



Pompe Disease: What You Need to Know^{©2010}

"Extraordinary Measures" is a touching movie released in January of 2010 about one family's experience with Pompe disease. The movie is based on the true story of New Jersey entrepreneur John Crowley -- played by Brendan Fraser -- who raised millions in capital and started a biotech company to develop a life-saving drug for his two young children, both of whom suffer from Pompe disease, a rare genetic disease. Harrison Ford plays an unconventional scientist whose discoveries are thought to be the key to finding a cure.

According to an article in the January 14th *Chicago Tribune* (<http://www.chicagotribune.com/entertainment/chi-0114-harrison-fordjan14,0,7594433.story>), "Facts were tweaked, the timeline was condensed and multiple scientists were rolled into one character, played by Ford. Press materials say the film is "inspired by" real events. Despite changes, Ford feels that "we were truthful to the necessary elements."

For anyone seeing the movie, please keep in mind that the movie is *based* on real events, but not entirely factual. For that reason, we have provided medical information about Pompe disease here.

What is Pompe disease?

The name Pompe (**pronounced "pom-PAY"** in the United States or "POM-puh" in Europe) comes from the Dutch pathologist J.C. Pompe, who first described an infant with the disease in 1932. Pompe disease is a genetic lysosomal storage disorder that affects about 1 in 40,000 individuals. Pompe disease is also known as Acid Maltase Deficiency or Glycogen Storage Disease type II. This condition is caused by the buildup of a complex sugar called glycogen in the body's cells. The accumulation of glycogen in certain tissues, especially muscles, impairs their ability to function normally. This can be life-threatening when the breathing and heart muscles are affected.

Pompe disease is caused by mutations in the GAA gene located on chromosome 17. This gene normally provides instructions to produce an enzyme called alpha-glucosidase (also called acid maltase). The severity of the disease and the age of onset are related to the degree of enzyme deficiency. There is an infantile-onset and late-onset form of Pompe disease.

The **infantile-onset type of Pompe disease** is severe and onsets in the first few months of life. The rapid development of Pompe-related health problems occurs from complete or nearly complete deficiency of alpha-glucosidase (GAA). About one-third of all individuals with Pompe disease have the infantile-onset form. Symptoms include:

- Poor feeding
- Failure to thrive (inability to gain weight and grow at the usual rate)
- Muscle weakness (myopathy)
- Poor muscle tone (hypotonia)

- Poor or absent reflexes
- Breathing problems
- Inability to hold head up or move normally
- Difficult swallowing
- Enlarged tongue (macroglossia)
- Enlarged liver
- Enlarged heart
- Early death caused by heart or breathing complications (often by the age of 1 or 2)

Some infants have an atypical form of infantile-onset Pompe disease, where symptoms begin later in the first year of life. In this atypical form, damage to the heart muscle progresses more slowly, and they may survive beyond their first birthday.

The **late-onset form of Pompe disease** is milder than the infantile form, and usually the heart is not affected. This is because there is only partial deficiency of GAA. Symptoms may not begin until childhood, adolescence, or adulthood (as late as the seventh decade). About two-thirds of all individuals with Pompe disease have the late-onset form. Symptoms include:

- Slow, progressive muscle weakness, especially in the legs and trunk, including the muscles that control breathing
- Difficulty walking
- Difficulty climbing stairs
- Difficulty raising arms
- Breathing problems, particularly when lying down
- Fatigue
- Decreased life expectancy due to critical muscle failure
- Abnormal spine curvature (lumbar lordosis and/or scoliosis)

How is Pompe disease inherited? Can I be a carrier? How do I find out?

Pompe disease is inherited in an autosomal recessive manner, which means that two copies of an altered (mutated) gene, one inherited from each parent, is necessary to have the condition. Males and females are equally likely to be affected. Carrier parents have a 1 in 4 or 25% chance with each pregnancy, to have an affected child, a 50% chance to have a child who is a carrier, and a 25% chance to have a child who is not affected nor a carrier. Parents who have had a child with Pompe disease are obligate carriers. Other close relatives may also be carriers depending on their relation to the individual with Pompe disease. Carriers do not have any health problems as a result of being a carrier.

When you visit a Lysosomal Storage Disease Center (LSDC) or genetic center, the genetic counselor or geneticist will take a detailed family history of your immediate and extended family for several generations. This information will help identify anybody who might be at risk for Pompe disease so he or she can get testing and treatment. The identification of at risk family members is determined by looking at the way in which people are related.

