



## A Publication from your Healthcare Advocates

### Welcome

We hope that you enjoy reading this fall 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

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### What's New

*Upcoming meetings that your health care providers may be attending;*

**National Society of Genetic Counselors  
Annual Education Conference,**  
Los Angeles, CA  
October 23 – 27, 2008

**American Society of Human Genetics,**  
Philadelphia, PA  
November 11 – 15, 2008

**Lysosomal Disease Network World Symposium,**  
San Diego, CA  
February 18 – 20, 2009

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## 10 Important Questions to Ask Yourself and the Researcher before you Decide to Participate in a Clinical Trial

By Eleanor Botha, MS, CGC, CCRC  
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People participate in clinical trials for many reasons. They may think the trial will benefit themselves or other family members, either now or in the future. They may have hope for a newer or better therapy, or even a cure for their disease. They may just want to contribute to the body of information about their health condition. How does a person decide whether a particular clinical trial is right for them? All clinical trials include a required informed consent process that provides details about the study and includes important information (often in the form of questions) to help you decide whether you want to participate. There is also an opportunity to ask questions about the study. This process where you learn about and establish an understanding about what the study involves may require several discussions and considerable thought before a consent form, indicating willingness to participate, is signed. This article highlights some of the questions that we suggest asking yourself and the researcher before signing on for a clinical trial.

- 1) Will I/ my child benefit from the research? Will there be possible benefits for others with the same disease or condition?
- 2) Can I/my child be hurt by the research? It is important to consider potential risks of procedures and side effects of medication. How likely is it that they will occur? Is it possible that the condition could get worse during the trial? If it does what happens? Has the experimental treatment been tested before? What did these studies show?

- 3) Will I/ my child possibly get placebo (a "sugar pill") instead of the medication? If so, how might I feel if I found out I was getting placebo?
- 4) Who is paying? Is the drug investigational and provided by the study sponsor? Are there required procedures and, if so, is the cost covered by the study or my insurance? Are there extra costs (i.e., gas, parking, childcare for other children)? If I get hurt during the study, who pays for my medical care?
- 5) Why is the research being done? If a new drug is being tested, will I have the option of staying on the investigational medication at the end of the study?
- 6) How much of my time will the study take? How long is the study? How often are the visits? How will it affect my daily life?
- 7) What happens to my personal information when I am taking part in a study? Who knows I am participating? Who has access to results of the study? Will I get any results from the study?
- 8) What if I choose not to be in the study? What are the alternatives to being in the study? What if I start the study and change my mind?
- 9) Who is in charge of my care while I am in the study? My regular doctor? The investigator? Other specialists?
- 10) If I have questions during the study, who do I call? The coordinator? The investigator?

Patient participation in research trials is necessary for the advancement of science and the development of new therapies. Participation involves a real commitment on the part of the individual and their family. If a particular trial interests you, it is important to participate actively in the informed consent process where you have ample time to develop a clear understanding about what the trial involves, review the consent form and have your questions answered to determine if the trial is right for you.

## Patient Story

### Looking back at a Clinical Trial; why did I participate? by Irene Marshall

"I want a normal mommy". This is a statement from my 7 year old daughter 16 years ago, one that made me passionate to get well and stay well, to be a pioneer. To a seven year old, I wasn't normal. She could see me having pain and using crutches for what must have seemed to her like an eternity.

It's kind of ironic that I was actually diagnosed with Type I Gaucher disease when I was almost 7. My parents were told that my spleen was dangerously enlarged and needed to be removed. They didn't know the actual diagnosis in 1954, but after my splenectomy, my "condition" improved and my frequent nosebleeds ceased. I'm sure that this hospitalization in Children's Hospital in Pittsburgh was a major influence in my becoming a RN in 1968. This was the timeframe in which I discovered the cause of my "condition" as some referred to it. Gaucher disease was the culprit. There was no family history of the disease and my older brother was not affected.

