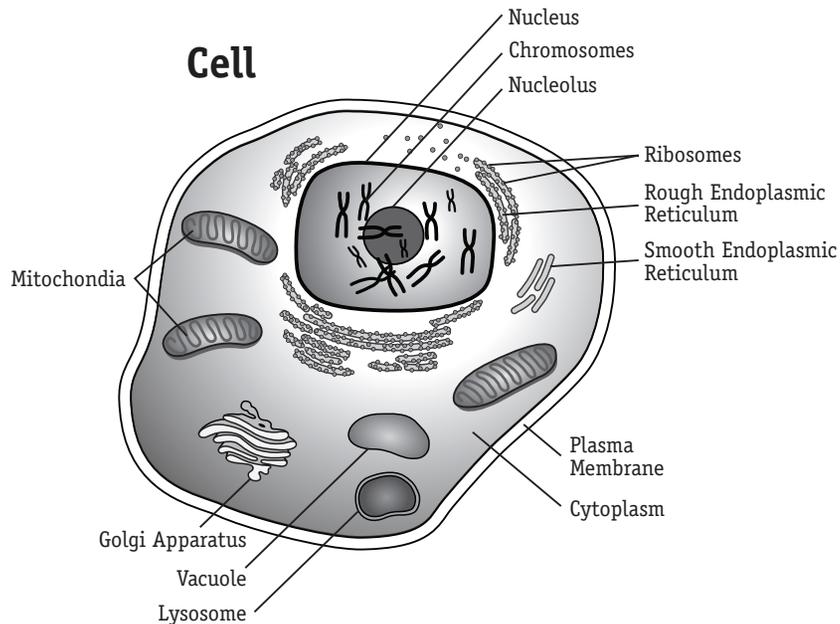


# Understanding Gaucher Disease

## 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 in order for our cells and body organs to work properly. Lysosomes are commonly referred to as the “garbage disposal” structure of our body. Since lysosomes are digestion machines, they go to work when the cell absorbs or eats some food. Once the material is inside the cell, the lysosomes attach and release their enzymes. 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)?

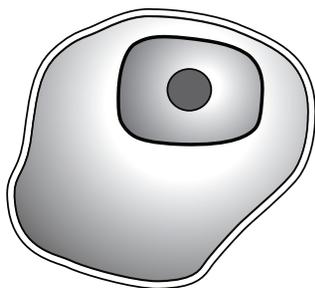
In LSDs, there is a build up of certain materials in lysosomes. As the substances build up over time, the symptoms of the disease may start to show. There are more than 50 known types of LSDs, some of which are Fabry disease, Niemann-Pick disease and Tay-Sachs disease.

## What is Gaucher Disease?

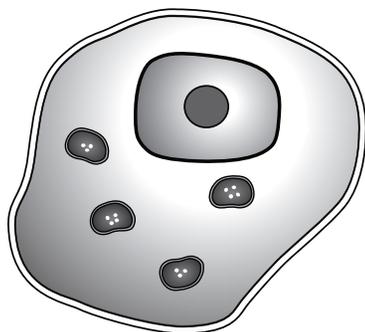
Gaucher (pronounced “Go-shay”) disease is an LSD caused by a defective **gene**. The defective gene prevents the body from producing proper amounts of an enzyme, called **glucocerebrosidase (GC)**. This enzyme removes and recycles a substance called **glucocerebroside**. When there is too little of this enzyme (GC), or when it does not work properly, special cells called **macrophages**, which are a type of white blood cell responsible for picking up and recycling glucocerebroside, fill up with the undigested material. The material continues to build up, mainly in the lysosomes of macrophages. These cells are referred to as **Gaucher cells**.

Gaucher cells are found mostly in the liver, spleen and bones, and sometimes in the lungs. When this happens, these body organs, especially the spleen and liver, can become enlarged and prevent them from working properly. In rare cases, Gaucher cells can also collect in the brain, resulting in more severe forms of the disease.

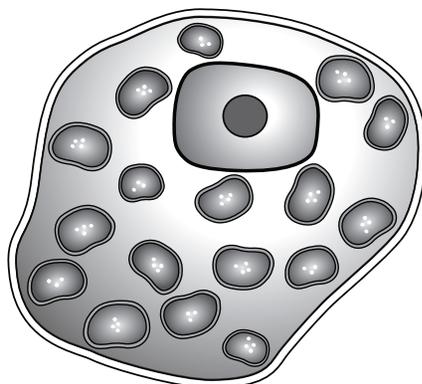
Healthy cell



Gaucher cell filled with undigested waste materials



Gaucher cell swollen beyond normal size with undigested waste materials, causing problems throughout the body



## How Many People Have Gaucher Disease?

Less than 1 in 40000 to 60000 people in the world have Gaucher disease. Among Jewish people of Ashkenazi (Eastern European) descent, the rate is higher: up to 1 in 450 people. The higher rate of Gaucher disease among this population has led to the false belief that this disease is a “Jewish genetic disease.” However, people of any ethnic or racial background may be affected.

