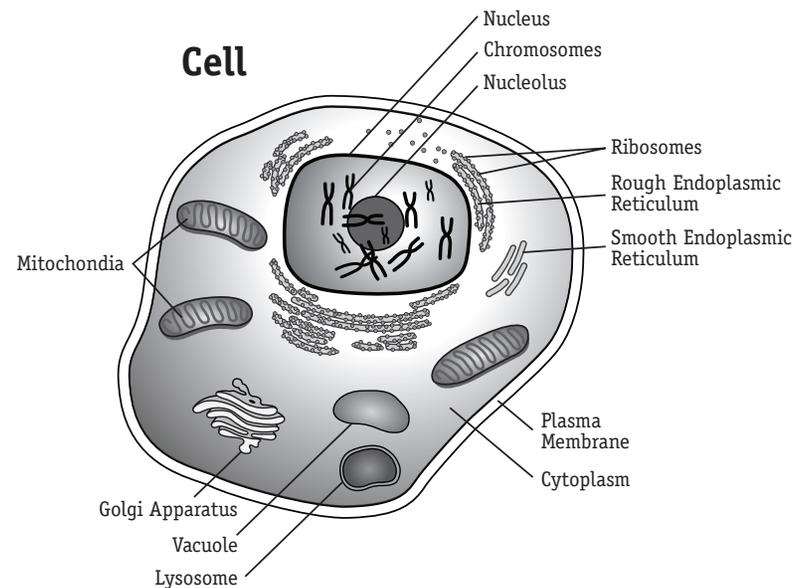


Understanding Late-Onset Pompe Disease

What Is a Lysosome?

Millions of tiny units called **cells** make up the human body. Each cell has its own job to keep the body running. Within each cell, there are **organelles**, tiny structures that perform specific jobs. **Lysosomes** are organelles that store **enzymes**, which are needed by our bodies to help break down nutrients and waste products. Lysosomes are commonly referred to as the “garbage disposal” structure of our body going to work when the cell absorbs food by releasing their enzymes and breaking down sugars, proteins, and fat. Each lysosome has over 40 enzymes. If one of these enzymes is missing or not working properly, the process of cleaning up the cell will not take place, and substances begin to build up in the cell.

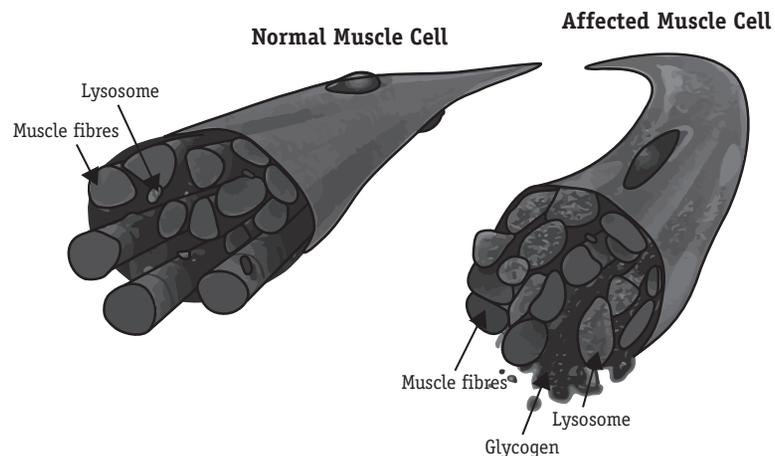


What Are Lysosomal Storage Disorders (LSDs)?

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, Pompe disease, Niemann-Pick disease, and Tay-Sachs disease.

What Is Pompe (“pom-PAY”) Disease?

Pompe disease is a genetic disorder that is caused by the absence or low levels of the lysosomal enzyme known as **acid alpha-glucosidase** (GAA). This enzyme is needed to break down **glycogen**, a storage form for sugar where the individual sugar molecules are stored in large sheets. Cells normally break down glycogen into smaller sugar pieces that are used as an energy source for muscles. In Pompe disease, because the process to break down these sugars is not working properly, there is an accumulation, or “storage”, of glycogen in the lysosomes. The result is that muscles, without an energy source, can begin to weaken. Pompe disease is also known as **Glycogen Storage Disorder type 2**.



