May 2007

LysoStories™

A Publication from your Healthcare Advocates

What's New

Take a look at the new Gaucher disease educational website at www.gauchercare.com

Don't miss the next NGF Webex meeting scheduled for June 3rd from 4–5:30 PM EST. Register for the meeting by June 1st by calling the NGF at 1-800-428-2437 or online at www.gaucherdisease.org click on register for meetings and events

We need to hear from YOU!

In an upcoming issue of Lyso Stories we will feature an "Ask the Expert" section. We want to include relevant questions from our readers. Please submit your questions for the expert LSD physicians to one of the Pub Comm members by July 30th 2007

Center News

Welcome

We hope that your enjoy reading this fourth 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 Publications Committee.

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Patient Interviews

What I Have Learned About My Bones

By Nadene Henderson MS, CGC

Since the theme of this issue of LysoStories is bone symptomatology in Gaucher disease, we have interviewed two individuals with Gaucher disease to ask them about their experiences. Mario Bono is a young 70 year old non-Ashkenazi Jewish man who was diagnosed with Gaucher disease at the age of 57. Stacey Feuer is a 31 year old Ashkenazi Jewish woman who was diagnosed with Gaucher disease at the age of 23. Both Mario and Stacey were pleased to contribute to this issue of LysoStories.

Was your initial diagnosis of Gaucher disease prompted by a bone problem or event?

- **MB** - Yes, I had bone pain in my hip for about two years until one day I was teaching in front of my class and my hip collapsed. I went to the ER and they saw it was fractured. I was then sent for an MRI before my hip surgery and the MRI doctor said it looked like Gaucher disease was affecting my hip.
- **SF** – My initial diagnosis of Gaucher Disease was due to a bone crisis. I was taken to the hospital in the middle of the night because my right knee was very swollen, red, and warm, and I was running a fever. For about two weeks previous to this, my knee had steadily grown more painful from a very slight pain to a pain that was so excruciating it hurt to breathe.

How long from that event to when you were officially told you had Gaucher disease?

- **MB** - My MRI was one week after my hip fracture so that was when I was told it was Gaucher disease.
- **SF** – From the first hint of pain until I was diagnosed was just under one month. From the time I was admitted to the hospital, it was ten days. After being misdiagnosed with a sports injury and leukemia, I was diagnosed from a bone marrow sample that was aspirated from my lower back.

How long after that event did you start enzyme replacement therapy? What dose were you placed on?

- **MB** - I was started on enzyme replacement therapy about 2 ½ years after my diagnosis. It took a while because of insurance issues but once that was approved I was started at 60 Units per kilogram every two weeks. I have stayed on that dose ever since and have not had any interruptions.
- **SF** – As soon as I was diagnosed, I was very lucky to be referred to John Barranger at the University of Pittsburgh. Because of this, I had immediate access to appropriate genetic counseling and expert advice regarding Gaucher. I started enzyme replacement therapy (ERT) approximately six weeks after I was diagnosed. I was put on the "normal" dose of 60 U/kg every two weeks. About one year after my diagnosis, I experienced another bone crisis in my right knee. I was immediately put on a double dose of enzyme and my symptoms subsided. After several months, we tried to lower my dose back to 60 U/kg, but I wasn't able to tolerate that dose anymore. For the last eight years I have been on 120 U/kg every two weeks. However, six months ago my dose was lowered to 90 U/kg and I have been tolerating the lowered dose well.

Have your symptoms resolved? Have you had any other bone problems or surgeries?

- **MB** - At the beginning, my one hip was replaced but it was also found that I had damage in my other hip and my shoulder. In total I have had all three joints

(cont.)

replaced. These joints have felt great since they were replaced. I only now get some aches in the muscles of my thighs (right above my knees). Other than that, I don't have any other pain. I now feel I can go 5-6 hours every day "lickety-split" and not have any pain. If it gets to be bothersome, I stop what I am doing and take a break. I do not take any medications for my pain.

- **SF** – Within the first year, my liver and spleen decreased dramatically to almost normal size. My blood counts (red, white, and platelet) also returned to normal ranges. My biggest problem throughout the past nine years has been with my bones, specifically my right knee. At the time of diagnosis, there was already significant osteonecrosis and arthritis in that knee. Despite such a large dose of enzyme over the years, the damage that was done prior to being diagnosed has caused a lot of problems. I have had a total of five arthroscopic surgeries and one bone graft on my right knee since I was diagnosed. However, in the last two years or so, these major problems seem to have subsided. I still deal with bone pain every day, and have to carefully monitor my activity levels to avoid being stuck in bed for days at a time, but it has become a manageable part of my life.