## What are the Signs & Symptoms of Gaucher Disease?

The signs and symptoms differ from one person to another. Some people have little to no symptoms and others may have very severe symptoms. They may also experience different symptoms at different times throughout their lives.

Common Signs & Symptoms	Less Common Signs & Symptoms
<ul style="list-style-type: none"> <li>• Easy bruising and bleeding</li> <li>• Bone pain</li> <li>• Fatigue (tiredness)</li> <li>• <b>Anemia</b> (low red blood cell count)</li> <li>• Easily broken bones</li> <li>• Delayed growth</li> <li>• Enlarged liver and spleen</li> <li>• Loss of appetite</li> <li>• Nosebleeds</li> <li>• Low blood <b>platelet</b> count</li> </ul>	<ul style="list-style-type: none"> <li>• Heart and lung problems</li> <li>• Seizures</li> <li>• Brain involvement</li> <li>• Tremors</li> <li>• Breathing problems</li> </ul>

- An overactive spleen can lower the number of blood platelets. A decrease in platelets lowers the body’s ability to form clots, increasing the chances for bleeding and bruising. Therefore, people with Gaucher disease may experience frequent nosebleeds, heavier menstrual periods, and bleeding gums more than other people.
- Some people with Gaucher disease may experience a loss of appetite. This can be caused by an enlarged spleen and/or liver putting pressure on the stomach, giving people a feeling of fullness after taking a few bites of food. Mineral or vitamin supplements may be recommended for nutritional deficiencies. The doctor may also recommend consulting with a dietitian.

- In Gaucher disease, the spleen becomes enlarged and overactive, breaking down too many red blood cells. This can lead to anemia. Anemia can make a person feel very fatigued. People often describe feeling tired, weak or lacking energy. It is important for these individuals to get a full night of sleep and take breaks during the day.
- Gaucher disease often affects bones. Over time, the disease can weaken bones and joints, which can cause pain and problems moving and functioning. It can also cause bones to break more easily. If not treated, bone problems can become permanent and lead to disability. Therefore, finding and treating bone problems early may help prevent pain and disability. Some people may be prescribed calcium supplements or other bone strengthening medications, such as those used to treat osteoporosis.
- Some people can experience “bone crises” when there is a sudden lack of oxygen in an area where Gaucher cells have blocked normal blood flow. This can cause pain that ranges from moderate to severe (described by some as feeling like a “heart attack of the bone”), which can last for hours to days. People experiencing severe bone pain may be admitted to the hospital to receive fluids and medications for pain control.

## What are the Different Types of Gaucher Disease?

Gaucher disease can affect different parts of the body with variable severity depending on the type of gene mutations that the person has as well as other factors that are not as well understood. Depending on which parts of the body are affected, Gaucher disease is subclassified into one of three types: Type I, II and III.

### Type I Gaucher Disease

This is the most common form of Gaucher disease, affecting approximately 94% of all people diagnosed. Type I Gaucher disease can involve body organs and tissues. The four main body organs that can be affected are the spleen, liver, bones, and lungs. Type I Gaucher disease does not have brain or spinal cord involvement.

### Type II & III Gaucher Disease

These are both less common forms of the disease, affecting about 1% to 4% of all people with Gaucher disease. Type II and III Gaucher diseases have CNS (brain and spinal cord) involvement with the Type I symptoms. The CNS involvement in Type III is less severe than Type II. Most patients with Type II & III Gaucher disease have symptoms which begin in the first few years of life.

