

About Pompe Disease

What is Pompe disease?

Pompe disease (also known as acid maltase deficiency or glycogen storage disease type II) is a rare and often fatal neuromuscular disorder affecting fewer than 10,000 infants, children and adults worldwide. Pompe disease is also a lysosomal storage disorder caused by a deficiency or absence of an enzyme that occurs naturally in cell lysosomes. This defect causes glycogen to accumulate within cell lysosomes, eventually resulting in lysosomal breakdown and consequently, progressive muscle damage.

What are the signs and symptoms of Pompe disease?

Pompe disease manifests as a continuous spectrum, ranging from a rapidly progressive and often fatal, infantile-onset disease to a steadily progressive, debilitating late-onset disease. The disease primarily manifests as deterioration of skeletal and respiratory function and cardiac function in infants. Clinical manifestations can present at any age.

Infantile-onset Pompe disease: Babies with this form of the disease typically present with symptoms during the first few months of life. Infantile-onset Pompe disease is more rapidly progressive and life-threatening. Without treatment, an infant with Pompe usually will become seriously ill and die from cardiac or respiratory complications before reaching age one. Common symptoms of infantile-onset Pompe disease include severe and rapidly progressive muscle weakness, generalized hypotonia, delayed motor development, cardiomegaly/cardiomyopathy, respiratory distress and feeding difficulties. Most babies with infantile-onset Pompe disease eventually require some type of mechanical ventilation to help them breathe, however, the use of a ventilator does not prevent early mortality.

Late-onset Pompe disease: Late-onset patients may present with muscle or respiratory weakness any time during childhood or adulthood. There is vast variability in the number, severity, and type of symptoms a patient experiences. These symptoms may initially appear suggestive of more common disorders such as the different types of muscular dystrophy. Many patients progress to respiratory failure and require mechanical ventilation to assist with breathing. Some may require mobility aids such as canes, walkers or wheelchairs. Common signs and symptoms of late-onset Pompe disease include progressive muscle weakness in the hips and legs, gradual loss of ability to walk, run or jump, respiratory distress, orthopnea, morning headaches, daytime sleepiness, and difficulty gaining or maintaining weight. Scoliosis and joint contractures may occur.

What causes Pompe disease?

Pompe disease is caused by a deficiency of an enzyme known as acid alpha-glucosidase (GAA). The enzyme is responsible for breaking down glycogen, a form of sugar stored in muscle cells throughout the body. The enzyme deficiency leads to excessive accumulation of glycogen in cells in the body, particularly in the muscles. The build up of glycogen causes lysosomes within muscle fibers to expand and their contents to leak, leading to muscle weakness that becomes more severe over time.

Who is at risk for Pompe disease?

Pompe disease is a genetic disorder passed from parent to child. Because Pompe is an autosomal recessive disorder, a child must receive two copies of the defective gene, one from each parent, in order to inherit the disease. If both parents are carriers of the defective gene, there is a 25 percent chance with each pregnancy that a child will develop Pompe disease.

Based on studies done in The Netherlands and in the United States, it is estimated that Pompe disease occurs in 1 in 40,000 live births worldwide. Pompe disease affects both males and females equally. It affects all ethnic groups, although it does appear at a higher incidence among African-Americans and in individuals of Chinese descent.

How is Pompe disease diagnosed?

Pompe disease can be difficult to diagnose because many of the symptoms are similar to those found in other diseases. Symptoms may also develop slowly and disease progression can vary widely, though the infantile-onset form of Pompe is more homogeneous and rapidly progressive. Given the rarity of the disease, many physicians have not encountered a patient with Pompe disease before. As a result, physicians may need to first eliminate other possible causes before beginning to consider a disorder as rare as Pompe disease.

A conclusive diagnosis of Pompe disease generally requires an enzyme assay test that demonstrates that the patient has deficient enzyme ([acid alpha-glucosidase, "GAA"](#)) activity. This is determined by performing tests on a tissue (muscle, skin) or blood sample to verify that the patient's GAA activity is low or absent. Infantile-onset patients often display total or near total deficiency of the normal enzyme activity levels in skin cells; late-onset patients generally display a wide range of enzyme activity (up to 40% of the normal enzyme activity levels when measured in skin cells).

Prenatal screening is also available for couples who may be at risk for having a child with Pompe disease. Two procedures may be used to provide samples for enzyme analysis to identify Pompe disease, amniocentesis and chorionic villus sampling (CVS). Couples should speak to their doctor to determine if prenatal screening is warranted. A referral to a genetic counselor may be recommended.

How is Pompe disease treated?

A new enzyme replacement therapy (ERT) called Myozyme[®] (alglucosidase alfa) received U.S. Food and Drug Administration (FDA) approval on April 28, 2006. Myozyme is the first and only approved drug in the United States and Europe for the treatment of Pompe disease. ERT is intended to replace the deficient enzyme that causes Pompe disease. The replacement enzyme is genetically engineered and it is administered intravenously.

Myozyme is indicated for use in patients with Pompe disease (GAA deficiency). Myozyme has been shown to improve ventilator-free survival in patients with infantile-onset Pompe disease as compared to an untreated historical control, whereas use of Myozyme in patients with other forms of Pompe disease has not been adequately studied to assure safety and efficacy. The product labeling includes a **boxed warning** increasing the prominence of information about the potential risk of hypersensitivity reactions. The boxed statement includes the following information: "Life-threatening anaphylactic reactions, including anaphylactic shock, have been observed in patients during Myozyme infusion. Because of the potential for severe infusion



reactions, appropriate medical support measures should be readily available when Myozyme is administered.”

The most common serious treatment-emergent adverse events (regardless of relationship) observed in clinical studies with Myozyme were pneumonia, respiratory failure, respiratory distress, catheter-related infection, respiratory syncytial virus infection, gastroenteritis, and fever.

See full prescribing information for complete product information.

In addition to Myozyme, are there other ways for patients to manage Pompe disease?

In addition to drug therapy and depending on the level of severity of their disease, many patients with Pompe disease may benefit from physical therapy, occupational therapy, speech therapy, respiratory therapy, nutritional monitoring, and psychosocial therapy.

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