

# Pompe Disease

By Dawn Harris Kendall

Elizabeth Nunnery takes her infant daughter, Zoe, to the hospital at 8:30 in the morning. A nurse verifies Zoe's medical information and hooks Zoe up to machines monitoring her blood oxygen level, heart rate, and respiration rate. They take Zoe's blood pressure and temperature. A numbing cream is put on Zoe's skin, above the port that she had surgically implanted in September. A doctor cleans and sterilizes the port, a needle is inserted, and everything is taped into place. Around 11 o'clock, the IV bag is placed on a pole and Zoe begins to receive her enzyme replacement. Six and a half hours later, Zoe is unhooked and sent home. They will repeat this process every two weeks for the rest of Zoe's life.

Dawn Kendall's husband, Chuck, picks her up from the chair and helps her walk to the bathroom. He helps her change into pajamas and he walks her to the couch. He removes her socks and picks her feet up so that she can lie down. He positions her so that she will not fall off the furniture. Usually Kendall can crawl up the stairs to the bedroom, but today is a bad day. Kendall cannot walk without assistance. She has diminished lung capacity. She gets headaches from straining the muscles in her shoulders and neck as she struggles to move. She is still recovering from misdiagnosis and medication that caused additional health issues, including high blood pressure, low blood sugar, anemia, Vitamin D deficiency, hot flashes, cold sweat, and digestive problems. She can no longer get out of chairs, lift her legs, or raise her arms straight over her head.

Zoe Nunnery and Dawn Kendall have Pompe disease. There is no cure.

## What is Pompe Disease?

Pompe disease is a rare, fatal illness affecting the heart and muscles. Pompe is caused by a defect in the gene that produces the enzyme alpha-glucosidase (GAA) (also known as acid maltase). This enzyme breaks down glycogen to be used as energy for the body. Pompe patients cannot properly process glycogen. Excessive amounts of glycogen accumulate in the muscle cells, eventually overtaking their function. The cells then break open, causing irreversible damage to the muscles.

Pompe disease is a recessive genetic disorder. Both parents must carry the gene for it to be transmitted to a child. Mutations in the gene determine when and how the active illness will appear. Studies indicate that Pompe disease occurs in 1 in 40,000 live births worldwide. The number of people with Pompe disease is estimated at approximately 5,000-10,000 patients. Pompe disease affects both men and women.

There is no cure for Pompe disease. Most patients die from cardiac or respiratory failure.

There are two classifications for Pompe disease: early onset (infantile) and late onset.

## Early Onset

Early onset is characterized by a nearly-complete deficiency of the enzyme. Most babies born with Pompe disease die from cardiac or respiratory complications before their first birthday. Symptoms appear almost immediately after birth. Babies often appear "floppy" due to muscle weakness. The heart and liver are enlarged. Respiratory problems occur and a ventilator will eventually be required to assist breathing. Many infant patients have enlarged tongues, which impacts feeding, swallowing, and weight gain. All major organs may be impacted. Regular development, such as rolling over, crawling, or sitting up, is delayed, if possible at all. The heart progressively thickens and enlarges and respiratory distress is common.

Early onset patients may benefit from enzyme replacement therapy (ERT). In 2006, the Federal Drug Administration (FDA) approved an ERT made by the pharmaceutical company Genzyme. The ERT infuses a man-made version of the enzyme directly into the veins of patients.

Zoe Nunnery was born prematurely on April 9, 2009. She was diagnosed with early onset Pompe Disease in July of that year. The geneticist at the hospital offered information about the only treatment option—ERT. Elizabeth and Shane Nunnery, Zoe’s parents, struggled with the decision. According to Elizabeth, “My husband and I were so torn on what to do. Do we try the IV therapy to prolong her life or do we let nature take its course and just keep her as pain-free as possible?” They decided to try the ERT, but their insurance did not want to pay for a treatment that would not definitively change the course for a terminally ill child. Only after prolonged discussions did the insurance company agree to cover the cost of Zoe’s treatment.

