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 use enzymes to help break down sugars, proteins, and fat for our cells and body organs to work properly. Lysosomes are commonly referred to as the “garbage disposal” structure of our body.

A lysosome has over 40 enzymes. If one of these enzymes is missing or not working properly, the process of cleaning up the cell does not take place, and substances begin to build up in the lysosomes.

What are Lysosomal Storage Disorders (LSDs)?

In LSDs, there is a build up of materials in lysosomes. As the substances accumulate, the organs can’t work as well and symptoms of the disease start to show. There are more than 50 known types of LSDs, some of which are Gaucher disease, Niemann-Pick disease, Tay-Sachs disease and Fabry disease.

What is Fabry (“Fa-bray”) Disease?

Fabry disease is a rare, inherited LSD that results in the absence or deficiency of a lysosomal enzyme called **alpha-galactosidase A**, or alpha-GAL A. Alpha-GAL A 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 go undiagnosed.
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 with 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 A in the blood. Genetic testing needs to be done on females to make a diagnosis as they may have normal levels of alpha-GAL A in the blood. 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 A is found on the X chromosome.

If a male X chromosome contains the mutated gene, he will produce little or no alpha-GAL A 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 A.

Historically, females with the fabry gene were called carriers and not considered affected. We now know that they too can display full symptoms of the disease.

X-linked inheritance pattern

- **Fabry Disease**
- **Unaffected**

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*Black “X” is the mutated gene & the grey “X” is the normal gene*

A father with an X-linked dominant condition will not pass the affected gene to his sons but will pass it to all his daughters.

A mother with an X-linked dominant condition has a 50% chance of passing the affected gene to all her children.
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, there are two treatment options that are available to some people with Fabry disease who meet disease-specific criteria based on the severity of their symptoms and their specific genetic mutation. These treatment options can help with symptom management, slow the disease progression and increase quality of life.

Enzyme replacement therapy (ERT)
The goal of ERT, given by intravenous (IV), is to replace alpha-GAL A in people who are lacking or missing it. Replacing the enzyme enables lysosomes to break down the GL-3 that has built up in the cells and caused symptoms of the disease. Freeing the organs of GL-3 allows them to work properly again, reducing symptoms.

Chaperone therapy
Many people with Fabry disease have some alpha-GAL A but due to a genetic mutation, can’t transport it into the lysosome to do its work. The goal of chaperone therapy, taken in pill form, is to stabilize the person’s own enzyme and transport or “chaperone” it into the lysosome so it can break down the GL-3.

Talk to your Fabry specialist about these and other emerging therapies to see if they are right for you.

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 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 go 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
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 A** (alpha-GAL A or Alpha-gal): 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.