



A Publication from your Healthcare Advocates

Welcome

We hope that you enjoy reading this issue of LysoStories, a newsletter designed by Health Care Advocates for patients and families with lysosomal storage disease (LSDs). If you have a suggestion for an article or would like to tell your story please contact a member of the Publication Committee. Happy Spring!

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What's New

Upcoming meetings that your health care providers may be attending;

Society of Inherited Metabolic Disease Annual Meeting,
San Diego, CA

August 29 - September 2, 2009

Child Neurology Society meeting,
Louisville, KY

October 15 - 17, 2009

American Society of Human Genetics meeting,
Honolulu, HI

October 20 - 24, 2009

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LysoStories™

Working Toward a More Complete Understanding of Pompe Disease

Increasing the Understanding of Pompe Disease

The Pompe registry, which is sponsored by Genzyme, was created to gather information to improve the understanding and evaluate the treatment of Pompe disease. Because Pompe disease is uncommon, it can be difficult to collect information on how the disease and its treatment affect different people. The Pompe registry is a database for gathering this critical information.



All people who have Pompe disease are eligible to participate, regardless of whether they are on disease-specific treatment. Your physician is the one who will enroll you in the Pompe Registry. He or she will explain the program and will ask you to sign an authorization to participate in the registry. Your participation is completely voluntary. When you volunteer to participate in the Pompe registry, your medical information is pooled with other participants' and is used to assist physicians in studying trends and addressing specific questions about Pompe disease. This information may contribute to better care for you and other people living with Pompe disease.

Benefits of the Pompe Registry

In addition to helping physicians understand Pompe disease, the registry can also benefit you. For instance, it can help you and your physician monitor your disease, whether or not you are on treatment.

When you are enrolled in the registry, your physician can produce a patient care report to help prepare for your appointments. This report uses charts, graphs, and text to show how you are progressing on important measures, including:

- Your muscle function
- Your lungs
- Your heart
- Your quality of life

The report contains an overview of your health status as it relates to Pompe disease. Your physician can review it with you to give you a picture of your health.

Take an active role

When you take an active role in your health care, you feel more in control. Talking to your doctor is an important first step. Here are some ways you can use the Registry to keep the lines of communication open:

- Ask your physician if he or she is enrolled in the Pompe registry*
- Let your physician know you are interested in participating in the registry*
- Ask your physician or nurse to share your patient Case Report with you at your next visit*

To learn more about the Pompe Registry, talk to your doctor or visit www.pomperegistry.com



A program sponsored by Genzyme

Patient Story

A Personal Odyssey with Pompe Disease

By John Cole
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I have dealt with Pompe Disease for over 35 years. First I watched my older brother pass away with the disease when I was nine. Then at thirty I experienced the onset of the disease myself. For the next twelve years I rode the downhill slide of increased muscle weakness and loss of muscle function which leads to isolation and, in my case, the disintegration of personal relationships and ultimately my marriage.

For those unfamiliar with Pompe Disease, it is also known as Glycogen Storage Disease Type II as there is a build up of glycogen in the lysosomes because the body does not produce enough of the enzyme required to breakdown all of the glycogen entering the lysosomes. This build-up results in progressive muscle weakness and muscle wasting. Once one muscle or muscle group begins to have problems, other muscles begin to take over the function of the weaker muscles. That is to say, the body compensates for the damaged muscles. Eventually it becomes difficult to get out of chairs, walk up stairs, etc.

In my case, while I have always had some muscle weakness, the first major problem was weakness in my diaphragm. From there the disease began to affect my chest and upper

back muscles – those my body recruited to help with breathing – and down to my hip girdle – those muscles used for walking. Now, any time I lay down, I have to be on bi-pap ventilation assistance. To get out of a chair, I have to use a walker or table. Stairs require a handrail.

Despite this seemingly dreary description of my life, I remained positive. I sought information that would help me and I maintained mild exercise and a high protein diet. In 2005 I was able to enroll in a clinical trial for an enzyme replacement therapy."

