

What is...

# Pompe Disease

**Pompe disease, also known as acid maltase deficiency (AMD) or glycogen storage disease II, is a rare, inherited glycogen storage disease** that affects the heart and skeletal muscles. There are two types of Pompe disease: infantile-onset and noninfantile-onset (juvenile or adult).

Pompe is classified as a **metabolic muscle disorder**, one of a group of diseases that interferes with processing and storage of complex sugars (carbohydrates). The build-up of sugar molecules in muscle cells causes them to break down.

This rare disease is estimated to occur in approximately **1 in every 22,000 births** based on studies of newborn screening efforts in the United States.

Mutations in a gene that carries the genetic instructions to make an enzyme called **acid maltase, or acid alpha-glucosidase (GAA)**, are the underlying cause of Pompe disease.

Normally, the body uses the GAA enzyme to break down **glycogen** (stored sugar used for energy). The enzyme performs its function in intracellular compartments called lysosomes, which gather several substances, including glycogen. There GAA converts glycogen into **glucose**, which is used to fuel cells. In Pompe disease, mutations in the GAA gene reduce or completely eliminate this essential enzyme.

**Muscle weakness** is a main symptom in both forms of Pompe disease.

Pompe disease **severity** and **age of onset** are related to how much functional GAA enzyme is present in cells.

Excessive amounts of lysosomal glycogen accumulate everywhere in the body, but the cells of the **heart and skeletal muscles** are the most seriously affected. Accumulation of glycogen in these tissues destroys healthy muscle and heart tissues.

Researchers have identified at least **550 different mutations** in the GAA gene that cause the symptoms of Pompe disease.

Although Pompe is a single disease, it is classified into two forms. The early-onset **infantile form** is the more severe of the two. It starts before 12 months of age and involves the heart muscle. The later-onset **juvenile or adult** form may start at any age after 12 months of age, and the heart is less likely to be severely affected.

There is no cure for Pompe disease, but medication and therapy can help manage some symptoms and potentially slow the course of the disease.

Alglucosidase alfa has been used for ERT for more than 15 years. It improves ventilator-free survival as well as cardiac and skeletal muscle function in patients. Avalglucosidase alfa, which has similar efficacy to alglucosidase alfa, has been approved as a second option for ERT.



# What are the signs and symptoms of Pompe disease?

Pompe disease is a multi-systemic condition, affecting many parts of the body and resulting in weakness of the skeletal, cardiac (heart), and pulmonary (lung) muscles.



## What should I know about Pompe disease?

**1** Pompe disease symptom onset may occur at any time from infancy to adulthood. It is slowly progressive and less severe in its noninfantile-onset forms.

**2** The infantile-onset form of Pompe results from a complete or near complete deficiency of GAA. Symptoms begin in the first months of life with feeding problems, poor weight gain, severe muscle weakness, "floppiness" (a lack of muscle tone, called hypotonia), and head lag. The heart may be enlarged, and respiratory difficulties are often complicated by lung infections. Many infants with Pompe disease also have enlarged tongues and livers (hepatomegaly). Without treatment, heart failure can cause life-threatening complications by the age of 12 to 18 months. The infantile-onset form of Pompe can present a non-classic phenotype; hypotonia without cardiomyopathy, during the first one to two years of life.

**3** Noninfantile-onset Pompe disease is the result of a partial deficiency of GAA. Symptoms may begin at any age. The primary symptom is muscle weakness, typically in the legs and trunk, as well as in the muscles that control breathing, progressing to life-compromising respiratory weakness. Problems with the heart are less likely in this form of the disease.

**4** In general, the later the age of onset, the slower the progression of the disease. Ultimately, the prognosis is dependent upon the extent of respiratory muscle involvement.

**5** A diagnosis of Pompe disease can be confirmed by measuring the level of GAA enzyme activity in a blood sample, and through screening for common genetic mutations.

**6** In May 2013, Pompe disease was added to the list of conditions that states screen for in newborn babies, based on the availability of reliable tests for screening and diagnosis and of an effective treatment (enzyme replacement therapy).

