A VISUAL GUIDE TO UNDERSTANDING POMPE DISEASE

INFORMATION FOR PEOPLE LIVING WITH POMPE DISEASE

Amicus Therapeutics has developed this educational resource in collaboration with the rare disease community and thought leaders.

Amicus Therapeutics

What is Pompe disease?

(Note: 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**.[1-3]

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.[2,3]

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[5,6]

Pompe disease is caused by certain variants in a specific gene (called the *GAA* gene)[1]

People who have gene variants that cause Pompe disease have difficulty making a specific **lysosomal enzyme**[2]

The purpose of lysosomal enzymes is to help process or break down specific substances within the **lysosomes** of cells[2]

In Pompe disease, the affected enzyme is acid α-glucosidase, also known as GAA[8]

Normally, the GAA enzyme breaks down a complex carbohydrate called glycogen and converts it into a simple sugar[8]

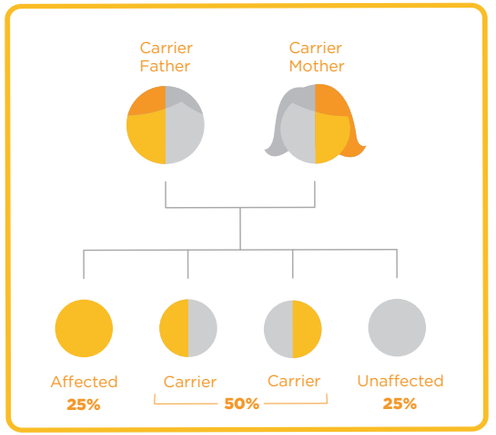
But people who have Pompe disease have very little GAA, or almost none at all. The GAA they do have also may not work properly. This causes glycogen to build up in the cells of muscles, as well as other tissues and organs[8,9]

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[8]

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

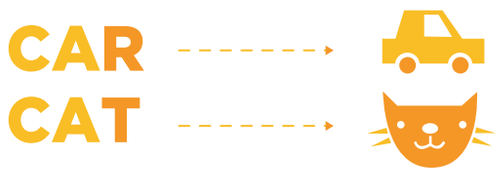
Other scenarios also can occur, depending on the parents' genes. For example, if one parent has Pompe disease and the other parent is unaffected, none of their children will develop Pompe disease, but all of them will be carriers.

What causes Pompe disease?

Everyone has information called **DNA** coded into his or her cells.

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 makes up a particular gene that can change the way the gene functions.



Think of it like spelling. One wrong letter can completely change the meaning of a word!

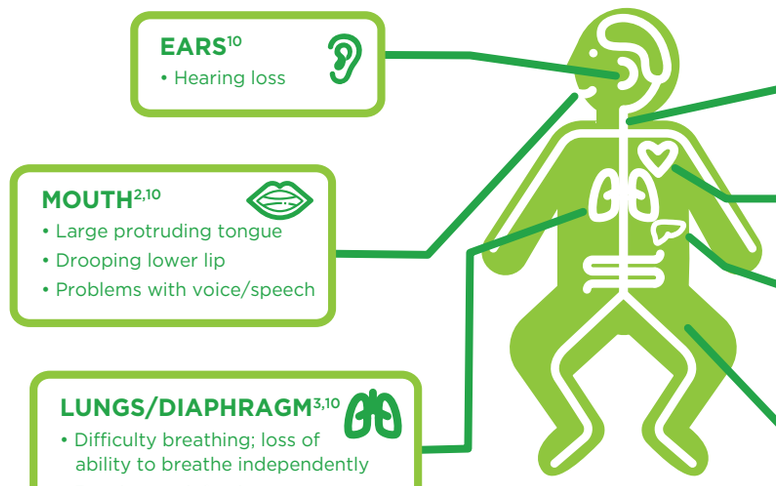
Some people with Pompe disease have gene variants that cause their bodies to make very little or no GAA.[8]

Others have different variants that cause their bodies to make some GAA, but not enough, and/or GAA that does not function correctly.[8]

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.[5] Not every person who has Pompe disease will experience every sign and symptom listed below.

