Disorder name: Pompe disease  
Acronym: GSD II

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This fact sheet contains general information about Pompe disease. Every child is different and some of this information may not apply to your child specifically. Certain treatments may be recommended for some children but not others. If you have specific questions about Pompe disease and available treatments, you should contact your doctor.

What is Pompe disease?

Pompe disease is also called GSD II, which stands for “glycogen storage disease type II.” It is an inherited disorder that affects many parts of the body, especially the heart and muscles. People with Pompe disease have problems breaking down a sugar called glycogen. Pompe disease belongs to two groups of diseases: glycogen storage disorder and lysosomal storage disorder.
**Glycogen Storage Disorder:**

Glycogen storage disorder (GSDs) are a group of inherited disorders. They are caused by enzymes that do not work properly.

Certain enzymes in the body are involved in the buildup and break down of a sugar called glycogen. When these enzymes are missing or are not working properly, glycogen can build up in the body. The buildup of glycogen causes a variety of symptoms.

Symptoms and treatment vary between GSDs. They can also vary from person to person with the same GSD.

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**Lysosomal Storage Disorders:**

Lysosomal storage disorders (LSDs) are a group of inherited disorders. They are caused by enzymes that do not work properly.

Lysosomes are like recycling centers for cells. They are small sacs filled with enzymes. These enzymes help break down large molecules into smaller molecules that the body can re-use. People with LSDs are missing enzymes or have non-working enzymes. As a result, these people have problems breaking down certain large molecules into usable forms. This leads to a buildup of these molecules, which causes a variety of problems.

The symptoms and treatment vary between LSDs. They can also vary from person to person with the same LSD.

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**What causes Pompe disease?**

Pompe disease is caused when an enzyme, called “acid alpha-glucosidase” (GAA), is either missing or not working properly. This enzyme is located in the lysosomes. Its job is to break down a complex sugar (glycogen) into a simple sugar (glucose). Glucose is a simple sugar and is the main energy source for the body.

When the body wants to store this energy so it can be used later, glucose molecules are linked together into a tree-like molecule called glycogen. Glycogen is mainly stored in the muscles and in the liver. Some glycogen is transported to the lysosomes, where GAA breaks it down into glucose. When GAA is missing or not working properly, glycogen builds up in the lysosomes. This excess glycogen causes the lysosomes to swell and damage the cellular structures around them. The lysosomes can eventually swell so much that they burst, further damaging cells and the body. This buildup of glycogen and the accompanying damage causes the symptoms of Pompe disease.
What are the symptoms of Pompe disease?

The symptoms of Pompe disease vary from person to person. Symptoms can begin at different ages. Symptoms may start in infancy or not until late adulthood. Without treatment, the symptoms of Pompe disease are often fatal. It is important to remember that each child is different and may experience symptoms differently.

There are three types of Pompe disease:
- classic infantile-onset
- non-classic infantile-onset
- late-onset

About one-third of people with Pompe disease have one of the infantile-onset types. These people tend to have no GAA enzyme activity. About two-thirds of people with Pompe disease have the late-onset type. These people tend to have some GAA activity, but less than people without Pompe disease. Generally, the older the child is when symptoms begin, the slower the disease will progress, and the better they will do.
Classic infantile-onset Pompe disease

Signs of classic infantile-onset Pompe disease usually appear before the baby is born or within the first two months of life.

These signs and symptoms may include:
- A large heart (cardiomegaly)
- Thickening of the heart muscle (Hypertrophic cardiomyopathy)
- Low muscle tone (Hypotonia)
- General muscle weakness
- Feeding problems, which may be the result of:
  - Low muscle tone in the face (facial hypotonia)
  - A large tongue (macroglossia)
  - Tongue weakness
  - Difficulty using the lips, tongue, and jaw (poor oromotor skills)
- Not gaining weight, or not growing at a healthy rate (failure to thrive)
- Breathing problems
- Hearing problems
- A large liver (hepatomegaly)

Without treatment, these symptoms can lead to fatal heart (cardiac) and lung (respiratory) failure within the first year of life.

Non-classic infantile-onset Pompe disease

Symptoms of non-classic infantile-onset Pompe disease usually appear within the first year of life.