What advice do you have for other individuals with bone issues or to the medical professionals taking care of them?

- **MB** - To individuals who have pain, go have it checked out right away. Don't do what I did by horsing around for two years and think the problem will go away. To the medical profession, learn as much as you can and look up Gaucher disease before you meet someone that has the diagnosis.
- **SF** – The first thing I would say is that it is important to see the experts. Most doctors do not understand Gaucher Disease, and certainly do not understand the bone involvement with this disease, even "bone" doctors or "pain" doctors. Secondly, trust your instincts—even the experts can be wrong. If you are in pain, be persistent because the reason may not be visible to your doctors. Third, and related, my experience has been that most of dealing with bone issues and Gaucher is managing the pain. If one method doesn't help, try another until something works (with the guidance of a Gaucher expert, of course!). Finally, have hope … I believe we are still in the beginning stages of learning how to deal with bone issues and Gaucher.

Summer is Coming!
Tips for Safe, Hassle-Free Travel
By Lisa Sniderman King, M.Sc., CGC

For many, summer conjures up images of family trips to the beach, visiting relatives, camping, exploring new cities and countries or road trips in your own state/province. When you have a medical condition, traveling can be simple and easy for some and extremely overwhelming for others. But no matter what your needs are, the tips below will help you plan for a smooth trip. Your home LSD center and also your Patient Services Representative of the appropriate pharmaceutical company can help you coordinate most of the steps below.

Identify Local LSD Resources

Whether you have a child with an MPS who needs medical attention or you're an adult with Gaucher disease having a bone crisis, being away from your home medical support system can be very scary. Having a local medical team familiar with your condition is very helpful at the least and can be lifesaving in the worst-case scenario. Your home LSD center or Patient Services Representative can help you find knowledgeable medical providers wherever your travels take you. They can contact these providers ahead of time to let them know you'll be in their area and might need to call on them for help. If you want to do your own legwork, check out the GeneTests website to find a genetics clinic in a city you're interested in. Even if GeneTests does not have the exact city listed, any genetic counselor in that area can help connect you with a physician who sees patients with your LSD. Go to www.genetests.org and click Clinic Directory at the top of the webpage to search.

Arrange ERT Well Ahead of Time

If you are receiving enzyme replacement therapy and are hoping to have an infusion in the city you're traveling to, there are a few things that need to happen ahead of time.

1. **Insurance coverage**. Check that your plan will cover out-of-network treatment.
2. **Local LSD treatment center**. Your home LSD team needs to connect with the center that will be infusing you to make appropriate arrangements. They will need to send medical records, infusion orders and any other requested information.
3. **Making an appointment**. Your home LSD team will give you the contact person to call for an appointment. Each center has different ways of organizing their infusion patients so you may need to be flexible about the day and time you go in.

If you're receiving ERT and you're not sure if you'll need an infusion while you're away, call your home LSD team to see how your travel dates fit with your infusion schedule.

Carry Medical Documentation

You should carry two letters with you when you go on vacation:

1. **In Case of Emergency Letter**. This letter contains information that anyone providing emergency care to you or your child would need to know. For example, anaesthesia risks due to narrow airways, medication allergies, how to manage a bone crisis, that you have a pacemaker or metal joint/bone replacements and cannot have an MRI, etc.
2. **Travel Letter**. This letter outlines the medications and/or medical supplies you need to carry with you. Include information about your pacemakers and metal joint replacements. This letter is primarily for the benefit of airline security personnel, border patrol etc.

Both letters should be written by your health care team and briefly explain the disorder, recommendations for management, reasons why you need to carry the medications/supplies with you, and contact information/paging information for your home physician.

Habla Español? Parlez-Vous Français?

If you are traveling to another country, consider having the letters translated into the majority language. Most major hospitals have translations services that can assist if given enough time.

Consider getting a Medic Alert bracelet

For information, go to www.medicalert.org or ask your home LSD team to give you some information. The Medic Alert Foundation is an international, non-profit organization whose symbol is recognized world-wide and can provide your medical information in over 100 languages.

What is Allowed on an Airplane?

All liquids, gels and aerosols must be in three-ounce or smaller containers and must be placed in a single, quart-size, zip-top (eg. Ziploc), clear plastic bag.

