A VISUAL GUIDE TO UNDERSTANDING POMPE DISEASE

INFORMATION FOR PEOPLE LIVING WITH POMPE DISEASE
What is Pompe disease?
(Notes: some words that may be unfamiliar are highlighted and are defined in the glossary at the end of this brochure)

Pompe disease is a rare neuromuscular disorder. It is a serious genetic disorder that is inherited from both parents in what is called an autosomal recessive pattern.1

Other names are sometimes used for Pompe disease, including acid maltase deficiency and glycogen storage disease type II. It is a type of condition known as a glycogen storage disease, and is also part of a larger group of conditions called lysosomal disorders.1, 2

There are 2 main types of Pompe disease: infantile-onset and late-onset. The infantile-onset type of Pompe disease begins during the first year of life and has a classic form and a nonclassic (less severe) form. Late-onset Pompe disease appears later in childhood or during adulthood.2, 3

Usually, the earlier the signs and symptoms of Pompe disease appear, the more quickly they get worse and the more severe they may eventually become.2, 4

Sometimes it’s difficult for doctors to diagnose Pompe disease, since many of its symptoms can be mistaken for those of other neuromuscular disorders.2, 5

How does Pompe disease affect families?7

People have two copies of most of the genes in their cells. One of these copies is inherited from their father and one from their mother. If BOTH copies of a person’s GAA gene have a variant associated with Pompe disease, he or she will have Pompe disease. But if ONLY ONE copy has a variant and the other copy is normal, he or she will be a carrier of Pompe disease. Carriers of Pompe disease can pass the disease down to their children, but usually do not have any of its signs or symptoms themselves.

Whether or not a person gets Pompe disease depends on their parents’ genes and how they are passed down. For example, if both parents are carriers (see graphic below), each of their children will have:

- A 1-in-4 (25%) chance of inheriting 2 normal genes and being unaffected
- A 1-in-2 (50%) chance of inheriting 1 copy of the variant and 1 normal gene, and being a carrier
- A 1-in-4 (25%) chance of inheriting 2 copies of the variant and having Pompe disease

Other scenarios also can occur, depending on the parents’ genes. For example, if one parent has Pompe disease and the other parent is unaffected, none of their children will develop Pompe disease, but all of them will be carriers.

What should I know about Pompe disease?

Depending on where you live, Pompe disease is estimated to affect as many as 1 in every 20,000–40,000 births.6

Pompe disease is caused by certain variants in a specific gene (called the GAA gene).

People who have gene variants that cause Pompe disease have difficulty making a specific lysosomal enzyme.

The purpose of lysosomal enzymes is to help process or break down specific substances within the lysosomes of cells.

In Pompe disease, the affected enzyme is acid α-glucosidase, also known as GAA.

Normally, the GAA enzyme breaks down a complex carbohydrate called glycogen and converts it into a simple sugar.

But people who have Pompe disease have very little GAA, or almost none at all. The GAA they do have may also not work properly. This causes glycogen to build up in the cells of muscles, as well as other tissues and organs.2, 5

This buildup of glycogen in the lysosomes of cells increases over time, gradually causing more and more damage to tissues and organs (especially muscles) and leading to the signs and symptoms of Pompe disease.6


4. 20,000-40,000 births.5, 6

5. Deoxyribonucleic acid (DNA):

6. Cell:

7. lysosome:

8. Lysosome:

9. Enzyme:

10. Other copy is normal, he or she will be a carrier of Pompe disease. Carriers of Pompe disease can pass the disease down to their children, but usually do not have any of its signs or symptoms themselves. Whether or not a person gets Pompe disease depends on their parents’ genes and how they are passed down. For example, if both parents are carriers (see graphic below), each of their children will have:

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9. A 1-in-2 (50%) chance of inheriting 1 copy of the variant and 1 normal gene, and being a carrier

10. A 1-in-4 (25%) chance of inheriting 2 copies of the variant and having Pompe disease

11. Other scenarios also can occur, depending on the parents’ genes. For example, if one parent has Pompe disease and the other parent is unaffected, none of their children will develop Pompe disease, but all of them will be carriers.

12. Depending on where you live, Pompe disease is estimated to affect as many as 1 in every 20,000–40,000 births.

13. Pompe disease is caused by certain variants in a specific gene (called the GAA gene).

14. People who have gene variants that cause Pompe disease have difficulty making a specific lysosomal enzyme.

15. The purpose of lysosomal enzymes is to help process or break down specific substances within the lysosomes of cells.

16. In Pompe disease, the affected enzyme is acid α-glucosidase, also known as GAA.

17. Normally, the GAA enzyme breaks down a complex carbohydrate called glycogen and converts it into a simple sugar.

18. But people who have Pompe disease have very little GAA, or almost none at all. The GAA they do have may also not work properly. This causes glycogen to build up in the cells of muscles, as well as other tissues and organs.

19. This buildup of glycogen in the lysosomes of cells increases over time, gradually causing more and more damage to tissues and organs (especially muscles) and leading to the signs and symptoms of Pompe disease.
What causes Pompe disease?

DNA is inherited through genes that are passed down from the person’s mother and father.

Sometimes, gene variants (also called mutations) occur in the DNA code that can change the way the gene functions.

Some people with Pompe disease have gene variants that cause their bodies to make very little or no GAA.