How Many People Have Pompe Disease?

It is estimated that Pompe disease affects approximately one in 40,000 live births. The number of people with Pompe disease could be higher due to: misdiagnosis, lack of a diagnosis, onset of signs and symptoms presenting at different ages, and the disease not being well known. The probability is high that there are people living with Pompe without knowing it.

What is Late Onset Pompe Disease?

The term “late onset” refers to Pompe disease that presents in childhood or adulthood. Disease progression is often slow and affects each person differently. People with late onset Pompe disease may have some working enzyme but a lesser amount than what is considered normal. Due to this, it is hard to predict the onset of symptoms. Some individuals may experience mild muscle weakness, whereas some may have breathing difficulties and require more support. Because the disease varies or differs from person to person, disease progression is often hard to predict. It is important to note that Pompe disease does not affect brain function.

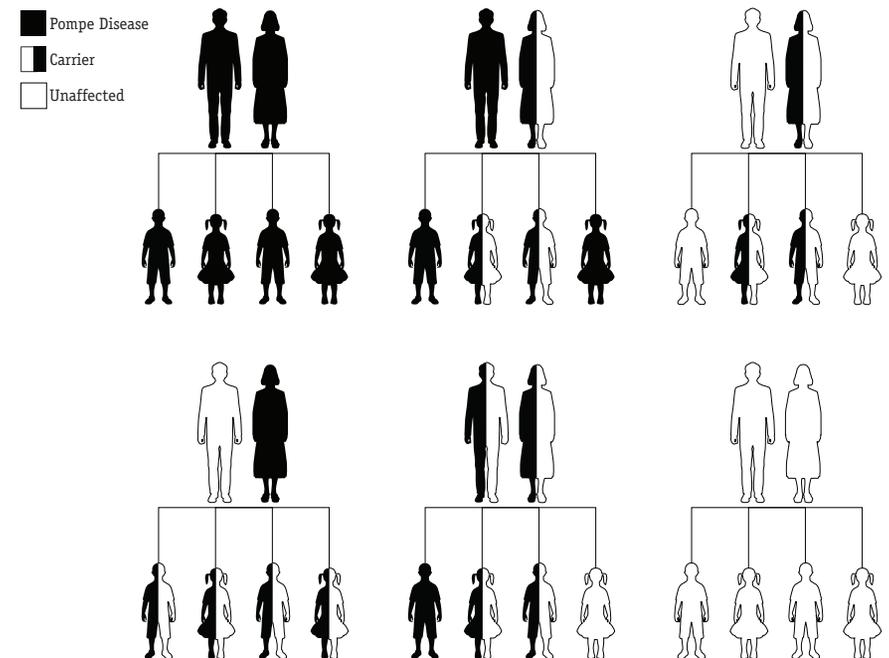
What Are the Signs and Symptoms of Pompe Disease?

Late onset (Childhood through adulthood)

Musculoskeletal
Progressive muscle weakness in trunk and lower limbs
Gait abnormalities
Muscle pain
Difficulty climbing stairs
Frequent falls
Respiratory
Respiratory failure/insufficiency
Shortness of breath
Exercise intolerance
Respiratory infections
Daytime drowsiness
Morning headache
Pauses in breathing when sleeping (sleep apnea)
Gastrointestinal
Feeding and swallowing difficulties
Difficulty maintaining weight
Difficulty chewing
Jaw muscle fatigue

Inheritance

Pompe disease is inherited, meaning it is passed on from parents to their children. Every cell in our body contains **DNA**, which is comprised of **genes**. Genes give our bodies instructions. A **mutation** is an abnormal change in a gene. When a mutation occurs, it may cause a disease or increase the chance of developing a genetic disorder. In Pompe disease, there is a problem with the gene that makes the enzyme acid alpha-glucosidase (GAA). Pompe 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 show the disease or disorder but can pass the mutated gene onto their children.



How Is Pompe Disease Diagnosed?

