A guide for people living with Pompe disease

UNDERSTANDING AND MANAGING

Digestive Tract Signs and Symptoms

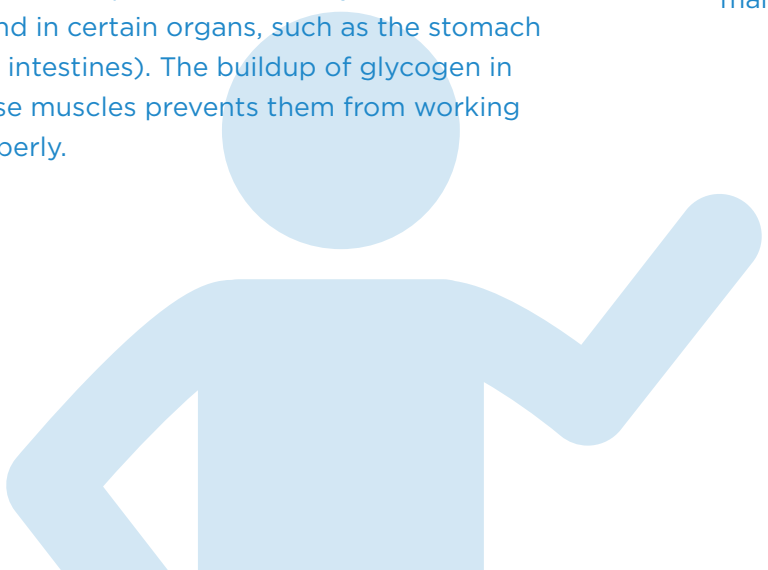
Amicus Therapeutics®

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

ABOUT POMPE DISEASE

Pompe disease is a rare, inherited lysosomal disease. It is caused by variants (also known as mutations) in a gene that carries instructions for the production of a lysosomal enzyme. Lysosomal enzymes are responsible for breaking down waste materials within cells. The specific enzyme affected in Pompe disease is called acid alpha-glucosidase (GAA). GAA is necessary for the conversion of a complex carbohydrate called glycogen into a simple sugar called glucose, which is the primary source of energy for most cells.[1,2]

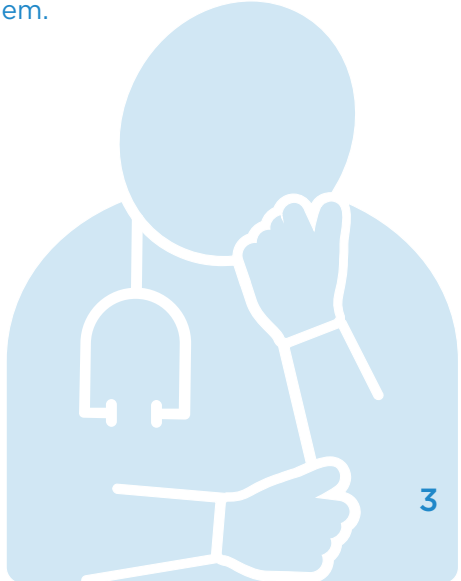
The lack of functioning GAA results in a buildup of glycogen within cells throughout the body, especially in the muscles. This happens in several different types of muscle: skeletal muscle (muscles that help move bones and joints), cardiac muscle (muscle tissue that forms the heart), and smooth muscle (a type of muscle that is not under a person's voluntary control; it is found in certain organs, such as the stomach and intestines). The buildup of glycogen in these muscles prevents them from working properly.



Because Pompe disease affects many different kinds of muscles, its signs and symptoms can impact many basic body functions, including the ability to move, breathe, eat and digest food.[2-4]

There are two main types of Pompe disease: infantile-onset Pompe disease (IOPD), which usually begins within the first year of life, and late-onset Pompe disease (LOPD), which appears later in childhood or during adolescence or adulthood. IOPD tends to be a more severe form of the disease than LOPD.[1] However, the severity of signs and symptoms, and how fast they get worse over time, can vary significantly from person to person in both forms.[2]

This brochure is designed to provide information about the digestive tract signs and symptoms that Pompe disease can cause, and to offer guidance on working with health-care professionals (HCPs) to manage them.



ABOUT THE DIGESTIVE SYSTEM

Understanding how the digestive system works can make it easier to understand why Pompe disease can cause digestive tract signs and symptoms.