	Description	Symptoms
<b>Type I</b>	Most common type Can affect body organs and tissue Does not involve the central nervous system (brain, spine, and nerves)	Symptoms can begin to develop in early childhood or adulthood, and include: <ul style="list-style-type: none"> <li>• Enlarged spleen</li> <li>• Enlarged liver</li> <li>• Anemia (low red blood cell count)</li> <li>• Low platelet count</li> </ul>
<b>Type II</b>	Affects the brain as well as the body organs and tissue that can be affected in Type I. This type is a very rare, rapidly progressive form of the disease that affects infants.	Symptoms begin in infant years, and include: <ul style="list-style-type: none"> <li>• Enlarged spleen</li> <li>• Enlarged liver</li> <li>• CNS involvement</li> <li>• Anemia</li> <li>• Low platelet count</li> </ul>
<b>Type III</b>	Other than the involvement of the brain, Type III symptoms resemble those of Type I. Does not progress as fast as Type II and the impact on the brain varies from major dysfunction to little evidence of brain involvement.	Symptoms can begin in childhood to early adulthood, and include: <ul style="list-style-type: none"> <li>• Enlarged spleen</li> <li>• Enlarged liver</li> <li>• CNS involvement</li> <li>• Anemia</li> <li>• Low platelet count</li> </ul>

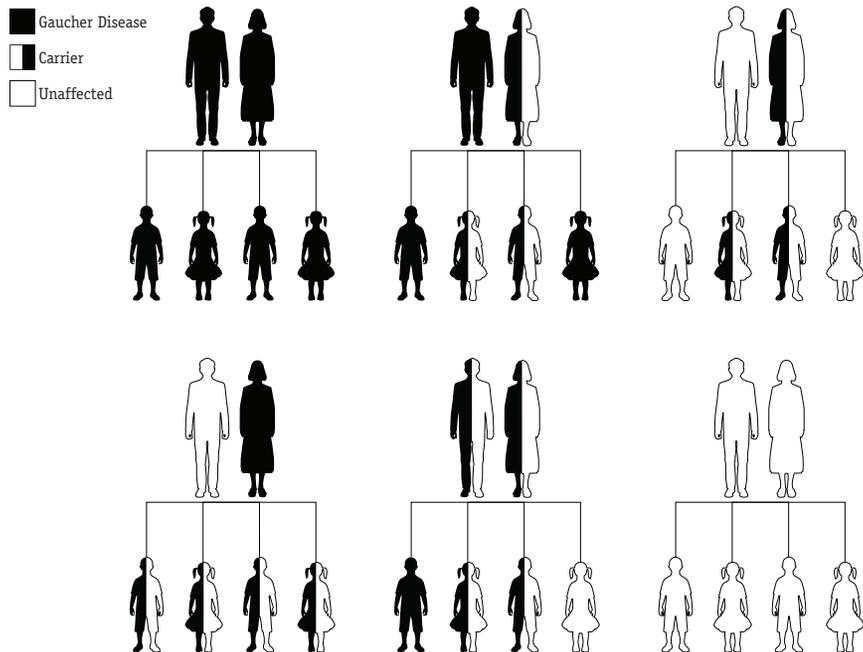
## How Do People Get Gaucher Disease?

Gaucher disease is inherited, meaning it is passed down from one generation to the next through the **genes** of one's parents. Our genes come in pairs because we receive half of our genes from our mother and the other half from our father. Genes are found in all of the cells, tissues, and organs of our bodies. When there is an abnormal change in a gene, also known as a **mutation**, it may cause a disease or increase a person's risk of developing a genetic disorder. In Gaucher disease, the gene (GBA) for the production of enzyme glucocerebrosidase is defective, so it is not able to work normally.

Gaucher disease is an **autosomal recessive disorder**, which means it is caused by receiving two copies of the mutated gene, one from the mother and one from the father. If the person only has one copy of the mutated gene, the person is a **carrier**. A carrier does not have the disease but can pass the mutated gene on to their children.

The following diagram of the inheritance pattern is a way of seeing how a gene is passed down from generation to generation. This diagram shows how different combinations of people, those with and without the disease, as well as carriers can pass Gaucher disease on to their children.

For example, if both parents are carriers, there is a 25% chance of their child being unaffected; a 25% chance of their child being affected; or a 50% chance of their child being an unaffected carrier.



## How is Gaucher Disease Diagnosed?

Recognizing that someone has Gaucher disease can sometimes be hard because the symptoms of Gaucher disease are often confused with those of other common diseases. For example, joint pain may be linked to arthritis or “growing pains” instead of Gaucher disease. Therefore, an affected person may at first be misdiagnosed. Some people may have symptoms for many years without knowing they have Gaucher disease. For these reasons, it can take time before a diagnosis is made.

### Blood Test

When Gaucher disease is suspected, the diagnosis can be confirmed by a blood test that measures the activity of the enzyme glucocerebrosidase in the blood. In individuals with Gaucher disease, enzyme activity is much lower than normal.

