysosomes to work properly, they need enzymes. A lysosome has over 40 enzymes, and if one of these enzymes is missing or not working properly, the process of cleaning up the cell will not take place, and the substances will begin to build up in the cell.

## What are Lysosomal Storage Disorders (LSDs)?

In LSDs, there is a build up of materials in lysosomes. As the substances build up over time, the symptoms of the disease may start to show. There are more than 50 known types of LSDs, some of which are Gaucher disease, Niemann-Pick disease and Tay-Sachs disease.

## What is Fabry (“Fa-bray”) Disease?

Fabry disease is a rare, inherited LSD that results in the absence or deficiency of an enzyme called **alpha-galactosidase A**, or alpha-GAL. Alpha-GAL breaks down a substance called globotriaosylceramide (GL-3). In Fabry disease, GL-3 builds up in a person’s cells and tissues throughout the body. When this happens, body systems and organs such as the heart, kidneys and central nervous system may be unable to work properly. The incidence of Fabry disease is estimated to be 1 in 40 000 to 1 in 117 000 live births, however, this number might be underestimated as patients with milder forms of the disease may not be diagnosed.



## What are the Signs of Fabry Disease?

The following can be signs and symptoms of Fabry disease

- **Angiokeratomas:** Pin-point red skin lesions that have a reddish to black look.
- **Acroparesthesiae:** Burning pain in the arms and legs (but not limited to these areas).
- **Corneal whorling:** Star shape pattern on the eye that an eye doctor can see with a slit lamp test.
- Hearing problems.
- Stomach problems such as diarrhea and stomach cramps.
- Heart problems.
- **Stroke** and TIA (**transient ischemic attack**), which include sudden loss of strength or sudden numbness in the face, trouble speaking, blurred vision and dizziness.
- Kidney problems.
- Heat intolerance, which can include impaired sweating.

## How is Fabry Disease Diagnosed?

Recognizing that someone has Fabry disease can sometimes be hard because its symptoms are often confused for other common diseases. For example, stomach cramps or diarrhea may be thought to be irritable bowel syndrome. An affected person may at first be misdiagnosed and in fact, may have symptoms for many years without knowing they have Fabry disease.

Males can be diagnosed through a blood test that measures the amount of alpha-GAL in the blood. A female who has Fabry disease may have normal levels of alpha-GAL in the blood, and needs genetic testing to determine whether or not they have the disorder. Genetic testing looks at a person's DNA to see if they carry the Fabry mutation.

## Inheritance

Fabry disease is an X-linked inherited disorder. Inherited means it is passed down from parents to their children. Every cell in our body contains DNA, which is like a ``code`` that tells the cell what to do. DNA is organized into genes, which are then organized into chromosomes.

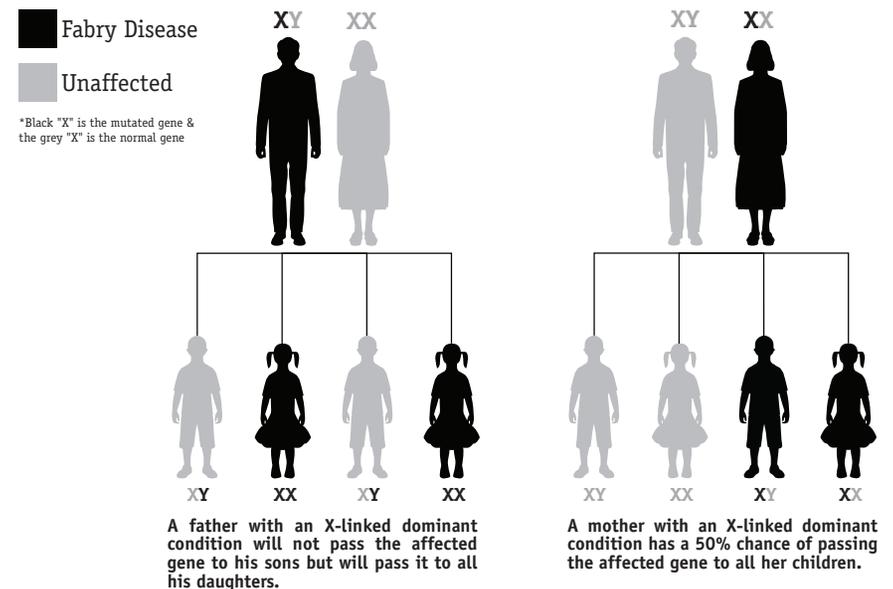
Females have two X chromosomes (XX) and males have an X and Y chromosome (XY). The gene that codes for alpha-GAL is found on the X chromosome.

If a male X chromosome contains the mutated gene, he will produce little or no alpha-GAL and will develop symptoms of Fabry.

A female has two X chromosomes, so one chromosome may have the mutated gene, but the other one will still produce some amount of alpha-GAL.

Females with the mutated gene have been called ``carriers`` because they have the mutated Fabry gene. We now know that they too can display full symptoms of the disease.

