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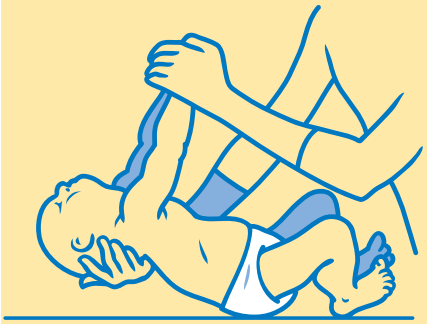
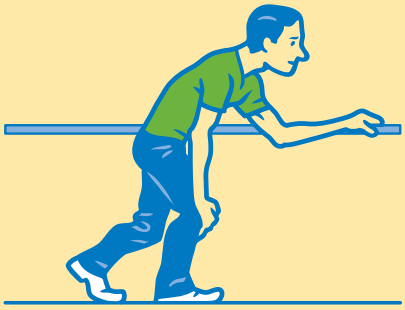
Pompe Disease Awareness Resource



Infants with Pompe disease often have weak head and neck control.

Muscle weakness and trouble breathing can make it difficult for adults with Pompe disease to climb stairs.



What is Pompe disease?

Pompe disease is a rare, hereditary, often fatal condition that disables the heart (in the infantile-onset form of the disease) and skeletal muscles (in both the infantile- and late-onset forms). Symptoms include weakness in the muscles closest to the body's midline (proximal muscles), difficulty with physical activity (such as climbing stairs or running), and difficulty breathing. When evaluated by a doctor, many patients are found to have elevated levels of creatine kinase (CK), an enzyme involved in muscle movement.

What causes Pompe disease?

Pompe disease is caused by mutations in a gene that makes the enzyme acid alpha-glucosidase (GAA). Normally, the body uses this enzyme to break down glycogen, a form of sugar used for energy. In Pompe disease—one of a number of glycogen storage diseases—gene mutations reduce or eliminate GAA, limiting the body's ability to break down glycogen. As a result, a buildup of glycogen is stored in muscle cells, causing muscles to weaken. Researchers have identified up to 300 different mutations in the GAA gene that can cause Pompe disease. The severity and age of onset are related to the degree of enzyme deficiency.

How is Pompe disease inherited?

Both parents of a child with Pompe disease must be carriers of a mutant gene for GAA. Each child of such parents will have a 25-percent chance of having Pompe disease, a 50-percent chance of being a carrier, and a 25-percent chance of neither having the disease nor being a carrier.

How common is Pompe disease?

Pompe disease affects approximately 1 in 40,000 births. It affects both sexes equally.

What are the forms of Pompe disease?

Infantile-onset Pompe disease involves a complete or nearly complete deficiency of GAA. Symptoms, which begin in the first months of life, include feeding problems, poor weight gain, muscle weakness, floppiness, poor head and neck control, breathing problems, and an enlarged heart. Many infants also have enlarged tongues. Most children with early-onset Pompe disease die because of heart or breathing problems within the first year of life.

Late-onset Pompe disease involves a partial deficiency of GAA. Onset ranges from the first years of life to the late sixties. The primary symptom is gradually worsening muscle weakness, which can progress to breathing problems. Late-onset Pompe disease often causes death due to respiratory failure over the course of several years.

POMPE DISEASE SYMPTOMS

Tear out this checklist to discuss symptoms with your doctor

Infantile-Onset:

- ☐ Feeding problems
- ☐ Poor weight gain
- ☐ Muscle weakness
- ☐ Floppiness
- ☐ Weak head and neck control
- ☐ Breathing problems
- ☐ Enlarged heart
- ☐ Heart conditions
- ☐ Enlarged tongue

Late-Onset:

- ☐ Progressive muscle weakness (for example, difficulty lifting a gallon of milk one month and difficulty getting up from a low seated position a few months later)
- ☐ Difficulty breathing
- ☐ Frequent respiratory infections
- ☐ Heart conditions
- ☐ Difficulty swallowing

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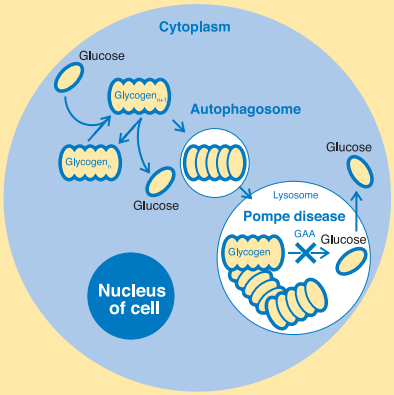
How is Pompe disease diagnosed?

Until recently, Pompe disease could be diagnosed by measuring GAA in a muscle biopsy. In 2006, a dried blood-spot test called a GAA activity assay was developed. The American Association of Neuromuscular and Electrodiagnostic Medicine and the Pompe Disease Diagnostic Working Group recommend giving the GAA activity assay to all patients with the symptoms of Pompe disease. Genetic analysis of the GAA gene provides definitive diagnosis. Experts also recommend screening all family members of people diagnosed with Pompe disease for the common genetic mutations.

Pompe disease mimics other neuromuscular diseases, often resulting in a delayed diagnosis. Some of the diseases that can be mistaken for early-onset Pompe disease include Werdnig-Hoffman disease (spinal muscular atrophy I); congenital muscular dystrophy; Danon disease; endocardial fibroelastosis; glycogen storage diseases IIIa (Debrancher deficiency/Cori or Forbes disease) and IV (branching enzyme deficiency/Andersen disease); hypothyroidism; idiopathic hypertrophic cardiomyopathy; mitochondrial/respiratory chain disorders; myocarditis; and peroxisomal disorders.