It's only after you've gone through such a very personal odyssey that you can look back to see what really got you through it all. While the physical struggle is monumental, it's really your mental strength that gets you through. I hadn't given this much thought until my father was on his deathbed. The last thing he said to me privately was that he admired me for my strength of character because of how I dealt with my condition. He respected that fact that I never let it get me down and I never gave up.

His simple statement – that he admired my strength of character – made me recognize that while I was aware of how I had endured the physical nature of my condition, I really hadn't put much thought into how I had dealt with the emotional aspects of having a chronic disease. When my physical therapist offered me a job as "Patient Representative", I thought this was an opportunity to explore this area. The clinic I now work at treats a great number of patients who have chronic, neurologic conditions like spinal cord injuries, stroke and MS.

From my personal experience and conversations I have had with our patients, I have embraced four basic guidelines to help live with a chronic disease:

1. Never, ever ask "Why me?" There is no answer and if there was, you probably wouldn't like it anyway. Focusing on such things is a waste of time and emotional energy.
2. Hold on to as much as you can. Do what is needed to manage your symptoms. Work to keep as much of your physical strength and flexibility as you can. In addition to possibly decreasing pain, it will keep you independent as long as possible and give you more to work with if a treatment does come along.
3. Get back as much as you can. Try to take control of your situation by trying to get back as much of what you have lost as possible.
4. Remember that the disease or disability is a part of you but it does not define you. Just as you wouldn't let having brown hair or blue eyes rule your life, don't let the chronic condition rule your life.

I know these guidelines may seem simplistic, but they are just that, guidelines. There are many other things that make life easier, such as the love and support of family and friends and faith in a higher power. These are very personal and individual. Do what you need to do to stay in as much control as possible. And always, always try to enjoy life to its fullest.



Pressure to Breathe

by Ford Greene, CRT, LRCP
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Mr. Greene is also a person living with Pompe

Patients with Pompe disease often experience difficulty breathing. This occurs mostly when sleeping or lying down due to progressive muscle weakness in the diaphragm (the muscle separating the lungs from the abdomen). When patients are first presented with options regarding treatment for their breathing it sounds like a foreign language with meaningless words like CPAP and Bi-PAP. The purpose of this article is to help explain some of the more commonly used terms and how they apply to you.

Respiratory therapists are key individuals who may help you achieve your maximum breathing potential. At initial diagnosis, the RT can teach you breathing exercises to help you regulate your breathing and maintain muscle strength. For patients with Pompe disease, it is not uncommon to also need breathing assistance from medical devices, particularly when sleeping. There are two methods of helping one breathe using medical equipment, invasive ventilation and non-invasive ventilation.

Invasive Ventilation: This is used when a person is not able to breath on their own, (respiratory failure). A tube is either inserted directly into the lungs via the nose or mouth, or directly into the trachea (windpipe) via a surgically placed opening in the trachea. A mechanical breathing device is then connected to the tube.

Non-invasive Ventilation: Non-invasive ventilation can be used to treat obstructive sleep apnea (pauses in breathing that occur from the collapse of the throat muscles), central sleep apnea (pauses in breathing that occur because the brain does not provide the correct breathing signals to the lungs), or neuromuscular disorders, such as Pompe disease, that result in muscle weakness. This type of ventilation involves the use of a mask being placed over the nose and mouth, or inserting nasal pillows into the nose and then connecting a mechanical device to it. The main devices used in the non-invasive modes of ventilation are Bi-PAP (bi-level positive airway pressure), or CPAP (continuous positive airway pressure).

- CPAP pushes air into the throat at one continuous pressure as you inhale and exhale. It is most commonly used to treat mild obstructive sleep apnea by preventing the throat muscles from collapsing. It will also reduce snoring.
- Bi-PAP uses two different pressures; one that will help keep your lungs open when you are breathing in and a second, usually lower, pressure that will keep your airways open when you breathe out. This mode of ventilation is used for more advanced breathing problems.

Persons with a neuromuscular disorder often need to use a Bi-PAP or CPAP unit while sleeping. The breathing muscles are very weak causing you to experience a decrease in normal breathing patterns at night, or when you lie down to sleep.