The items below can be greater than 3 ounces each but must be carried separately from the shampoo etc that's in your quart-sized Ziploc bag:

- Baby formula and breast milk if a baby or small child is traveling.
- All prescription and over-the-counter medications (liquids, gels, and aerosols) including KY jelly, eye drops, and saline solution for medical purposes.
- Liquids including water, juice, or liquid nutrition or gels for passengers with a disability or medical condition.
- Life-support and life-sustaining liquids such as bone marrow, blood products, and transplant organs.
- Items used to augment the body for medical or cosmetic reasons such as mastectomy products, prosthetic breasts, bras or shells containing gels, saline solution, or other liquids.

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- Gels or frozen liquids needed to cool disability or medically related items used by persons with disabilities or medical conditions.

Be prepared to present your letter regarding your meds or equipment to the security officer.

For more detailed information, consult the Federal Aviation Administration website. http://www.faa.gov/passengers/

Be sure to inform your airline about the specific needs you will have and check-in at least 2-hours before your flight if you need special assistance.

Have Too Much Gear? Don't Lug it! Rent it!

This website contains state-by-state listings of baby and child equipment rentals. http://www.thenewparentsguide.com/baby-equipment-rentals.htm

Suggested Timeline:

In my experience, the timeline below gives you plenty of time to put your needs in place. I recognize that not all travel is planned in advance, however, so as soon as you know you will take a trip, call your LSD center so they can start helping you make arrangements.

6-8 weeks prior to trip:

- Request travel and emergency letters if you need them. Now is also the time to mention it if you need them translated into another language.

4-6 weeks prior to trip:

- Contact your Patient Support Services Representative to verify your insurance coverage.
- Contact your LSD center to discuss arranging off-site infusions if necessary. You will need to provide your dates of travel and what city(ies) you'll be visiting. If you are followed in a clinic with a small number of LSD patients, your health care team might need guidance to make arrangements for you. Your industry Patient Support Services Representative can help you and your clinic.

3-4 weeks prior to the trip:

- Make infusion appointments if necessary.
- Join Medic Alert if you are planning to. It takes 7-10 days to receive your bracelet once they receive your application. You may want input from your doctor on what information to have engraved, so factor in some time to request this of your doctor.
- Look into renting any equipment you don't want to carry.

2 weeks prior to the trip:

- Request prescription refills if you will need them.

1 week prior to the trip

- Call your airline to inquire about check-in requirements if you have special needs.
- Relax and have fun!!!

Brinksmanship and Your Bone

By John A. Barranger, MD, PhD

The author is a professor of Human Genetics at the University of Pittsburgh and a consultant to governments and industry.

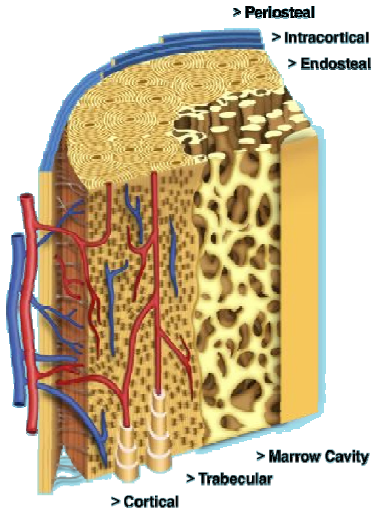
In 1977, a young child diagnosed with Gaucher disease, was evaluated for the profound enlargement of his liver and spleen, anemia, low platelets, bruising, and nose bleeds. He felt tired, but had little bone pain. Regular x-rays showed no lesions in the skeleton.

Just about this time a new technique was beginning to be evaluated for its ability to measure changes in the shape and consistency of organs. It had been used to examine soft tissue tumors. This x-ray technique was called Nuclear Magnetic Resonance (NMR) imaging or just MRI which is how it is most frequently known today.

The technique was applied to the seven year old to see if something could be learned about the nature of Gaucher disease. What a surprise! His skeleton, which looked pretty normal by regular x-rays showed a host of lesions by MRI. Multiple areas of osteonecrosis and osteosclerosis in the interior of the large leg bone (femur) could be seen. There were also abnormal collections in the neck and head of the femur and disorganization of bone growth. All of this, when the regular x-ray was normal. It was clear that the MRI was a great tool for evaluating the bone in Gaucher disease. Dr. Daniel Stowens gathered up clinical and x-ray data in 327 Gaucher patients and performed correlated findings on bone biopsies.