These symptoms may include:
- Muscle weakness, which leads to breathing problems
- Delayed motor skills (such as rolling over and sitting)

Unlike the classic type of infantile-onset Pompe disease, heart failure is not usually seen in children with non-classic infantile-onset disease.

Without treatment, these children usually develop fatal respiratory failure in early childhood.

Late-onset Pompe disease

Late-onset Pompe disease is sometimes divided into childhood, juvenile, and adult-onset types. These categories are based on when the symptoms begin.

Symptoms are similar among the different types of late-onset Pompe disease. However, symptoms start at different ages and progress at different rates, depending on the type of late-onset Pompe disease.
Symptoms include:
- Muscle weakness that gets worse
- Breathing problems, which can lead to fatal respiratory failure
- Difficulty exercising
- An enlarged liver (hepatomegaly)
- Difficulty chewing or swallowing

Generally, the later symptoms begin, the more slowly they progress. People with late-onset Pompe disease may develop life-threatening respiratory failure. How well people do ultimately depends on how much the breathing muscles are affected.

**What is the treatment for Pompe disease?**

People with Pompe disease should be treated by a team of specialists who are familiar with the disorder. Which specialists are needed will depend on the person's symptoms. All people with Pompe disease should be seen by a metabolic genetics doctor. Their team may also include a cardiologist (heart doctor), pulmonologist (breathing doctor), neurologist (brain doctor), neuromuscular specialist (muscle doctor), orthopedist (bone doctor), rehabilitation specialist (like a physical therapist or speech therapist), and genetic counselor. This team can support the family and help manage the symptoms of Pompe disease.

People with Pompe disease should generally have a cardiac, respiratory, musculoskeletal, neurological, and general health assessment at least every six months, unless very mild, slowly progressive disease is present. Certain treatments may be recommended for some children but not others. The following treatments and management are often recommended for children with Pompe disease:

1. **Enzyme Replacement Therapy (ERT)**
   Pompe disease is caused by not having enough of an enzyme called acid alpha-glucosidase (GAA). Enzyme replacement therapy gives people a replacement form of that enzyme. This new enzyme replaces the GAA enzyme missing in people with Pompe disease. This is a long term treatment option. ERT improves both symptoms and long-term survival but it is not a cure. ERT should be started as soon as the diagnosis of Pompe disease is made.

2. **Respiratory Support**
   Respiratory failure is the most common cause of early death in people with Pompe disease, so breathing symptoms should be checked regularly. Breathing support may include using a machine to help the weakened breathing muscles (this is called “mechanical ventilation”), giving extra
oxygen, making sure the airway is clear, changing how a person eats to make sure they do not choke, and, in the most severe cases, tracheostomy (using a tube to help a person breathe) is sometimes recommended. As symptoms get worse, most people will need mechanical ventilation to help with breathing.

3. **Cardiac Care**
   Infants should be seen frequently by a cardiologist familiar with Pompe disease. Medications may be used to treat cardiomyopathy (a large heart).

4. **Physical Rehabilitation**
   Physical therapy exercises can help strengthen weakened muscles, improve range of motion, and develop motor skills. Strengthening exercises for breathing muscles can help with breathing. Speech therapy may be recommended for people with weak facial and oral muscles. Occupational therapy can help develop and maintain motor skills needed for daily tasks.

5. **Psychosocial Support**
   Individual and family counseling, disease education, and participation in patient organizations, advocacy groups, and support groups are important for managing the emotional and psychological impact of Pompe disease.

6. **General Medical Care**
   People who have problems eating may need help managing their nutrition and weight. This may include physical therapy to strengthen the facial muscles, choosing foods that are easier and safer to eat, maximizing nutrients, and tube feeding (in severe cases). If a person with Pompe disease needs surgery, the use of anesthesia needs to be thought about carefully. This is because anesthesia could cause a heart problem. People with Pompe disease also need to avoid getting infections. They can do this through routine immunizations, strict hand washing, prompt medical attention for any signs of infection (such as cough or fever), and aggressive treatment for infections.

**What happens when Pompe disease is treated?**

In children with infantile-onset Pompe disease, ERT may improve survival. It can also reduce heart size, help the heart work better, help the muscles work, decrease the need for a ventilator, and help some people gain motor skills. In individuals with late-onset Pompe disease, ERT may help the muscles and lungs continue to work. With early detection and treatment, children with Pompe disease have a better chance of living healthy lives.