Recognizing that someone has Pompe disease can be difficult because the symptoms are often confused with other diseases involving muscles and body movement. An affected person may at first be misdiagnosed. Some people may have symptoms for many years without knowing they have Pompe disease. For these reasons, it can take time before a diagnosis is made. There are multiple methods to diagnose Pompe disease. The most common practice is a dried blood spot test.

Blood Test

When Pompe disease is suspected, the diagnosis can be confirmed by a blood test. A few drops of blood are placed on a special filter paper that is called a “dried blood spot card”. This measures the activity of the enzyme acid alpha-glucosidase in the blood. In individuals with late onset Pompe disease, enzyme activity is much lower than normal. If the enzyme level is low, the doctor will order a second blood test to see if the person carries Pompe mutations. It takes about 8 to 10 weeks to obtain enzyme level and mutation analysis results.

My Family Member Has Pompe Disease, Should I Get Tested?

If a person has a family history of Pompe disease, they can see their family doctor and request to be referred to a Pompe specialist for a discussion of the risks and to determine if testing is needed. It is especially important for siblings of an affected person to be tested, as their risk of having Pompe disease is 1 in 4.

Pompe and Exercise

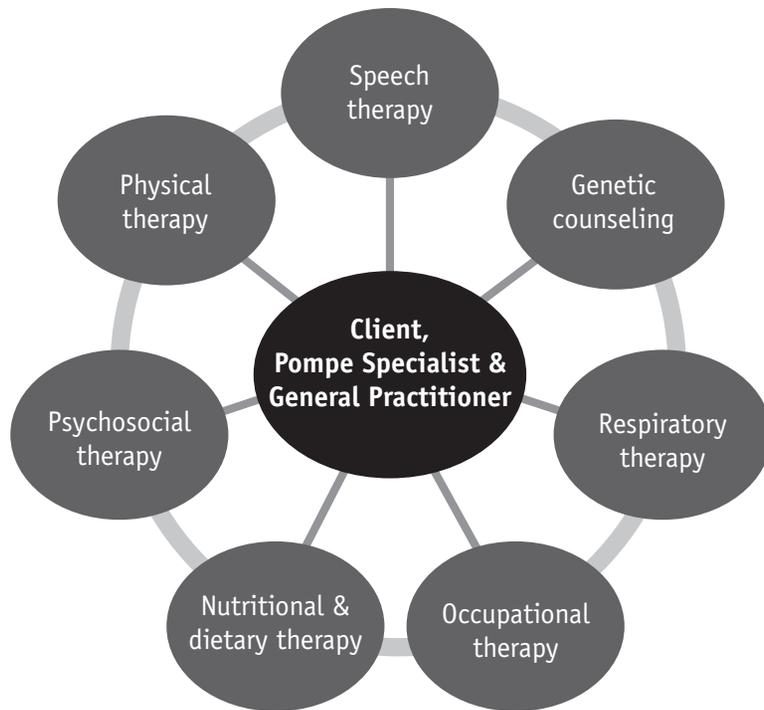
Exercise can greatly improve the quality of life by strengthening muscles and reduce stiffness that might occur due to a lack of activity. Exercises that use large muscle groups and increase the heart rate will have the added benefit of improved breathing strength. Resistance training such as light weights or elastic bands will benefit bone health. A consistent cardiovascular and strength training program can be tailor-made for patients with Pompe disease by physiotherapists with expertise in neuromuscular disorders. By exercising, the risk of falls and injury is reduced, as balance and strength are improved.

Treatment Options

Although there is currently no cure for Pompe disease, **enzyme replacement therapy (ERT)** can help manage some symptoms and slow progression of the disease. Not all people with Pompe disease require ERT. This medication provides the enzyme people lack and allows the lysosomes to break down the substrates that have built up in the muscle. ERT is given by **intravenous (IV)** infusion every 2 weeks for life. It is hoped that by giving ERT, people begin to experience some relief of their symptoms. In British Columbia, ERT is decided on a case-by-case basis. A discussion with a Pompe specialist will determine whether ERT is right for you.