Non-invasive ventilation will allow you to get the restorative sleep that is needed for normal activities during the day.

There have been many advances in the field of non-invasive ventilation over the last decade. Today's machines are very sensitive to individual needs. These new systems are able to adjust automatically to the pressure that you need to keep your airway open. The pressure can start out at a lower amount and gradually increase over an adjusted period of time until the prescribed pressure is reached. This allows you to become comfortable with the maximum pressure prescribed by your physician. Some units can actually log information about your compliance with the therapy, and transmit the data to the sleep lab thereby allowing changes to be made via telephone. In past years this would have required a trip to the sleep lab for another sleep test. Transmitted data also helps the clinical personnel understand how well you are tolerating the therapy.

The masks that have been developed have also advanced from the days of "one size fits all". Today you have an array of nasal masks, full face masks, nasal pillows and what is referred to as a Jason mask. The Jason mask covers the face from forehead to the chin! These types of masks and nasal pillows come in a variety of materials that include air filled, foam filled, gel filled, and even water filled. The type of equipment that is used is somewhat dependent on your preferences. The most important thing is for you to be compliant with the physician - prescribed therapy.

The changes and differences in CPAP and Bi-PAP therapy have been extensive over the last 5 to 10 years. As we learn more about sleep therapy there will be even greater advances made in patient comfort and compliance with the prescribed therapies. Quality of life and overall health are improved with appropriate restorative sleep.

Keep this thought in mind: We spend approximately one third of our lives sleeping, and give almost no thought to our sleeping environments. It is imperative that you understand the differences in sleep therapies. Make sure that you ask questions when you do not sleep well or do not feel rested upon waking in the morning. Talk to your doctor or ask if sleep therapy might help. Take charge of your health and get the SLEEP YOU NEED!

Approaches to Treatment for Lysosomal Storage Diseases

Nadene Henderson, MS, CGC
Ms. Henderson works at the University of Pittsburgh
and also as a Registry Associate for Genzyme

Lysosomal Storage Diseases (LSDs) are conditions with different symptoms affecting various organ systems. These conditions have excessive storage of a compound in the lysosomes of the body's cells. What is the lysosome? The lysosome can be thought of as the recycling center of the cell. Compounds come in, get broken down into smaller parts which are then used to make new compounds. If they don't get broken down properly, then they start to accumulate in the lysosome, thereby overloading it and causing the cell to dysfunction.

Whose job is it to break down these compounds? That is where the word enzyme comes into play. Each LSD is caused by a missing, decreased, or malfunctioning enzyme, but for each LSD there is a different enzyme involved. An enzyme's job is to either help break down or to build up compounds in our bodies. For example, enzymes in our saliva and stomach break down the food we eat. Similarly, enzymes are found within the lysosomes of our cells and are responsible for breaking things down within the lysosome. This process maintains a balance within the cell. In persons affected with these conditions, the enzyme can't do this job properly, either because it is missing or because it is not produced correctly. The compound (or substrate) that the enzyme is supposed to break down cannot be broken down and it builds up in the lysosome which results in excessive storage and unhealthy cells.

Why might an enzyme not be produced correctly? Part of the process of making a normal enzyme is the need to make it into a specific shape and to get it to the right place (in this case, the lysosome). One could compare this to the art of origami where you fold a piece of paper into unique designs. You would always start with the same piece of paper but if you make a mistake in folding it you will end up with the incorrect shape. Enzymes in LSDs are also folded in specific ways but sometimes the folding does not occur properly. In that case the misfolded enzyme is thought of as foreign and it is degraded quickly. The proper folding of the enzyme also allows the active site (this is the place the enzyme needs in order to attach correctly to the compound it has to break down) to be available. If the active site is blocked or not shaped correctly then the enzyme can not perform its job very well.