Other treatments can help with some of the symptoms of Pompe disease. Mechanical ventilation helps the breathing problems. It can also help people with
respiratory failure live longer. Physical therapy can improve a person’s motor skills and independence. Cardiac care reduces the risk of heart problems. Psychosocial support can improve overall patient well-being. Nutrition support makes sure the muscles and the rest of the body get the nutrients they need. Prevention and management of infections reduces the risk of pneumonia, bronchitis, and other infections, which can be life-threatening.

What causes the GAA enzyme to be absent or not working correctly?

Genes tell the body how to make enzymes. The GAA gene instructs the body to make the acid alpha-glucosidase enzyme. Everyone has two copies of the GAA gene. People with Pompe disease have changes, also called variants, in both copies of their GAA genes. Because of the variants in the GAA genes, the acid alpha-glucosidase enzyme either does not work properly or is not made at all.

How is Pompe disease inherited?

Pompe disease is inherited in an autosomal recessive manner. It affects both boys and girls equally.

Everyone has two copies of the GAA gene that make the GAA enzyme. In people with Pompe disease, neither of their GAA genes works correctly. These individuals inherit one non-working GAA gene from each parent.

Parents of children with Pompe disease usually do not have the condition themselves. Instead, each parent has one non-working GAA gene and one working gene for the GAA enzyme. The parents are called carriers. Carriers do not have Pompe disease because one of their GAA genes is working correctly. The working GAA gene is able to make enough GAA enzyme for the person to be healthy.

When both parents are carriers, each pregnancy has a 25% (1 in 4) chance of resulting in a child having Pompe disease. There is a 50% (1 in 2) chance for the child to be a carrier, just like the parents. There is a 25% (1 in 4) chance that the child will have two working genes.
Genetic counseling is available to families who have children with Pompe disease. Genetic counselors answer questions about how Pompe disease is inherited, choices during future pregnancies, and how to test other family members. Ask your doctor about a referral to a genetic counselor.

Is genetic testing available?

Genetic testing for Pompe disease can be done on a blood sample. Genetic testing, also called DNA testing, looks for changes (variants) in the pair of genes that causes Pompe disease. If a gene change has been found in other family members, testing can find out if your child has the same gene change.

DNA testing is not always necessary to diagnose your child, but is often performed after a positive newborn screen result. It is helpful to know the gene changes in a child with Pompe disease because it is essential for carrier or prenatal testing, discussed below. It is often needed to determine whether someone has a pseudodeficiency of GAA, also discussed below.

What other testing is available?
Screening Tests

Newborn Screening
Newborn screening for Pompe disease is done in some states. A blood spot from the baby’s heel is used to screen for many different conditions. Newborn screening detects Pompe disease by looking for GAA enzyme activity. GAA enzymes are active in every healthy newborn’s blood. Since babies with Pompe disease have GAA enzymes that are either missing or not working properly, they will have reduced GAA enzyme activity.

If a baby has a positive result on the initial Pompe screen, it does not yet mean that he or she has Pompe disease. It just means that they have lower GAA enzyme activity as measured by the newborn screening test. Low GAA enzyme activity levels can sometimes be found in people who never develop Pompe disease. This is called pseudodeficiency. This is observed in about 4% of East Asian populations. A positive screening result means that further testing must be done to confirm or rule out Pompe disease. Rarely, there can also be false positives with additional testing.

When one or both parents are known to be carriers of Pompe disease, newborn screening results are not enough to rule out Pompe disease in a newborn baby. In this case, more sensitive diagnostic testing should be done in addition to newborn screening, even if the newborn screening result is negative.

Serum Creatinine Kinase (CK) Concentration
This blood test measures the amount of an enzyme called creatinine kinase (CK) in the blood. People with Pompe disease will often have more CK in their blood than expected. Many other conditions also cause elevated CK levels in the blood, so this test cannot be used to make a definite diagnosis of Pompe disease. Also, late-onset Pompe disease that presents itself in late childhood may be missed by this test.

Urinary Glucose Tetrasaccharides
This urine test looks at certain carbohydrates in the urine. Individuals with Pompe disease will have more of a particular carbohydrate than expected in their urine. However, people with other glycogen storage diseases will have the same results, so this test cannot by itself diagnose Pompe disease.