Some of the diseases that can be mistaken for late-onset Pompe disease include Duchenne and Becker muscular dystrophies; Danon disease; glycogen storage diseases IIIa (Debrancher deficiency/Cori or Forbes disease), IV (branching enzyme deficiency/Andersen disease), V (muscle phosphorylase deficiency/McArdle disease), and VII (muscle phosphofructokinase deficiency/Tauri disease); mitochondrial myopathies; myasthenia gravis; polymyositis; rheumatoid arthritis; rigid spine syndrome; scapuloperoneal syndromes; and spinal muscular atrophy.



In Pompe disease, gene mutations reduce or eliminate GAA, limiting the body's ability to break down glycogen. As a result, a buildup of glycogen is stored in muscle cells, causing parts of those cells (lysosomes) to swell and muscles to weaken.

What treatments are available?

People with Pompe disease are best treated by a team of specialists— a neurologist, a cardiologist, a pulmonologist, a gastroenterologist, and a physical therapist—who are familiar with the disease.

In clinical trials, enzyme replacement therapy has been shown to reduce excess glycogen, decrease heart size, maintain normal heart function, and improve or stabilize muscle function, tone, and strength in about one-third of infantile-onset patients.

A drug called alglucosidase alfa (Myozyme) received approval from the U.S. Food and Drug Administration (FDA) in 2006 for the treatment of infantile-onset Pompe disease. Another alglucosidase alfa drug, Lumizyme, was approved for late-onset Pompe disease in 2010. Both drugs are administered intravenously and can be costly. Patient-assistance programs may be available.

Use of Lumizyme requires patient enrollment in a special program as well as training for both the physician and infusion center that administers the drug.

What research is being done into Pompe disease?

Much Pompe-related research focuses on finding better ways to prevent, treat, and ultimately cure this disorder. For more information on clinical trials, visit **1.usa.gov/15iS5jF** and **1.usa.gov/173056q**.

Organizations Offering Support for Families with Pompe Disease:

Acid Maltase Deficiency Association (AMDA)
P.O. Box 700248
San Antonio, TX 78270
tianrama@aol.com
www.amda-pompe.org
Tel: 210-494-6144
Fax: 210-490-7161

Association for Glycogen Storage Disease
P.O. Box 896
Durant, IA 52747
info@agsdus.org
www.agsdus.org
Tel: 563-514-4022
Fax: 563-785-6038

Muscular Dystrophy Association
3300 East Sunrise Drive
Tucson, AZ 85718
mda@mdausa.org
www.mda.org
Tel: 520-529-2000
800-572-1717
Fax: 520-529-5300

United Pompe Foundation
5100 N. Sixth Street #119
Fresno, CA 93710
www.unitedpompe.com
david@unitedpompe.com
Tel: (559) 227-1898
Fax: (559) 227-1898

Sources: Dubrovsky A, Corderi J, Karasarides T, et al. Pompe disease, the must-not-miss diagnosis: A report of 3 patients. *Muscle Nerve* 2013; 47(4):594-600; National Institute of Neurological Disorders and Stroke. Pompe Disease Information. Last Updated February 20, 2013. Available at: **http://www.ninds.nih.gov/disorders/pompe/pompe.htm**; Vissing J, Lukacs Z, Straub V. Diagnosis of Pompe Disease: Muscle Biopsy vs Blood-Based Assays. *JAMA Neurol*. 2013; 70(7):923-7; Kishnani PS, Steiner RD, Bali D, et al. Pompe disease diagnosis and management guideline. *Genetics in Medicine* 2006; 8(5):267-288; Rajan DS, Abdel-Hamid H. Child neurology: Pompe disease: new horizons. *Neurology* 2012; 79(23):E197-200; Kroos M, Pomponio RJ, van Vliet L, et al. GAA Database Consortium. Update of the Pompe disease mutation database with 107 sequence variants and a format for severity rating. *Hum Mutat*. 2008; 29:E13–E26.

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☐ Yes! I'm interested in receiving more information on Pompe disease from Genzyme.

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☐ Contact me via email ☐ Contact me via telephone ☐ Contact me via U.S. mail

1.Which category best describes you?

A. ☐ Person with a neurologic disorder
B. ☐ Caregiver/friend/family member of person with neurologic disorder
C. ☐ Other

2.Which neuromuscular disorder/symptoms do you have?

A. ☐ Congenital muscular dystrophy
B. ☐ Duchenne and Becker muscular dystrophies
C. ☐ Endocardial fibroelastosis
D. ☐ Glycogen storage diseases
E. ☐ Idiopathic hypertrophic cardiomyopathy
F. ☐ Limb girdle muscular dystrophy (LGMD)
G. ☐ Mitochondrial myopathy
H. ☐ Mitochondrial/respiratory chain disorders
I. ☐ Myasthenia gravis
J. ☐ Myocarditis
K. ☐ Polymyositis
L. ☐ Pompe disease
M. ☐ Rheumatoid arthritis
N. ☐ Rigid spine syndrome
O. ☐ Scapuloperoneal syndromes
P. ☐ Spinal muscular atrophy

3.How long ago was the neurologic diagnosis made?

A. ☐ Less than 3 months
B. ☐ 3-12 months
C. ☐ 1-3 years
D. ☐ 4-10 years
E. ☐ More than 10 years

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