INFANTILE-ONSET POMPE DISEASE



EARS[10]
- Hearing loss

MOUTH[2,10]
- Large protruding tongue
- Drooping lower lip
- Problems with voice/speech

LUNGS/DIAPHRAGM[3,10]
- Difficulty breathing; loss of ability to breathe independently
- Respiratory infections

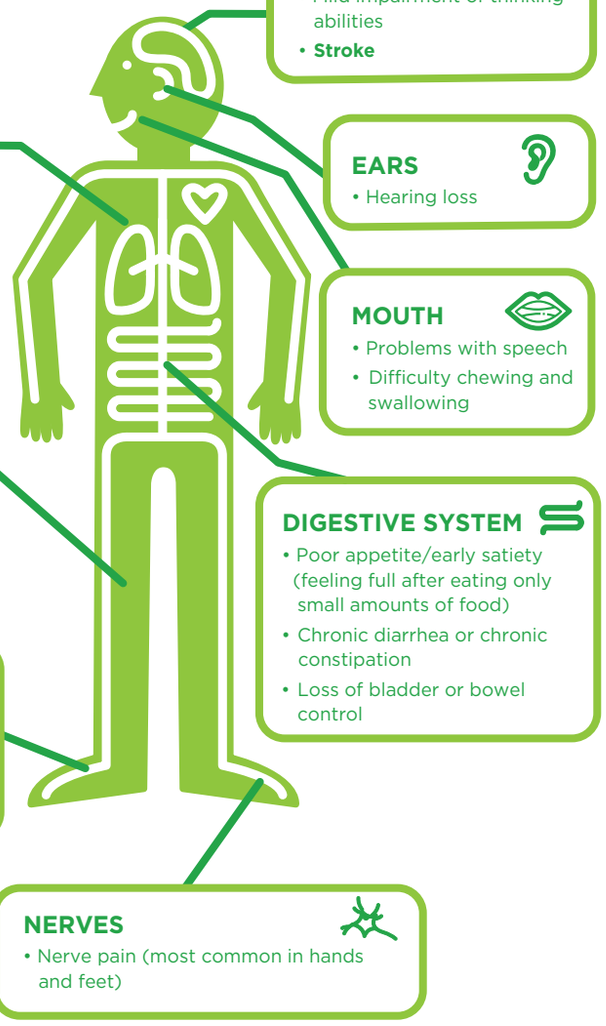
DIGESTIVE SYSTEM[2,3,10]
- Feeding difficulties
- Reduced gag reflex
- Difficulty swallowing
- Failure to thrive
- Loss of bladder or bowel control

HEART[2,3]
- Enlarged heart
- Abnormal heartbeat

LIVER[3]
- Enlarged liver

SKELETAL MUSCLE[2,3,10]
- Rapidly worsening muscle weakness
- Diminished muscle tone
- Floppy limbs
- Difficulty holding up head
- Motor delay (abnormally slow development of motor skills)
- Inability to sit up, roll over, or stand without assistance

LATE-ONSET POMPE DISEASE[2,11]



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

SKELETAL MUSCLE
- Weakness
- Exercise intolerance/fatigue
- Problems with walking (may result in wheelchair dependency)
- Winging of the shoulder blades
- Gait abnormalities
- Difficulty climbing stairs