Supportive Treatments

Each person with Pompe disease may experience different symptoms and require treatments and therapies based on their symptoms. Each person will therefore have an individualized team of healthcare professionals to ensure that health problems and disease symptoms are being managed. Healthcare professionals may include: Pompe specialists, genetic counsellors, registered nurses, speech therapists, physical therapists, respiratory therapists, occupational therapists, dietitians, and social workers.



Regular Check-Up with Doctor(s)

Pompe disease is a lifelong condition that currently has no cure. To manage the disease symptoms, it is important to have regular check-ups with doctors and specialists to identify any health changes immediately. Early detection allows doctors and specialists to adjust treatment plans to best manage care. Examinations may include blood work, breathing tests, swallowing tests, chest x-rays, bone density tests, and musculoskeletal and motor function tests.

How Can Family and Friends Help?

The health of people with Pompe disease may change day to day. Patients with Pompe disease may experience a lack of energy for simple tasks. It is important for family and friends to be supportive and encouraging. Family and friends can be supportive by learning about the disease and recognizing the signs and symptoms of Pompe disease. It is important to be aware of sudden changes such as breathing difficulties or increased muscle weakness and seek medical help immediately. Family and friends can also participate in Pompe disease awareness programs and campaigns to learn more about the disease and help spread awareness.

Where Can I Find Additional Support and Information?

Each person with Pompe disease is unique, and may require different resources to manage challenges. These resources may include family, friends, support groups, others with Pompe disease, and health care workers. In addition, several organizations and associations listed below can provide you with additional information:

Canadian Pompe Association

<http://www.pompecanada.com/>

Pompe Community

<http://www.pompe.com>

United Pompe Foundation

<http://www.unitedpompe.com/>

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: vchadultmetabolicclinic@vch.ca

www.adultmetabolicdiseasesclinic.ca

Glossary

- **Acid alpha-glucosidase:** The enzyme that is missing, ineffective, or lacking that is responsible for breaking down glycogen into usable glucose. It is normally found in the lysosomes.
- **Autosomal Recessive:** A pattern of inheritance where two non-working copies of the gene are needed to have the condition. Autosome refers to the 22 pairs of chromosomes that both males and females have; non sex-chromosomes (ie: X and Y). Autosomal conditions affect males and females equally.
- **Carrier:** Refers to a person that carries a non-working copy of a gene but is not affected by it. A carrier passes down the gene to its offspring.
- **Cells:** Basic organic unit of all living organisms.
- **Cytoplasm:** A gel like fluid in the cell that contains all material in the cell and outside of the nucleus.
- **DNA:** Hereditary material that acts like “instructions” which can tell a cell how to act and build a person. It is a biological “code” that contains information for cellular functions.
- **Enzyme Replacement Therapy (ERT):** A medical treatment in which an enzyme that a person is missing or lacks is given to patients through an IV infusion.
- **Genes:** Genes are made up of DNA, which act as instructions that tell the body how to grow and function.
- **Glycogen:** The storage form of sugar. It is stored in areas such as the liver and muscles.

- **Glycogen Storage Disorder:** Failure of cellular components to break down sugars into a usable form the body can use. Glycogen storage disorders are classified as genetic or acquired.
- **Intravenous (IV):** A patient receives medication through a plastic “needle” (called a cannula) connected to a tube that is inserted into a vein. This allows for immediate access to blood supply and rapid circulation.
- **Lysosome:** A structure in the cell that breaks down and “cleans” up unwanted substances that the cell no longer needs; referred to as the chemical plant of the cell.
- **Lysosomal enzyme:** A protein that breaks down other substances.
- **Lysosomal Storage Disorder:** Results from the accumulations of specific materials in lysosomes. Pompe disease is one of many lysosomal storage disorders.
- **Muscle Fibres:** The functional unit of muscle. Similar to “normal cells”, their function is to contract and relax causing movement of limbs or aid in breathing.
- **Mutation:** An abnormal change that happens to a gene, altering its function.
- **Protein:** The building blocks of cells involved in all essential life functions (ie: metabolism, cell growth).
- **Organelles:** Structures within cells that perform specific jobs.
- **Substrate:** The substance on which an enzyme acts.

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