To schedule an appointment or speak with a member of our lysosomal storage disease team, call 404-778-8565 or 800-200-1524. You can also email our genetic counselor who specializes in Pompe Disease at ebotha@genetics.emory.edu .

No one in my family has Pompe disease. Can I still be a carrier?

Yes. Pompe disease is seen in approximately 1 in 40,000 individuals. The rate varies slightly by ethnicity. Based on the 1 in 40,000 figure, the chance for someone without a family history to be a carrier is about 1 in 100.

Although Pompe disease can be seen in all racial and ethnic groups, it is more common in some groups than others. In the African-American population approximately 1 in 14,000 individuals are affected, while in the Caucasian population approximately 1 in 100,000 individuals have the infantile-onset form and 1 in 60,000 have the late-onset form. Studies have also shown that there are more cases of infantile-onset Pompe disease in Southern China and Taiwan.

Can Pompe disease be diagnosed before a baby is born?

Prenatal diagnosis is available for families who already have one affected child with Pompe disease if the disease-causing mutation has been previously identified. Genetic counseling is highly recommended for couples before achieving a pregnancy to discuss testing options. Standard prenatal chromosome analysis (from an amniocentesis or CVS) does NOT detect Pompe disease.

How many people around the world have Pompe disease?

It is estimated that between 5,000 and 10,000 have Pompe disease.

How is Pompe disease diagnosed?

A diagnosis of Pompe disease is first suggested by a person's symptoms such as muscle weakness, fatigue, and breathing problems. In adults, Pompe disease may be confused or misdiagnosed as other chronic muscle diseases such as multiple sclerosis, limb girdle muscular dystrophy and polymyositis. In infants and children, Pompe disease may be confused with other types of muscular dystrophy. Confirmation of the diagnosis can be made by examining the activity of acid alpha glucosidase in cultured skin cells, muscle, or blood. In Pompe disease, there will be reduced or absent activity of this enzyme. Children afflicted with infantile-onset typically have lower than 1% of normal GAA enzyme activity levels. Individuals afflicted with later-onset have lower than 40% of normal GAA enzyme levels.

Testing for genetic mutations in the GAA gene can also help to confirm a diagnosis. Carriers are most reliably identified via genetic mutation analysis.

Who takes care of patients with Pompe disease? An individual with Pompe disease needs specialized medical care from a team of specialists including geneticists, metabolic specialists/dietitians, cardiologists, pulmonologists, orthopedists, physical, speech, and occupational therapists, genetic counselors, and neurologists. The combination of specialists may vary depending on the patient. In addition, a specialized diet and exercise program may help adult-onset individuals with Pompe disease along with frequent medical evaluations as the disease progresses.

Is there a cure or treatment for Pompe Disease (acid maltase deficiency)?

At this time there is no cure for Pompe disease. There is one FDA approved treatment called Myozyme which is an enzyme replacement therapy produced by Genzyme Therapeutics. Enzyme replacement therapy (ERT) works by replacing some of the missing enzyme in Pompe disease patients' bodies through lifetime IV infusions of Myozyme every other week. ERT improves the symptoms of Pompe disease in many patients but not all. In some patients ERT will decrease heart size, maintain normal heart function, improve muscle function, tone, and strength, and reduce glycogen accumulation.

Several research studies are working on other types of therapies such as chaperone therapy, more effective enzyme replacement therapies, and ways to make current enzyme replacement more effective including small scale gene therapy and immune response decreasing treatments. Emory participates in several of these clinical trials. For more information on research trials for Pompe disease go to www.clinicaltrials.gov and type in the search term "Pompe disease".

What is the life expectancy for an individual with infantile-onset and late-onset Pompe disease?

Babies who are not treated with ERT die from cardiac failure or a respiratory infection before the age of 1 or 2.

The prognosis for an individual with late-onset Pompe disease depends on the age of onset. Generally speaking, the later the age of onset of symptoms, the slower the progression of the disease. Overall the prognosis depends on the extent of respiratory muscle involvement.

What is Emory doing to help treat patients with Pompe disease?

The Emory Lysosomal Storage Disease Center in the Department of Human Genetics is committed and devoted to remaining on the cutting edge of research and treatment, providing comprehensive and compassionate care for all of our patients affected by Pompe disease. Accordingly, we participate in many Pompe disease research trials and are working with the Centers for Disease Control and Prevention (CDC) to bring newborn screening for Pompe disease for the state of Georgia. Newborn screening (NBS) is a test done from a small blood sample on a newborn in the first 24-48 hours of life to test for inherited disorders.