Others have different variants that cause their bodies to make some GAA but not enough, and/or GAA that does not function correctly.

What are the signs and symptoms of Pompe disease?

How mild or severe the signs and symptoms of Pompe disease are—and how quickly they get worse—may vary from person to person in both the infantile-onset and late-onset types of the disease. This may be determined by how much GAA enzyme a person has and how well it is functioning, as well as other possible factors. Not every person who has Pompe disease will experience every sign and symptom listed below.

INFANTILE-ONSET POMPE DISEASE

- GAA activity is normal AND/OR there is no glycogen buildup
- The test detects a variant that causes Pompe disease
- The person has Pompe disease

- GAA activity is absent or reduced AND/OR there is glycogen buildup
- DNA testing is done to look for common gene variants associated with Pompe disease
- The test does not detect a variant that causes Pompe disease, but the doctor still suspects Pompe disease
- The person does NOT have Pompe disease

- The test detects a variant known to cause Pompe disease
- A GAA gene sequencing test is done

DIGESTIVE SYSTEM
- Malabsorption
- Reduced ability to breathe independently
- Respiratory infections

LUNGS/DIAPHRAGM
- Reduced ability to cough
- Shortness of breath
- Sleep apnea
- Breathing difficulties; loss of ability to breathe independently

NERVES
- Nerve pain (most common in hands and feet)

BONES/JOINTS
- Osteoporosis (weakened, fragile bones)
- Fractures
- Soiliness (abnormally curved spine)
- Protruding shoulder blades

How is Pompe disease treated?

Currently, enzyme replacement therapy (ERT) is the only FDA-approved treatment for Pompe disease.

ERT works by replacing the nonfunctioning or missing GAA with functioning GAA.

CRIM
- An infant’s cross-reactive immunological material (CRIM) status can help determine his or her response to treatment. CRIM-positive infants make some GAA while CRIM-negative infants make no GAA.

People with Pompe disease also may receive supportive treatments to help manage the signs and symptoms of the disorder. For example, physical therapy can help improve muscle strength, and the use of a walker or wheelchair may help improve mobility. Mechanical ventilators or feeding tubes may be necessary in some cases.

Other potential therapies for Pompe disease are being researched. These include new forms of ERT, as well as another type of treatment called gene therapy. Although some of these investigational therapies have shown promise, their safety and efficacy in Pompe disease have not been proven, and they are not currently approved to treat the disease.

A doctor suspects Pompe disease—here’s an example of what can happen

A blood test is done to measure the level of GAA enzyme activity

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**What do these words mean?**

**Autosomal recessive:** an inheritance pattern in which two copies of a gene variant must be present in order for the trait or disorder to develop

**Cell:** basic building block of all living things

**Cross-Reactive Immunological Material (CRIM):** a measurement of natural GAA enzyme production

**Deoxyribonucleic acid (DNA):** substance within genes that contains instructions, or code, for making proteins, including enzymes

**Diaphragm:** a thin sheet of muscle that separates the chest from the abdomen

**Enzyme:** a special type of protein that speeds up chemical reactions that take place within a cell

**Enzyme replacement therapy (ERT):** a treatment that replaces missing or nonfunctioning enzymes

**Gene:** the basic unit of heredity contained within each cell, made up of DNA, that group of more than 70 diseases that result from accumulation of waste products in lysosomes

**Lysosomal enzyme:** a special protein found within the lysosome of cells

**Lysosome:** a sac found in cells that contains enzymes that digest cell waste

**Neuromuscular disorder:** a disorder that affects the nerves that control voluntary muscles and the nerves that communicate sensory information back to the brain

**Sign:** objective evidence of a disease or condition that can be recognized by the patient as well as others

**Skeletal muscle:** muscle connected to the skeletal system that helps move the limbs and other parts of the body

**Sleep apnea:** a disorder in which a person’s breathing repeatedly stops briefly during sleep

**Symptom:** subjective evidence of a disease or condition that can be recognized only by the patient

**Stroke:** damage to the brain resulting from blockage of blood flow or rupture of a blood vessel

**References:**


**Other resources that may be helpful are listed below.**

**International**

**International Pompe Association**
worldpompe.org

**The Association for Glycogen Storage Disease UK**
agsd.org.uk

**Australian Pompe’s Association**
australianpompe.com

**Canadian Association of Pompe**
pompecanada.com

**Selbsthilfegruppe Glykogenose Deutschland e.V.**
glykogenose.de

**Spierziekten Nederland**
spierziekten.nl

**EURODIS**
eurodis.org

**Pompe Support Network**
pompe.uk

**Associazione Italiana Glicogenosi (AIG)**
aiag-aig.it

**New Zealand Pompe Network**
znpomenetwork.weebly.com

**United States**

**United Pompe Foundation**
unitedpompe.com

**Acid Maltrate Deficiency Association**
amda-pompe.org

**Muscular Dystrophy Association**
mda.org

**National Organization for Rare Disorders**
rarediseases.org

**Global Patient & Professional Advocacy**

- **Amicus Therapeutics, Inc.**
  1 Cedar Brook Drive
  Cranbury, NJ 08512
  USA

- **Amicus Therapeutics UK LTD**
  One Gobehide
  Fieldhouse Lane
  Marlworth SL7 1HZ
  United Kingdom