Confirmatory testing
Confirmatory testing is needed for a diagnosis of Pompe disease. Each person may not need every one of the confirmatory tests listed below.
**GAA Enzyme Activity**
In this test, a small sample of blood is taken and the amount of GAA enzyme activity is measured. Test results are confirmed if necessary by again measuring the GAA enzyme activity in tissue (usually a skin sample).

**GAA Protein Quantitation**
In this test, a small sample of skin is taken and the amount of GAA protein is measured. Decreased GAA indicates Pompe disease. Normal GAA does not exclude Pompe disease. This test can be useful in determining whether someone with Pompe disease is likely to develop antibodies and reduced response to ERT treatment.

**Muscle Biopsy**
In this test, a small sample of muscle is taken. Increased glycogen storage in the lysosomes of the muscles cells can indicate Pompe disease. If results are normal, this test cannot rule out Pompe disease.

**Can you test for Pompe disease during a future pregnancy?**
Prenatal genetic testing for Pompe disease is only available if a genetic cause has already been identified in the family. If not done prior to pregnancy, genetic testing to identify the genetic cause can be performed during the pregnancy. Once a genetic cause has been identified, DNA from the fetus can be tested. The sample for this testing is obtained by either CVS or amniocentesis.

Parents may choose to have testing during pregnancy or wait until birth to have the baby tested. Parents may also choose to use assisted reproductive techniques to decrease the chance that their future children would have Pompe disease. A genetic counselor can talk to you about your choices and answer questions about prenatal testing or testing your baby after birth.

**Can other members of the family have Pompe disease or be carriers?**

**Having Pompe disease**
Each full sibling (brother or sister with the same mother and father) of a baby with Pompe disease has a 25% (1 in 4) chance of also having Pompe disease. Even older siblings who have not shown any symptoms of the disease could have late-onset Pompe disease that has not caused symptoms yet, but will in the future. All siblings of an individual with Pompe disease should be tested.
Carrier for Pompe disease

Each full sibling of a baby with Pompe disease has a 50% (1 in 2) chance of being a carrier. Full siblings who do not have Pompe disease have a 66% (2 in 3) chance of being a carrier.

If you are a parent of a child with Pompe disease, your brothers and sisters have a 50% (1 in 2) chance of being a carrier. It is important for other family members to be told that they could be carriers. There is a small chance that they are also at risk to have children with Pompe disease.

Not all states offer newborn screening for Pompe disease. This makes it especially important to tell your family members if they are at risk for having a child with the disease.

Can other family members be tested?

Diagnostic testing
Siblings of a child with Pompe disease should be tested to see if they also have Pompe disease. Talk to your doctor or genetic counselor if you have questions about testing for Pompe disease.

Carrier testing
If both gene variants have been found in your child, other family members can have DNA testing to see if they are carriers. If you have questions about carrier testing, ask your genetic counselor or doctor.

How many people have Pompe disease?

It is estimated that 1 in every 40,000 live births in the United States is a baby with Pompe disease.

Does Pompe disease happen more often in a certain ethnic group?

Pompe disease occurs in people of all ethnicities and races. However, it does occur more often in certain groups. Infantile-onset Pompe disease is more common among African Americans and people from southern China and Taiwan. Late-onset Pompe disease is more common in the Netherlands. Pompe disease is less common among people of Australian and Portuguese descent.

Does Pompe disease go by any other names?

Pompe disease is also called:
- Glycogen storage disease type II (GSD II)
• Acid maltase deficiency disease (AMD)
• Alpha-1,4-glucosidase (GAA) deficiency
• Deficiency of alpha-glucosidase
• Glycogenosis type II

Where can I find more information?

Sanofi Genzyme (Pompe Community)
http://www.pompe.com

Genetic Home Reference

International Pompe Association
http://www.worldpompe.org

Acid Maltase Deficiency Association
http://www.amda-pompe.org

Association for Glycogen Storage Disease
http://www.agsdus.org/type-ii.php

Muscular Dystrophy Association

United Pompe Foundation
http://www.unitedpompe.com

National Organization for Rare Disorders
https://rarediseases.org/rare-diseases/pompe-disease/