### X-linked inheritance pattern



## **My Family Member has Fabry Disease. Should I Get Tested?**

If a person thinks they have Fabry disease, either due to family history or presentation of Fabry signs and symptoms, they can see their family doctor and request to be referred to a Fabry specialist.

## **Treatment Options**

Although there is currently no cure for Fabry disease, enzyme replacement therapy (ERT) can help manage some patients' symptoms. Not all people with Fabry disease require ERT. ERT involves giving people the glucocerebrosidase enzyme that their bodies are missing or deficient in by intravenous (IV) infusion. This medication allows the lysosomes to break down the substance that has built up in the cells. Therefore, the cells and body organs can begin to work properly, and people can begin to experience some relief of their symptoms. The Fabry specialist is the best person to decide which treatment, if required, might be best for the patient.

## **Supportive Treatments**

People with Fabry disease may suffer from depression, so people often are followed by mental health teams or therapists. Fabry disease can affect different organs of the body and those affected may have high blood pressure or irregular heartbeats. They may be prescribed medications such as those to reduce the risk of heart disease, control blood pressure or irregular heart beats. If people who are affected with Fabry experience pain, it is important for them to consult with their medical practitioner if medication is required. Non- pharmacological methods of pain management can also help with pain management and some examples include distraction and imagery (such as watching TV or reading books), applying cold compresses to the area of pain, massage therapy, music therapy, deep breathing, laughter and aromatherapy.

## **Regular Check-Up with Doctor(s)**

Fabry disease is a lifelong condition, therefore managing the disease and meeting treatment goals will involve regular testing. These tests help track changes in the body so new symptoms can be caught early and treated before they cause permanent damage. Tests for Fabry disease can involve checking the heart, kidneys (through blood and urine tests) and possibly MRIs (brain scans). The frequency of testing is determined by the Fabry specialist.

## **How Can Friends and Family Help?**

People with Fabry disease can have fluctuating health, so family members can be supportive by being patient and encouraging. Family members should learn to recognize signs of heart problems, such as dizziness, chest pain and shortness of breath. Family should also learn to recognize the signs and symptoms of a stroke or TIA, which can include sudden onset of one or more of the following symptoms: blurred vision, weakness of the face, limbs, especially on one side of the body, confusion, severe headache or balance problems. If a person with Fabry disease experiences these symptoms, they should report to the Emergency Room as soon as possible. Those affected with Fabry may not be able to perspire very much or at all and may be sensitive to their environment's temperature. Ensure they have blankets if cold, or provide fans if hot. Staying cool and well-hydrated in hot weather is important to avoid a possible pain flare-up.

## Where Can I Find Additional Support?

Just as each person with Fabry disease is unique, each person will seek a unique combination of internal and external resources to manage challenges. These resources may include family, friends, support groups, others with Fabry disease, and health care workers. In addition, several organizations and associations that are listed below can provide you with additional information:

Canadian Fabry Association  
<http://www.fabrycanada.com/>

Treatment Guidelines  
<http://www.garrod.ca/?s=FABRY+DISEASE&task=search>

The Adult Metabolic Diseases Clinic  
Vancouver General Hospital  
Level 4 - 2775 Laurel Street  
Vancouver, BC V5Z 1M9  
Phone: 604-875-5965  
Fax: 604-875-5967  
Email: [adultmetabolicclinic@vch.ca](mailto:adultmetabolicclinic@vch.ca)

## Glossary

- **Acroparesthesiae:** Pain characterized by tingling, burning and/or numbness.
- **Angiokeratomas:** Pin-point red skin lesions that have a reddish to black look.
- **Alpha-galactosidase:** An enzyme that breaks down a substance called globotriaosylceramide (GL-3).
- **Chromosome:** Long strands of DNA that are found in the cells of the body. Humans have 23 pairs of chromosomes, half of our chromosomes are inherited from the mother and the other half are inherited from the father.
- **Corneal whorling:** A starburst like pattern that appears on the eye that can be seen with an ophthalmoscope by an eye doctor.
- **Cells:** Basic unit of all living organisms.
- **DNA:** Hereditary material that acts like “instructions” which tell a cell how to act and build a person.
- **Enzyme replacement therapy:** A medical treatment in which an enzyme that a person is missing or deficient in is given to patients through an IV infusion.
- **Electrocardiogram:** A test that uses electrical waves to measure the activity and function of the heart.
- **Genes:** Genes are made up of DNA, which act as instructions that tell the body how to grow and function.
- **Globotriaosylceramide (GL-3):** Compound that builds up in the lysosome in a person who is affected with Fabry disease.
- **Glycolipids:** Fats that are attached to a carbohydrate.
- **Intravenous (IV):** A patient receives medication through a needle or tube inserted into a vein. This allows immediate access to the blood supply.

- **Lysosomal enzyme:** A protein that breaks down other substances.
- **Lysosome:** Structure in the cell that breaks down and “cleans” up unwanted substances that the cell no longer needs.
- **Stroke:** A stop in blood flow to the brain which causes sudden loss of brain function.
- **Transient ischemic attack (TIA):** Sometimes referred to as a “mini stroke”. It is the temporary loss of blood flow to the brain caused by clots in the blood.

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