Type 1 Gaucher disease was the first LSD to have a direct treatment. This treatment, enzyme replacement therapy (ERT), is based on early experiences with Bone Marrow Transplant (BMT) in genetic diseases. The lessons learned from Gaucher disease have led the way for other treatments to be developed. Other more recent approaches such as Substrate Reduction Therapy (SRT) and Chemical Chaperone Approach (CCA) are discussed below, along with ERT and BMT.

Bone Marrow Transplant (BMT)/ Stem Cell Transplant (SCT)

Rationale for the approach: Provide an affected individual with donor cells from a confirmed unaffected individual so that the donor cells can supply some functional enzyme. The donor enzyme is made by cells derived from the bone marrow and travels throughout the body via the bloodstream in order to perform its proper function. Stem cells are within the bone marrow and are the originators of all subsequent bone marrow cells. By using stem cells, there is less of a chance for the recipient's body to think of the transplanted cells as foreign and thus reject them.

When is it used? Lysosomal storage diseases, like severe MPSI, that involve the central nervous system. BMT may also be considered for conditions that do not have other treatment approaches. BMT may not be appropriate for all lysosomal storage diseases.

How is it done? The process involves a conditioning regimen of various drugs to prepare the body for accepting donor cells and follow-up to ensure acceptance of the donor cells (or engraftment). The actual transplant of cells involves an injection of the donor cells into the blood stream.

Enzyme Replacement Therapy (ERT)

Rationale for the approach: Replace the enzyme that is deficient, non-functional, or absent so that the accumulated substance can be broken down into its smaller components.

When is it used? For individuals with diagnosis of the conditions listed in the table. ERT is not expected to be beneficial for the neurologic compromise that occurs in some lysosomal storage diseases. These conditions may use ERT in conjunction with BMT. Clinical trials are currently underway to look at injecting the enzyme directly into the central nervous system since injecting the enzyme into the bloodstream does not allow it to cross the blood-brain barrier because enzymes are too large.

How is it done? Intravenous infusions at regular intervals (these intervals vary with each product and sometimes by the physician's preference).

Substrate Reduction Therapy (SRT)

(also known as Small Molecule Therapy or Substrate Synthesis Inhibition)

Rationale for approach: Prevent the compound from building up in the first place. This is achieved by slowing down the earlier steps in the pathway that eventually lead to the compounds involved in each disease.

When is it used? For individuals with an established diagnosis. Currently an approved product is available for patients with type 1 Gaucher disease. Clinical trials of this approach for other lysosomal diseases are currently taking place.

How is it done? Oral drug

Chemical Chaperone Approach (CCA)

Rationale for approach: This approach provides chemical assistance to the abnormally folded enzyme. By "chaperoning" the enzyme through its production process, it helps to protect it from being broken down and discarded. Once it gets to the lysosome, then the chaperone can be washed off and the enzyme can then do its assigned job.

When is it used? For diagnosed individuals who have genetic changes or mutations that result in an abnormally folded enzyme.

How is it done? Oral drug

SUMMARY OF CURRENT TREATMENT APPROACHES

	BMT/SCT	ERT		SRT		CCA	
	Procedure used in	Drug Product Available	Clinical Trials Ongoing†	Drug Product Available	Clinical Trials Ongoing†	Drug Product Available	Clinical Trials Ongoing†
Gaucher Disease type I	✓*	✓	✓	✓	✓		✓
Fabry Disease		✓	✓				✓
MPS I	✓	✓	✓				
MPS II	✓	✓	✓				
MPS VI	✓	✓					
Pompe Disease		✓	✓				✓

* BMT/SCT for Gaucher disease is rarely used now since there are other established treatments
† The status of clinical trials changes frequently. Please check the clinical trials website (address below) for updates

Please contact your treating physician if you are interested in more information or have questions about these treatment approaches.

Resources:

www.clinicaltrials.gov
National Gaucher Foundation (www.gaucherdisease.org)
MPS Society (www.mpsociety.org)
http://genzyme.com/research/research_home.asp
<http://www.amicustherapeutics.com/clinicaltrials/overview.asp>
<http://www.shire.com/shire/RandD/>
<http://www1.actelion.com/en/patients/index.page>