What is Pompe disease?

Pompe disease is a genetic disorder that leads to problems with breaking down glycogen. Glycogen is a type of sugar that is stored in our cells. Another name for Pompe disease is Glycogen Storage Disease Type II (GSD II). Pompe disease is part of a group of diseases called lysosomal storage disorders (LSDs).

Pompe disease is divided into two groups based the age when symptoms started and how severe they are. The two types of the disease are:

1. **Infantile-onset Pompe disease (IOPD)** – when the disease appears within a few months of birth
2. **Late-onset Pompe disease (LOPD)** – when the disease appears later in childhood, adolescence, or adulthood.

How common is Pompe disease?

In the United States, about 1 in 40,000 people have Pompe disease but it is much more common among African Americans. It is estimated that 1 in 14,000 African Americans have Pompe disease.
Basic Genetic Concepts

In order to understand the cause of Pompe disease, it is important to understand some basic genetic concepts. The human body is made up of many cells, each cell contains 23 pairs of chromosomes (or 46 altogether). One chromosome from each pair comes from mom and one from dad.

Chromosomes carry our genes. Genes are like the instruction book for the body. They tell the body how to grow and function.

DNA (Deoxyribonucleic acid) are like the letters in the instruction book. Genes are pieces of DNA that explain how to make many types of chemicals, which are used to make sure the body works properly. One type of chemical is called an enzyme. Enzymes help with reactions, such as breaking glycogen (a type of stored sugar).
What causes Pompe Disease?

Pompe disease occurs when a gene called the **GAA gene** is not working properly. This nonworking gene prevents the cells from making enough of an enzyme called **acid alpha glucosidase**.

![Diagram showing normal and Pompe cell with working and nonworking GAA gene](image-url)
There are structures in the cell called lysosomes. **Lysosomes** are the **recycling centers of the cell**. One of their jobs is to break down **glycogen**. Normally, an enzyme called **acid alpha glucosidase** is used to break down the glycogen in the lysosome (pictured below).
If the cells do not make enough acid alpha glucosidase and are not able to break down the glycogen, then glycogen builds up the lysosome.

The buildup causes damage to the body, particularly to the heart and muscles.
How is Pompe disease inherited?

Pompe disease is a genetic condition. A person affected with the disease inherits two nonworking genes – one from each parent. This is called autosomal recessive inheritance.

When a child has Pompe disease, it means that both parents are “carriers” of a nonworking gene. Each parent has one working copy of the gene and one nonworking copy of the gene. The nonworking copy cannot properly produce the enzyme needed to break down glycogen. Since they still have one normal working copy, the parents do not show symptoms of the disease. Being a carrier does not cause health problems. When both parents are carriers, there is a 1 in 4 (25%) chance of having a child with Pompe disease. This is true for each pregnancy.
What are the different forms of Pompe disease?

Infantile-onset Pompe disease (IOPD)
This form of Pompe disease begins within the first few months of life. Babies usually show signs of muscle weakness and have heart problems. Without treatment, this form of Pompe disease can lead to death within the first year of life. Children with this form of Pompe disease have normal intelligence.

Medical problems of infantile-onset Pompe disease

- **Weak sucking and swallowing muscles** can make eating difficult. This can lead to problems gaining weight.

- **Overall muscle weakness and poor muscle tone**. This can cause a “floppy” appearance and problems with movement.
• **Weak breathing muscles** can cause difficulty breathing. The weakness also increases risk for infections. These muscles are located below and near the ribs (diaphragm).

• **Heart problems** – Babies usually have larger hearts (cardiomegaly) and thicker heart muscle (cardiomyopathy). These heart problems can cause heart failure.
Late-onset Pompe disease (LOPD)

The late-onset type form of Pompe disease can begin anytime from around the age of 1 year old through adulthood. It is less severe because there are usually no heart problems.

Symptoms include increased muscle weakness, especially in the legs, and breathing problems. People with this form of Pompe disease have normal intelligence.

Medical problems of late-onset Pompe disease

- **Eating difficulties** – Weak jaw and swallowing muscles can make eating difficult. This can lead to trouble gaining or maintaining weight.

- **Muscle weakness** – Gradual weakening of leg and hip muscles can cause walking difficulties and possible need for support.

- **Breathing concerns** – Weakness of the muscles needed to breathe can cause difficulty breathing, higher risk for infections, low energy and sleep difficulties.
How is Pompe Disease diagnosed?
It is very important to diagnose Pompe disease early to begin treatment. Early treatment is critical to delay some of the permanent damage caused by the disease.

Tests Before and During Pregnancy
It is possible to have tests before or during a pregnancy to find out if the baby is affected.

Testing for Pompe can be done before pregnancy by a process called pre-implantation genetic testing.

Testing while pregnant (prenatal testing) can be done using a tissue sample taken from the placenta or from the fluid that surrounds the unborn baby (amniotic fluid). Prenatal testing can be performed as early as the 10th week of pregnancy.

Decisions about prenatal testing are personal and can be complicated. It can be helpful to speak to a genetic counselor or physician to learn more about these options and discuss what is best for your family.