## **Late Onset**

Late onset is the result of a partial enzyme deficiency. The heart is not usually enlarged and may not be impacted at all. Symptoms and severity can vary widely from one patient to another. The primary symptom is muscle weakness. Many patients walk with a “waddle” as their body compensates for weakness in the torso. Reflexes and balance are affected and patients may fall frequently. Basic daily activities become limited and ultimately lost, including bending, reaching overhead, climbing stairs, or rising from a seated position. The patient may experience lower back pain and curvature of the spine. Breathing may become difficult, leading to headaches, fatigue, and sleep apnea. In advanced cases, the diaphragm will become paralyzed. Infections such as bronchitis and pneumonia frequently occur. The patient may have difficulty maintaining weight—gaining weight because of lack of mobility or losing weight due to problems chewing or swallowing. All of these conditions worsen over time.

Unless they participated in Genzyme’s early clinical trials, late onset patients have no treatment options. Neurology and pulmonary specialists can treat the symptoms which result from the disease, but not slow the progression of it. A diet low in carbohydrates, which introduce glycogen into the body, and high in protein is sometimes recommended; however, patients with difficulty chewing and swallowing may require a feeding tube to keep their weight stable. Because patients have such limited mobility and damage to muscles is permanent, doctors discourage intense exercise. Temporary respirators are often used at night to keep oxygen levels stable and allow the patient to have a restful night’s sleep.

Patients with late onset deteriorate at varying rates, depending upon the age of onset and the progression of the disease.

## **Diagnosis**

Because doctors do not include rare illness markers in routine tests, Pompe disease is usually misdiagnosed. Pompe symptoms are similar to other neuromuscular illnesses, including muscular dystrophy, multiple sclerosis, arthritis, amyotrophic lateral sclerosis (Lou Gehrig's disease), or myositis. Patients with respiratory symptoms are often misdiagnosed with chronic obstructive pulmonary disease (COPD). Treatments for these illnesses can actually worsen the symptoms for Pompe patients. Additionally, Pompe symptoms may be dismissed as part of the normal aging process.

A diagnosis of Pompe disease may be confirmed by a simple blood test that measures the level of acid maltase in the system; this test is 100% accurate but very few doctors know about it. Muscle biopsies may be used to determine the buildup of glycogen in the muscle cells.

Even with an accurate diagnosis, many Pompe patients have to take the initiative to find treatment options for themselves. Most doctors have not heard of Pompe disease and do not know how to proceed.

## **Patient Care**

Research is ongoing for treatment of Pompe disease. Genzyme's ERT is the only available therapy for Pompe disease. It slows the progression of the illness, but does not cure it.

The ERT is given through infusion—intravenously—much like chemotherapy is given to cancer patients. The ERT has been proven to slow progression of the illness, reduce heart size, improve both heart and muscle function, and reduce glycogen accumulation in the cells. Pompe patients who benefit from the ERT require an infusion every two weeks for the duration of their lives. The cost of the ERT is approximately \$300,000 per year. Because of the cost and complexity of creating the enzyme, it is currently available only to children under the age of 17 and to patients participating in the company's clinical trials. Genzyme continues to work toward making its ERT available in larger quantities, thus also offering it to late onset patients. The FDA is currently considering a larger-scale production of the enzyme for commercial use. The same drug has been approved for use in approximately 40 other countries.

Amicus Therapies had initiated early phase clinical trials for an oral chaperone therapy involving the use of small molecules that selectively bind to and stabilize proteins in cells. Those trials were suspended because of reactions experienced by the participants.

ZyStor Therapeutics is beginning clinical trials for another oral chaperone therapy that relies on an alternative approach to getting the enzyme into the patient's system.

All efforts to treat Pompe disease fall under the FDA's Orphan Drug Act. The Orphan Drug Program was developed to address treatments for diseases that impact less than 200,000 people in the United States. Orphan designation qualifies the producer for tax credits and marketing incentives. Because there is no expectation that costs of research and development of the orphan drug can be recovered by sales of the drug in the United States, an orphan drug designation grants the maker a seven-year exclusive marketing period for that drug.

Specific symptoms are treated individually and patients will have a team of medical specialists supporting their care.