## Genetic Testing

Because Gaucher disease is a genetic disorder, all close relatives of people with Gaucher disease are at risk of having the disease, or are potential carriers of the “Gaucher gene.” Families with a history of Gaucher disease may want to discuss the possibility of genetic testing with their doctor. A blood test can determine if a person has Gaucher disease or is a carrier. Prenatal testing for Gaucher disease is also available early in pregnancy. Genetic testing is also available to couples who are found to be carriers or who have a family history of Gaucher disease.

## How is Gaucher Disease Treated?

Although there is currently no cure for Gaucher disease, treatment can help manage some of the symptoms of the disease. Not all people with Gaucher disease require treatment. If a patient meets criteria for treatment, one of two therapies are available: enzyme replacement therapy (ERT) or substrate reduction therapy (SRT). The Gaucher specialist is the best person to decide which therapy, if required, might be best for the patient.

### Enzyme Replacement Therapy (ERT)

ERT involves giving people the glucocerebrosidase enzyme that their bodies are missing 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 a person with Gaucher disease can begin to experience some relief of their symptoms.

### Substrate Reduction Therapy (SRT)

In addition to ERT, SRT is available to treat Gaucher disease. The goal of SRT is to lower the production and build up of glucocerebrosidase within the cells. SRT works by decreasing the amount of glucocerebrosidase the cells make, so less waste builds up in the cells. SRT is taken by mouth in a pill form.

## How is Gaucher Disease Managed?

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

Gaucher disease is a lifelong condition. Therefore, managing the disease and meeting treatment goals will involve regular monitoring tests. These tests help track changes in the body so new symptoms can be caught early and treated before they cause permanent damage. Tests for Gaucher disease can involve checking the bones, blood, liver, and spleen. Please consult the doctor to learn more about the frequency of tests.

### How Can Family & Friends Help?

- Recognize that people with Gaucher disease may have physical limitations and may get tired more easily. Most people find they can participate in normal activities if they pace themselves and if they plan their day with family, friends, teachers, and others involved. It is important to include these individuals in activities and not treat them differently.
- Family and friends can make offers of help more concrete. For example, instead of saying, “Do you need help with anything?”, give clear offers, such as “I will do the household chores today” or “I will pick up the kids from school today.” Concrete offers like these are easier to accept than offers the person may perceive as you just “trying to be nice”.
- Learn the signs and symptoms of Gaucher disease and help explain it to others. This will not only increase the awareness of Gaucher disease but also prevent the person affected with Gaucher disease from explaining it over and over again.
- If the person is having a bone crisis (extreme bone pain) get them to seek medical attention as soon as possible.
- Some children with Gaucher disease are advised to avoid contact sports if they have an enlarged spleen.

Instead, they may be encouraged to take up non-contact sports, such as swimming, dance, and bicycle riding.

Families can work with their child’s doctor to determine which activities are most appropriate for children with physical limitations.

## Where Can I Find Additional Support?

Just as each person with Gaucher 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 Gaucher disease, and health care workers. In addition, several organizations and associations that are listed below can provide you with additional information:

National Gaucher Foundation  
[www.gauchercanada.ca](http://www.gauchercanada.ca)

Treatment Guidelines  
[www.garrod.ca](http://www.garrod.ca)

Gaucher disease information  
[gaucherconnection.ca](http://gaucherconnection.ca)

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

- **Anemia:** A decrease in the number or concentration of red blood cells or hemoglobin.
- **Enzyme Replacement Therapy (ERT):** A medical treatment in which an enzyme that a person is missing or deficient in is given to people through an IV infusion.
- **Gaucher cell:** A macrophage that is enlarged from the build up of the substance glucocerebroside.
- **Genes:** Are found in all of the cells, tissues, and organs of our bodies. Genes are responsible for the way you look, such as eye color, height, and likelihood of having a disease.
- **Glucocerebrosidase:** the enzyme that is lacking in Gaucher disease; its job is to break down the substance glucocerebroside.
- **Glucocerebroside:** The substance that builds up mostly in special cells called macrophages in people who are affected with Gaucher disease.
- **Hemoglobin:** A part of red blood cells that carries oxygen. A low hemoglobin level is a sign of anemia, which results in fatigue.
- **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:** A sac-like compartment in cells where enzymes break down substances; this is where glucocerebroside builds up in Gaucher disease.
- **Macrophage:** A type of white blood cell that recycles waste and other harmful materials.
- **Platelet:** A cell that helps blood clot; bruising and bleeding may happen when platelet count is low.

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