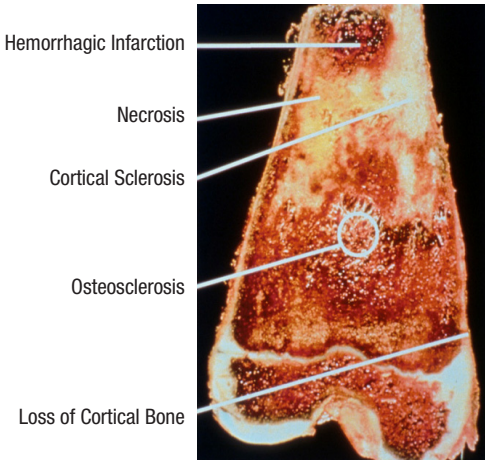
What he showed in this study was that the mechanisms of bone disease were complex and that both the hardest part of bone (the cortex) and the bone marrow (medulla) were involved.

Figure 1. Understanding the Bone Structure



With the help of Drs Arnold Kuhn and Steven Teitelbaun, leaders in the field of bone metabolism, we learned that the bone in patients with Gaucher disease doesn't grow properly. An exaggerated sign of abnormal growth and lack of strengthening of bone is the ehrlenmeyer flask deformity.

Figure 2. Femur with ehrlenmeyer flask deformity, infarction and sclerosis



Many other signs of bone disease are evident by MRI. Drs Henry Mankin, Samuel Doppelt and Daniel Rosenthal at the Massachusetts General Hospital helped us use and interpret this tool – not only for diagnosis of bone pathology, but also in judging response to enzyme replacement therapy (ERT). In this regard, the combination of X-rays and MRI provided new definitions of the nature of the bone disease and the response to treatment.

Even though these developments were ground breaking, they have not been used by all physicians taking care of Gaucher patients. One of the problems in their use is that the lesions of the bone may have progressed too far and have resulted in scar and deformity. Thus, some caregivers and patients, as well, remark that bones and pain are not getting any better. This is an unfortunate misconclusion. The

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graphic example below is useful to understand the process of bone disease, in fact, most aspects of Gaucher disease and other lysosomal disease as well.

These steps in the injury to the bone in patients with Gaucher disease are operating from the beginning of life. Clinical evidence of this toxic process may not be immediately obvious or could be missed if not measured. Many cases of bone disease are missed or ignored because this simple principle is not understood and testing is not done. The specific testing needed is published and available even on line at www.gaucherregistry.com.

These recommendations include testing for bone disease, specifically x-rays, MRI's, and bone mineral density as measured by DEXA scans. Very recent data obtained by the Gaucher Registry and published by Dr. Richard Wenstrup in collaboration with the Gaucher Registry board of advisors (ICGG), reveals what many of us have expected from the beginning – for bone, dose matters. In this article based on the collection of data from 342 treated patients and 160 untreated patients, bone density achieves a normal level only at a dose of ERT of 60U/kg/2 weeks. Lower doses do not reach this degree of improvement over a period of study of 8 years. Other recently published studies have revealed that areas of bone death (bone infarcts) stop completely when ERT is instituted (Charrow, J Clinical Genetics, 2007)

So if ERT is so good, why am I having so much bone pain? This question was posed by a patient in the Wall Street Journal about a year ago. The answer is simple. If you consider the mechanism of tissue injury shown above in figure 3. Lysosomal storage and the poisons released from storage cells is like a fire. Thrust your hand into it and it will burn. How badly is a consequence of how long the fire burns your hand. If your injury is so intense that the skin and flesh are burned away, then even if you put out the fire with ERT, the residual injury will be disfiguring and painful for life. This is how it is for bone. Delay treatment too long and some aspects of the disease may be irreversible.

Fortunately the tools are available to recognize bone involvement early. Dr. Kaplan showed in a study of 887 children that 72% had bone disease before the age of 5 years and that by adulthood essentially all had signs of bone involvement. In children treated early, the extent of the involvement of the skeleton is halted and much of the bone tissue, except for the scars, can be reversed and they will catch up in their growth. Follow up for 28 years in the earliest treated Gaucher patients shows that the well monitored patient does not develop bone problems even if the disease is severe early in life.

Waiting for an irreversible bone event to occur is brinkmanship. Be sure to talk with your physician about how your bones are being monitored. Keep in mind that every case is different and your treatment needs to be individualized. Your bone is not something to risk.

Recent References:

- Charrow et al (2007) The effect of enzyme replacement therapy on bone crisis and bone pain in patients with type 1 Gaucher disease. *Clin Genet.* 2007 Mar;71(3):205-11.
- Kaplan, P. et al (2006) The clinical and demographic characteristics of nonneuronopathic Gaucher disease in 887 children at diagnosis. *Arch Pediatr Adolesc Med.* 2006 Jun;160(6):603-8.
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