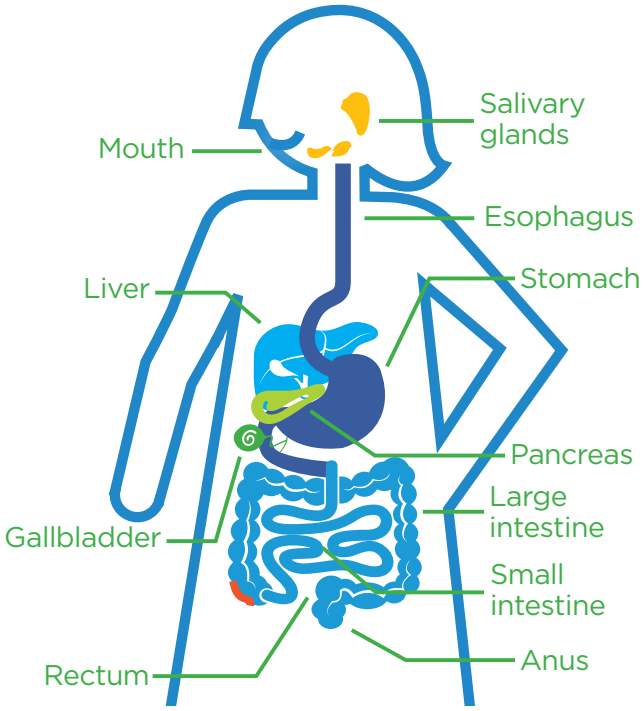
The digestive system consists of:[5]

- three solid organs (the pancreas, liver and gallbladder), and
- a series of connected hollow organs—the mouth, esophagus, stomach, small intestine, large intestine, rectum and anus—which form the digestive tract.

The digestive tract is designed to break food and liquid down into ever-smaller pieces so that the nutrients that the food contains can be absorbed by the body and the remaining matter can be eliminated as waste.[5]

Most parts of the digestive tract involve muscles that help mix food with digestive enzymes and keep moving it through the body.[5]

The digestive system and digestive process[5]



1. In the **mouth**, chewing and saliva help break food down into pieces that can be swallowed.
2. The smooth muscles of the **esophagus** push the pieces down to the **stomach**.
3. Acid and contractions of smooth muscle in the stomach walls help convert the pieces into a more liquid form.
4. This liquid is passed along to the **small intestine**, where nutrients are absorbed.
5. Smooth muscle in the **large intestine** (also called the colon) pushes the remaining undigested matter to the **rectum** and **anus** to be excreted.

HOW DOES POMPE DISEASE AFFECT THE DIGESTIVE TRACT?

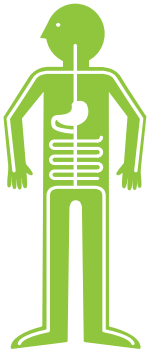
Pompe disease affects the functioning of muscles and organs throughout the body, including the skeletal and smooth muscles involved in eating and digesting food. When those muscles are not functioning properly, digestive tract signs and symptoms can result.

Digestive tract signs and symptoms of Pompe disease may include abdominal discomfort or pain, diarrhea, constipation, bloating, vomiting or acid reflux (heartburn).[3,4] Any of these problems can affect the ability to eat or drink normally and maintain proper nutrition.

The most common digestive tract signs and symptoms of Pompe disease are listed in the chart at the right. **However, signs and symptoms can vary among different people with Pompe disease; not everyone will have every sign and symptom listed.[2]**

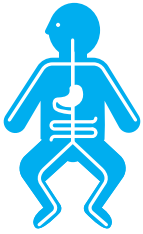
In addition to being uncomfortable or unpleasant, digestive tract signs and symptoms can have serious negative effects on health and well-being in people who live with Pompe disease.

Common signs and symptoms of Pompe disease



Many people with Pompe disease experience these signs and symptoms:

- Difficulty chewing or swallowing[2,6]
- Choking[2,6]
- Weakening jaw muscles[2]
- Chronic diarrhea[4]
- Constipation[7]
- Bloating[4]
- Abdominal pain[4]
- Acid reflux (heartburn)[4]
- Vomiting[4]



Infants and children may also experience signs and symptoms such as:

- Difficulty with sucking[2]
- Enlarged, uncoordinated tongue[2]
- Pooling of saliva and drooling[2]

PROBLEMS WITH NUTRITION

Good nutrition—including appropriate amounts of macronutrients (proteins, carbohydrates and fats) for energy, as well as micronutrients (vitamins and minerals) that are vital to many bodily functions—is required for the body to remain healthy and function well. Because digestive tract signs and symptoms can interfere with the ability to eat and obtain nutrients from food, they can affect growth and development in children[2] and can have a significant negative impact on overall health in adults and children alike.