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

BRAIN
- Mild impairment of thinking abilities
- **Stroke**

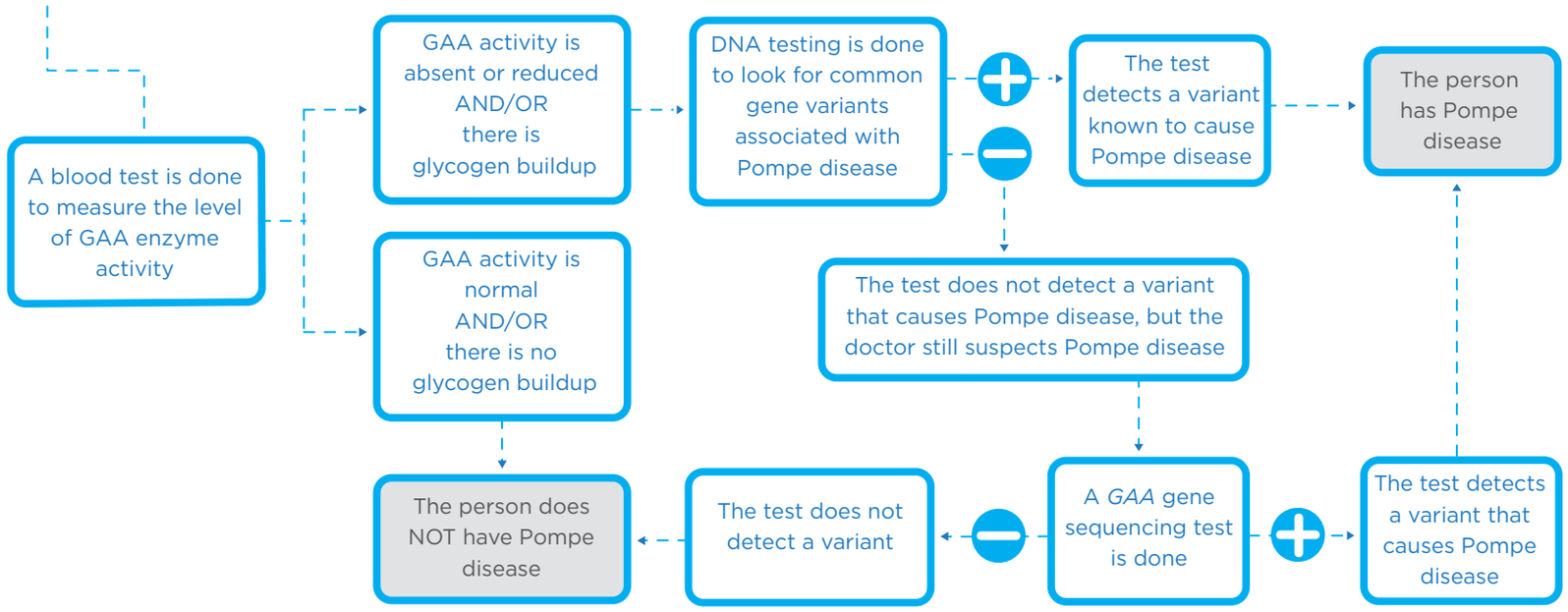
EARS
- Hearing loss

MOUTH
- Problems with speech
- Difficulty chewing and swallowing

DIGESTIVE SYSTEM
- Poor appetite/early satiety (feeling full after eating only small amounts of food)
- Chronic diarrhea or chronic constipation
- Loss of bladder or bowel control

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

A doctor suspects Pompe disease—here's an example of what can happen[12,13]

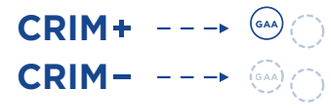


How is Pompe disease treated?

ERT

Currently, **enzyme replacement therapy (ERT)** is the only FDA-approved treatment for Pompe disease.[14]

ERT works by replacing the nonfunctioning or missing GAA with functioning GAA.[15]



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.[16]

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.[3]

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.[15]

More information about clinical research in Pompe disease can be found by visiting **clinicaltrials.gov** or **clinicaltrialsregister.eu**, or by talking with a health-care professional

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 and plays a vital role in the breathing process

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

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

EURORDIS
eurordis.org

Pompe Support Network
pompe.uk

Associazione Italiana Glicogenosi (AIG)
aig-aig.it

New Zealand Pompe Network
nzpompenetwork.weebly.com

United States

United Pompe Foundation
unitedpompe.com

Acid Maltase Deficiency Association
amda-pompe.org

Muscular Dystrophy Association
mda.org

National Organization for Rare Disorders
rarediseases.org

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Amicus Therapeutics Global Patient & Professional Advocacy

Please discuss any medical questions with a health-care professional (HCP).
If you would like to provide feedback on this educational resource or would like additional information please contact:
patientadvocacy@amicusrx.com.