## **Patient Life**

Finding a doctor to coordinate the diverse forms of care necessary for a patient is often difficult. Because the illness is so rare, most doctors have not heard of Pompe disease and are at a loss as to what to do. Many times, the patient has to teach the physician about the disease, at least to the point that the physician knows enough to research it on his own. Kendall says that most doctors she contacted seeking treatment options for Pompe symptoms told her "I've never heard of that." Tim Neuman of Great Falls, Montana, has late onset Pompe disease. His biggest disappointment was in trying to find a doctor that wanted to take a vested interest in treatment. He says there is "not very much interest in me or Pompe. I believe that this is probably because they do not know what to do."

Regional patient meetings are a useful way for Pompe patients to network. Physicians, specialists, pharmaceutical representatives, researchers, caregivers, and patients attend day-long or weekend meetings to share information, offer suggestions for symptom treatments, and provide support. There are also several patient-oriented organizations that provide information and support, including the United Pompe Foundation and the Acid Maltase Deficiency Association (AMDA).

Finding someone who fully understands what a patient goes through is also difficult. Kendall and Neuman met Karen Kacures through a Facebook group for Pompe patients. Spread out across the country, they are able to ask questions, share information, and provide personal support to one another. All are late onset patients, with varying symptoms. All three are mobile, although Neuman has more difficulty breathing and Kendall uses a

cane to walk. Kacures, the only one that receives the ERT, has benefitted from using a Biphasic Intermittent Positive Airway Pressure (BiPAP) machine at night. Like most patients, they were all misdiagnosed several times before receiving the proper diagnosis.

Insurance is another issue for Pompe patients. Kacures' insurance company initially rejected coverage for her. "I soon found out what it was like to fight for your life when it came to your health care," she says. "I am the only patient that my insurance company has ever had with this disease." She eventually received the ERT through a clinical trial. After a year of receiving beneficial physical therapy, Kendall's insurance notified her that they would no longer cover that service. Even with a justification from a specialist at Johns Hopkins, the insurance company reaffirmed their denial, claiming that physical therapy was not shown to make a significant change in the illness. Quality of life care does not fall under the insurance coverage.

Living with Pompe disease affects everyone in the family. Parents who unknowingly carried the recessive gene may feel guilt for having "given" their children the illness. Healthy children may resent the time and attention a sick sibling receives. Parents with Pompe disease may worry about being an embarrassment, especially to their children, and may be uncomfortable with the level of help they need to perform routine tasks. Patients with advanced symptoms may feel self-conscious about appearing in public with a ventilator or may be frustrated with the responses of other people. Spouses may be uncomfortable in a role as caregiver. The illness frequently causes depression in patients and caregivers. Pompe disease, like other terminal illnesses, may cause people to be more attuned to their faith or spiritual beliefs or may cause them to question or dismiss those beliefs.

## **Conclusion**

Because the clinical trials for the ERT are closed, Kendall can only treat her various symptoms. She has numerous specialists to support her care: a neurologist, a pulmonologist, a cardiologist, an oncologist, a registered dietician, a physical therapist, and an entire staff at a cardio-pulmonary rehab gym. She travels four hours out of state to a hospital equipped to handle her case. She is very self-conscious about the way that she moves. She worries about embarrassing her children. She hates the planning that has to go into any activity. "We have to plan everything," she says, "Is there handicapped parking, can I walk or do I need a wheelchair, are there bathroom facilities, will there be a crowd?" When asked what she misses most, Kendall becomes quiet. She says, "I miss being independent. I hate having to ask for help to do the simplest things, like picking up something that I've dropped or getting something out of a drawer. I miss ordinary things, like putting my hair up, wearing high heels, having picnics on the ground, playing games on the floor with my kids." She is also frustrated by the lack of handicapped accessibility, saying "It is amazing the number of places that meet the legal requirements for handicapped accessibility but are not accessible for me."

Zoe's parents threw a "Sweet 6 Month" birthday party for Zoe last fall. They are excited about spending their first Christmas with their daughter. They look forward to her first birthday. They take a lot of photographs and videos and Elizabeth has created a website dedicated to Zoe. But the struggle is ongoing. Elizabeth says, "I still can't believe Zoe has Pompe disease. I still cry every day."

For more information about Pompe disease or to donate to research efforts, refer to the following sites:

[www.amda-pompe.org](http://www.amda-pompe.org)  
[www.pompe.com](http://www.pompe.com)  
[www.unitedpompe.com](http://www.unitedpompe.com)  
[www.worldpompe.org](http://www.worldpompe.org)