**7** Early detection of Pompe disease allows for the earliest possible treatment, which can lead to better outcomes.

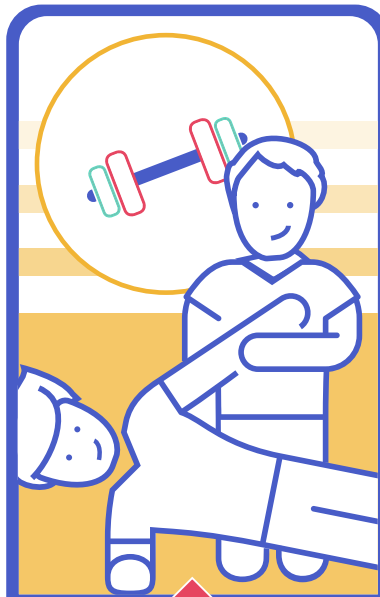
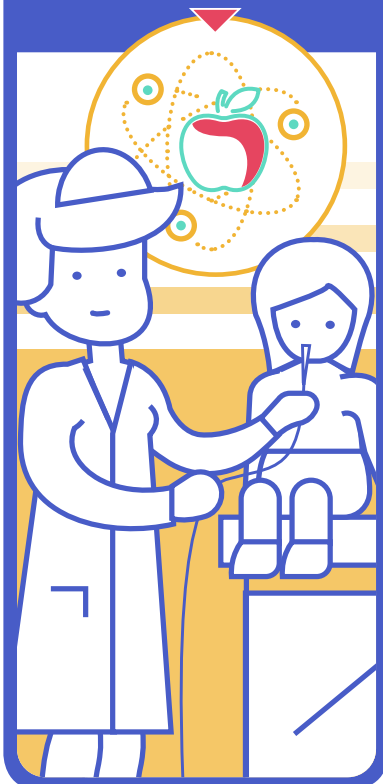
**8** Once Pompe disease is diagnosed, testing of all family members and a consultation with a genetic counselor are recommended.

# How is Pompe disease treated?

Treatment for Pompe disease should involve a **multidisciplinary team of specialists** (such as a cardiologist, neurologist, and respiratory therapist) who are knowledgeable about the disease and who can offer supportive and symptomatic care.

A **registered dietitian** can suggest well-balanced meals to help maintain the consumption of adequate calories and nutrients.

Insertion of a **gastrostomy tube, or g-tube**—either through the nose and down the throat or surgically into the stomach— can deliver food directly to the stomach or intestines.



Physical therapy helps to restore and maintain muscle strength and function through exercise, as well as to maintain range of motion through stretching.

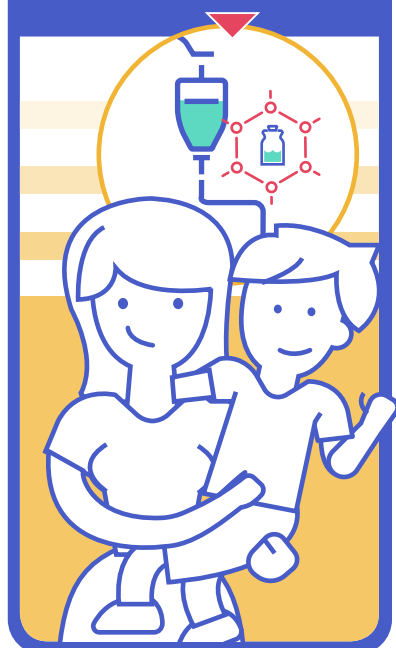
Breathing should be **monitored regularly** by a specialist, as weakened respiratory muscles make it difficult to cough, leading to increased risk of serious respiratory infection and pneumonia.

Symptoms such as unusual shortness of breath on exertion or morning headaches may indicate compromised breathing, which may require **supplemental oxygen** or **ventilatory assistance** at night.

A **speech or swallowing therapist** can recommend exercises to strengthen muscles needed for swallowing.

Enzyme replacement therapy (ERT) is the approved treatment for all patients with Pompe disease. In ERT, a synthetic form of the maltase enzyme is delivered to cells to substitute for the enzyme missing in Pompe disease. This may keep muscle cells from dying. The ERT drugs Myozyme and Lumizyme were the first options available to treat infantile-onset and late-onset Pompe disease, respectively. A second generation ERT, Nexviazyme, has also been approved to treat late-onset Pompe disease.

Since the approval of ERT, the outlook for people of all ages with Pompe disease is better, with reversal of cardiac damage and increased life expectancy in the infantile-onset form of the disease and improved respiratory function and walking endurance in older individuals.





## MDA Glossary

### **Cardiomegaly**

Enlargement of the heart

### **Glucose**

The simplest carbohydrate, formed from one sugar, and one of the body's preferred sources of fuel for cells — particularly muscle cells

### **Glycogen**

A form of sugar that is stored for future mobilization and use as energy

### **Glycogen storage disease**

A metabolic disorder, caused by enzyme deficiencies, that affects the production or breakdown of glycogen or glucose

### **Hepatomegaly**

Enlargement of the liver

### **Hypertrophic cardiomyopathy**

A condition in which part of the heart muscle becomes thickened, hindering its ability to pump blood to the body

### **Hypotonia**

Diminished muscle tone

### **Macroglossia**

Enlargement of the tongue

### **Mutation**

A flaw in the DNA code

**To learn more about Pompe disease, visit [mda.org](http://mda.org) or contact the MDA National Resource Center at 833-ASK-MDA1 (275-6321).**



Designated a Top-Rated Charity by the American Institute of Philanthropy, MDA is the first nonprofit to receive a **Lifetime Achievement Award from the American Medical Association** for "significant and lasting contributions to the health and welfare of humanity."



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