Newborn Screening
Newborn screening (NBS) is the process of testing newborn babies for some serious, but treatable, conditions. Newborn screening involves a heel prick for blood testing. For Pompe disease, a positive newborn screen alone does not mean the baby has the disease. Further testing is needed in order to diagnose Pompe disease. Each state decides which diseases and conditions to test for in their Newborn screening program. To find out if your state is screening for Pompe disease, you can visit: http://www.newsteps.org/pompe.
**Enzyme Testing**

In order to make a Pompe disease diagnosis, your doctor measures the **acid alpha glucosidase** enzyme activity. Usually activity is measured by taking a small amount of blood, however, skin and muscle can also be used. People with Pompe disease will show low levels of **acid alpha glucosidase** enzyme activity.

**Genetic Testing**

Genetic testing is also important for diagnosing Pompe disease. Your doctor will test for the **GAA** gene, the only gene that causes Pompe disease. The testing includes a small blood sample and looks for changes or missing pieces of the gene to help confirm Pompe disease.

In addition, once your doctor knows the exact change in the **GAA** gene, they can test other family members who may be at risk for Pompe disease.

**Tests During Childhood and Adulthood**

Doctors may test for late-onset type of Pompe disease when signs and symptoms of the disease are not explained by other causes. These signs include things like muscle weakness and breathing problems.

In order to diagnose Pompe disease, the doctor will order a blood test that measures the enzyme activity of **acid alpha glucosidase**.
Is there a cure?
At this time, there is no cure for Pompe disease. However, there are ways to treat and manage the disease. Enzyme replacement therapy (ERT) is a treatment that can help with the breakdown of glycogen. Research is currently being done to improve treatment options for Pompe disease.

What is Enzyme Replacement Therapy (ERT)?
There is no cure for Pompe disease. However, the best treatment option is Enzyme Replacement Therapy (ERT). ERT is a medical treatment that replaces the missing enzyme, acid alpha glucosidase, in patients with Pompe disease.

A drug called Lumizyme® was approved by the Food and Drug Administration (FDA) to treat all types of Pompe disease. Lumizyme® is an artificial version of acid alpha glucosidase enzyme.

ERT is given to patients by a slow intravenous infusion (IV). Your doctor will calculate the dose according to your child's weight and they will receive treatment every two weeks.

ERT improves muscle weakness, heart muscle, motor skills and breathing problems. Your child should start ERT as soon as the diagnosis of Pompe disease is confirmed. It cannot repair muscle or heart damage that has already occurred but it can help reduce further damage.
How ERT works within the cell:
What is the follow-up and disease management plan?

Children with Infantile-onset Pompe disease will have:

- Regular heart evaluations including echocardiogram (sound wave test) and electrocardiogram (electrical tracing of the heartbeat)
- Evaluation of muscle tone and skeletal problems
- Evaluation of development, growth and overall status twice per year
- Physical therapy and occupational therapy as needed
- Regular nutrition and food assessment and support
- Breathing assessment and support including:
  - sleep evaluation
  - lung function tests or surgery to make an airway in the windpipe (tracheostomy) for those having breathing difficulty
- Kidney tests
- Hearing test

Children with late onset Pompe disease will have:

- Physical therapy and occupational therapy for muscle weakness
- Hearing test
- Heart tests including echocardiogram and electrocardiogram
- Monitoring of overall muscle and bone status
- Breathing tests (sleep test if needed)
- Physical examination
- Kidney tests
What else should I know about Pompe disease diagnosis?

CRIM Status
CRIM stands for Cross-Reactive Immunologic Material. Before ever receiving treatment for infantile Pompe disease, your doctor must test your CRIM status using a blood or skin sample. When a patient makes some of their own acid alpha glucosidase enzyme, they are CRIM positive. When they do not make any of their own enzyme, they are CRIM negative.

About 66 out of 100 people with infantile Pompe disease make a small amount of acid alpha glucosidase. However, 33 out of 100 patients do not make any acid alpha glucosidase. People with late-onset Pompe disease are CRIM positive.

Your doctor must know your CRIM status because it will help to direct treatment. When a person is CRIM negative, they need extra medicine to help protect their immune system.

Pseudodeficiency
Pseudodeficiency ("pseudo" means "false" or "misleading") occurs when you have low enzyme activity when they test your blood in the laboratory. It happens when there is a specific type of change on both copies of the GAA gene. These changes do not cause you to have symptoms of Pompe disease.

This condition does not cause health problems but it can be stressful for families by causing "false positive" results. This means that the testing shows low acid alpha glucosidase enzyme levels but you do not actually develop Pompe disease. The prevalence of pseudodeficiency in the United States is less than 1 person out of 100.
Where can I find more information about research on Pompe disease?

- For information on clinical trials, visit [http://www.clinicaltrials.gov](http://www.clinicaltrials.gov) and search “Pompe disease”.

Where can I find more information about Pompe disease?

- Pompe Community (information provided by Genzyme Therapeutics)
  - [http://www.pompe.com](http://www.pompe.com)
- Acid Maltase Deficiency Association (AMDA)
  - [http://www.amda-pompe.org](http://www.amda-pompe.org)
- Association for Glycogen Storage Disease
  - [http://www.agsdus.org/type-ii.php](http://www.agsdus.org/type-ii.php)
- Association for Glycogen Storage Disorders UK
- National Organization of Rare Diseases or NORD
- Genetics Home Reference – Pompe disease
- Baby’s First Test
  - [http://www.babysfirsttest.org/newborn-screening/conditions/pompe](http://www.babysfirsttest.org/newborn-screening/conditions/pompe)