What can I do to help support Emory and their work with patients with Pompe disease?

The Emory Lysosomal Storage Disease Center is seeking additional funding and support to work toward newborn screening for Pompe disease in Georgia. The earlier in life that patients with Pompe disease are diagnosed, the sooner treatment can begin leading to a better outcome.

Who do I contact with questions about research programs for Pompe disease?

Someone is always available to discuss research projects for Pompe disease with interested individuals. To speak with a member of our lysosomal storage disease team, call 404-778-8565 or 800-200-1524. You can also email our genetic counselor who specializes in Pompe Disease at ebotha@genetics.emory.edu.

Where can I call to learn more about Pompe disease? A Lysosomal Storage Disease Center near you can be a great resource. The Emory Lysosomal Storage Disease Center can be reached at (404) 778-8518 or (800) 200-1534. Genzyme Medical Information (800-200-1534) can provide accurate information on enzyme replacement therapy for Pompe disease. There are several websites for additional information:

- **Pompe Community** (information provided by Genzyme Therapeutics)
http://www.pompe.com/patient/pc_eng_pt_main.asp
- **Acid Maltase Deficiency Association (AMDA)**
<http://www.amda-pompe.org>
- **Association for Glycogen Storage Disease**
<http://www.agsdus.org>
- **National Organization of Rare Diseases or NORD**
www.Rarediseases.org
- **Hide & Seek Foundation for LSD Research**
http://www.hideandseek.org/index.php?option=com_content&task=view&id=157&Itemid=75
- Information on **research for Pompe disease** can be found at:
<http://clinicaltrials.gov/search/term=Pompe%20Disease>
- Other information about the **treatment of Pompe disease** can be found at:
http://www.pompe.com/healthcare/treating/pc_eng_hc_treating.asp
- A father of a **Pompe patient's perspective** on the development of treatment for Pompe disease
<http://pompestory.blogspot.com/>

Where do I go for more information on the disease, treatment, and medical care for Pompe Disease?

The best way to obtain the most accurate, current, clear, and comprehensive information is to be seen at a lysosomal storage disease center (LSDC). LSDCs are genetic centers that specialize in the treatment of patients with lysosomal conditions such as Pompe disease. At most centers the affected individual will see a clinical geneticist, genetic counselor, and nurse who work as a team to answer your questions, discuss testing, identify your at risk family members, and develop a comprehensive evaluation and treatment plan. The LSDC will work with your family's current doctors to organize the treatment, tests, and specialists needed. There is at least one lysosomal storage disease center in every region of the United States. Please feel free to call the Emory Lysosomal Storage Disease Center at 800-200-1524 to locate a center near you. A partial listing of LSDCs is below.

Lysosomal Storage Disease Centers

British Columbia Institute, 604-875-2830

Cedars-Sinai Medical Center Lysosomal Storage Disease Center, (310) 423-9914
<http://www.csmc.edu/3574.html>

Cincinnati STAR Center for Lysosomal Diseases
<http://www.cincinnatichildrens.org/svc/alpha/l/lysosomal/>

Duke University Medical Center
<http://medgenetics.pediatrics.duke.edu/>

Emory University Lysosomal Storage Disease Center, 800-200-1524
http://genetics.web.emory.edu/LSDC/lfdc_index.php

The Hospital for Sick Children in Toronto, 416-813-8367

MGH Lysosomal Disease Program
<http://www.mghlysosomal.org/english/view.asp?x=1>

Mt. Sinai School of Medicine's lysosomal disease centers
http://www.mssm.edu/genetics/genetic_diseases.shtml

Royal Manchester Children's Hospital (UK), 44-161-727-2137

University of California San Francisco/Stanford, 415-476-5048
<http://medschool.ucsf.edu/lysosomal/fabry/>

University of Massachusetts Lysosomal Storage Disorders Treatment and Research Center
<http://www.umassmed.edu/entities/ldtr/>

University of Minnesota Bone Marrow Transplant and Gene Therapy Centers
<http://www.peds.umn.edu/Centers>

University of North Carolina at Chapel Hill, Division of Genetics and Metabolism
<http://www.med.unc.edu/>

University of Pittsburgh 800-334-7980
<http://www.hgen.pitt.edu/index.php>

University of Washington-CHRMC Lysosomal Disease Program, 206-616-1840
<http://www.uwmedicine.org/>