For example:

- In infants and children with IOPD, weak facial muscles or an enlarged tongue can make biting, chewing, sucking and swallowing difficult, causing feeding difficulties that can result in a failure to thrive or gain weight.[2]
- Similarly, in those with LOPD, weakened jaw muscles and malfunctioning smooth muscle in the esophagus can make it difficult to chew or swallow food. This can result in insufficient daily calorie, vitamin and mineral intake and make gaining or maintaining weight (or even maintaining normal muscle and organ function) difficult or impossible.[2]

REDUCED QUALITY OF LIFE

Digestive tract signs and symptoms also can have a negative impact on health-related quality of life, sometimes to the point of limiting the ability to perform normal daily activities.[3,4] For example:

- Bowel incontinence (caused by smooth muscle weakness and anal sphincter dysfunction) and diarrhea occur significantly more frequently in adults with Pompe disease than in the general population[8,9] and may make people reluctant to leave their homes for any significant amount of time.[8] (It is estimated that up to 25% of those with LOPD suffer from bowel incontinence.[9])
- Nausea and vomiting can diminish the ability to enjoy food and may limit participation in social occasions or reduce the ability to keep up with daily responsibilities.[8]

Digestive tract signs and symptoms are very common in Pompe disease. However, treatment approaches are available that can help! This is why it's important for people who have Pompe disease to talk to their HCPs about any digestive tract signs and symptoms they are experiencing. Working with an HCP can help people who live with Pompe disease find ways to reduce these signs and symptoms and make them more manageable.

WORKING WITH HCPs TO MANAGE DIGESTIVE TRACT SIGNS AND SYMPTOMS

Keeping a signs and symptoms diary is one of the best ways to gather the information HCPs need to develop the best management approach. A diary can make it easier to identify triggers and habits that could be helpful to change, and can help HCPs select the specific treatment options that may be most effective for a given individual. **A detachable digestive tract signs and symptoms diary is provided at the end of this brochure that can be used to gather information to share with an HCP.**

HCPs may recommend several different approaches to managing digestive tract signs and symptoms and improving nutrition. Consulting with a registered dietitian or nutritionist may also be suggested. Registered dietitians and nutritionists can offer specialized guidance to help people with Pompe disease safely address digestive tract signs and symptoms via dietary changes, while also helping to ensure adequate and balanced nutrition. They can also suggest dietary strategies for special situations—for example, they may provide ideas for healthy and appropriate meals or snacks for children to have at school or when eating with friends.

Other specific management approaches to digestive tract signs and symptoms may include:

- **Special food preparations and supplements**
  Easy-to-swallow food preparations or vitamin and mineral supplements may be recommended for those who are unable to get sufficient essential nutrients through a normal diet.[2]

- **A high-protein, low-carbohydrate diet**
  Some research suggests that a diet high in protein (eg, from meat, fish or dairy products) and low in carbohydrates (eg, from breads or other starchy foods) may help slow muscle wasting caused by glycogen buildup in people with Pompe disease. A registered dietitian or nutritionist can help design a balanced diet that follows these principals while also providing proper amounts of other essential nutrients.[7,10,11]

- **Assisted feeding**
  For infants who are unable to suck from the breast or a bottle, and for children or adults who are severely underweight or have serious swallowing, choking or breathing problems, a feeding tube may be recommended to facilitate food intake and nutrition.[11]

CONCLUSION

Digestive tract signs and symptoms can significantly reduce quality of life and overall health in people who live with Pompe disease. However, dietary modifications and other available treatment options can help manage these signs and symptoms and reduce their impact. For this reason, it's very important for people who have Pompe disease to talk with an HCP about any digestive tract signs and symptoms they may be experiencing. Filling out the detachable signs and symptoms diary provided on the last page of this brochure and sharing it with an HCP can help start the conversation. (Remember—*always* consult an HCP before making any changes to diet, medications, or any other aspect of treatment.)

GLOSSARY

Acid alpha-glucosidase (GAA): an enzyme that breaks down the complex carbohydrate glycogen into a simple sugar called glucose

Acid reflux (heartburn): a condition in which fluid from the stomach flows backward into the esophagus

Anal sphincter: muscles at the end of the rectum that surround the anus and control the release of stool

Bowel incontinence: the loss of bowel control that results in the unexpected passing of stool

Cell: basic building block of all living things

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

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

Feeding tube: a device inserted into the stomach to supply nutrition for those who have trouble eating

Gene: the basic unit of heredity contained within each cell, made up of DNA, that is passed from parent to child

Gene variant: (also known as mutation) a change to the structure of a gene that can alter the gene's function, sometimes resulting in diseases or conditions

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

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

Smooth muscle: a type of muscle found in internal organs that is not under voluntary control

References **1.** Pompe Disease. Genetics Home Reference. National Institutes of Health. U.S. National Library of Medicine. https://ghr.nlm.nih.gov/condition/pompe-disease. Accessed May 25, 2020. **2.** Kishnani PS, Steiner RD, Bali D, et al. ACMG Work Group on Management of Pompe Disease. Pompe disease diagnosis and management guideline. *Genet Med.* 2006;8(5):267-288. **3.** McCall A, Salemi J, Bhanap P, Strickland LM, Elmallah M. The impact of Pompe disease on smooth muscle: a review. *J Smooth Muscle Res.* 2018;54:83-90. **4.** Bernstein DL, Bialer MG, Mehta L, Desnick RJ. Pompe disease: dramatic improvement in gastrointestinal function following enzyme replacement therapy. A report of three later-onset patients. *Mol Genet Metab.* 2010;101(2-3):130-133. **5.** Your digestive system and how it works. National Institutes of Health. National Institute of Diabetes and Digestive and Kidney Diseases. https://www.niddk.nih.gov/health-information/digestive-diseases/digestive-system-how-it-works. Accessed May 25, 2020. **6.** Barba-Romero MA, Barrot E, Bautista-Lorite J, et al. Clinical guidelines for late-onset Pompe disease. *Rev Neurol.* 2012;54(8):497-507. **7.** Al Jasmi F, Al Jumah M, Alqarni F, et al. MENA Pompe Working Group. Diagnosis and treatment of late-onset Pompe disease in the Middle East and North Africa region: consensus recommendations from an expert group. *BMC Neurol.* 2015;15:205. **8.** Karabul N, Skudlarek A, Berndt J, et al. Urge incontinence and gastrointestinal symptoms in adult patients with Pompe disease: a cross-sectional survey. *JIMD Rep.* 2014;17:53-61. **9.** Remiche G, Herbaut AG, Ronchi D, et al, Incontinence in late-onset Pompe disease: an underdiagnosed treatable condition. *Eur Neurol.* 2012;682:75-78. **10.** Esposito K, Improta M, Guigliano D. The nutritional approach to Pompe disease. *Acta Myol.* 2011;30(3):208-209. **11.** Cupler EJ, Berger KI, Leshner RT, et al. Consensus treatment recommendations for late-onset Pompe disease. *Muscle Nerve.* 2012;45(3):319-333.

RESOURCES

Interested in learning more about Pompe disease? Please contact the Amicus Global Patient & Professional team at **patientadvocacy@amicusrx.com** to request additional educational materials, including ***A Visual Guide to Understanding Pompe Disease.***

Other organizations and 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

Pompe Deutschland e.V.
mpompe.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

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**.

Digestive tract signs and symptoms diary

Use this detachable diary to collect information about digestive tract signs and symptoms to share with an HCP (space to note the HCP's recommendations for management is provided on the back).

Record signs and symptoms below		
Sign/ Symptom	**How often does it happen?** *(eg, once a week, several times a week, daily, other)*	**How much does it interfere with daily life?** *(eg, slightly, somewhat, a lot, other)*
Abdominal discomfort or pain		
Bloating		
Difficulty sucking, biting or chewing		
Difficulty swallowing		
Choking		
Acid reflux (heartburn)		
Nausea		
Vomiting		
Diarrhea		
Constipation		
Difficulty maintaining weight		
Other		

Record HCP management recommendations below	
Sign/ Symptom	**Recommendations for management**
Abdominal discomfort or pain	
Bloating	
Difficulty sucking, biting or chewing	
Difficulty swallowing	
Choking	
Acid reflux (heartburn)	
Nausea	
Vomiting	
Diarrhea	
Constipation	
Difficulty maintaining weight	
Other	

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