Other than anemia and fatigue, my life was somewhat stable. I married, had two sons and was involved in all of their activities. In 1983, I was knocked off my feet with bilateral avascular necrosis of the hips. Thankfully, with hospitalization, analgesics, and crutches I was able

to spring back to normal activities. After the birth of my daughter in 1985, I did feel well for about 6 years, but then began experiencing stress fractures of the tibias, climaxing in 1992 to a collapsed knee.

Enzyme replacement therapy had been suggested to me in 1991 by Dr. John Barranger who had been involved in the research and development of treatment for Gaucher disease. How fortunate I was to live only 50 miles from a major treatment center with an amazing doctor! There were some insurance issues to resolve and once that was complete, I started enzyme replacement in June 1992.

Bone damage had already been done and I required a right total knee replacement in February, 1993. Post-op progress seemed so slow, but that Spring I was able to attend my daughter's First Holy Communion and my sons' high school and college graduations. Insurance again became an issue and I missed a few infusions before being assisted by the Charitable Access Program. Eventually I obtained an insurance policy with no lifetime max.

After several years, there was an opportunity to participate in a clinical trial of gene therapy. After lengthy discussions with Dr. Barranger and investigations of my own; I talked with the head oncologist at the hospice where I worked, and had numerous discussions with my son who is a PhD microbiologist, I felt that the trial was right for me. I wanted to contribute to science.

There was an extensive informed consent process that is important & helpful when making a decision about

participating in a clinical study. The gene therapy trial involved injections of GCSF and leukopheresis before receiving my cells that had been exposed to a retroviral vector carrying an unchanged copy of the Gaucher (glucocerebrosidase) gene. I understood that the vector could possibly activate an unwanted oncogene which could possibly cause cancer.

I received four gene transplants from July, 1995 to August, 1996. The plan was simple. If the corrected gene was seen in my blood, my dose of enzyme would be reduced by half several times until I was eventually weaned from the drug. My infusions were discontinued in October, 1997. I felt great and had no health issues but in January, 2000, the corrected gene was no longer seen in my labs which meant resuming enzyme therapy. Mine was the only trial out of four total patients in which the transplant was temporarily successful.

Presently I continue with enzyme infusions. I remain optimistic that as we learn more through present & future clinical studies, there will be new and improved medicines and ultimately, a cure for Gaucher disease...hopefully in my lifetime.

## Hearing Loss & Lysosomal Storage Diseases

By Gwendolyn O' Grady, PhD  
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Because hearing loss can be an issue, this paper will discuss the tests used to identify and describe the hearing loss sometimes found in patients with MPS I (Hurler Syndrome), MPS II (Hunter Syndrome), and Fabry disease.

Hearing loss is often not expected in infants with MPS I or II. These infants typically pass the newborn hearing screening test. However, early on in the disease, these infants may develop stuffy noses with discharge (chronic rhinitis), repeated ear infections that cause fluid to accumulate in the middle ear space (recurrent otitis media), enlarged tonsils and adenoids, and sometimes difficulty breathing while laying down for even short periods of time (obstructive sleep apnea). The above symptoms often lead families to seek medical attention from audiologists and otolaryngologists and often occur before the diagnosis of MPS I or II has even been considered.

In Fabry disease, which is usually identified much later in life, auditory symptoms, particularly ringing in the ears, are sometimes the first indication of a problem. However, auditory symptoms typically do not cause a patient with Fabry disease to seek medical treatment.

The task for the audiologist is to assess the structures involved in hearing, and to determine the effect of the disease in each individual. There is no way to predict the disease's impact on the hearing structures as there does not seem to be a correlation between disease severity and degree of hearing loss. Professionals well versed in the expected findings in individuals with lysosomal diseases know that the hearing structures affected by the disease vary by individual diseases and with each individual.

### Behavioral Hearing Tests

Most people are familiar with routine hearing testing in which earphones are used and the hand raised every time a tone is heard. In order to do that test reliably, a person must be cooperative, and be able to maintain attention for 20 – 30 minutes. The same information can be obtained from infants or young children by slightly altering the task. Although there are no formal behavioral hearing tests for infants and children younger than 5 months of age, when an infant can sit with minimal support, hearing can be assessed.

For young children, hearing is assessed by demonstrating to the child that a head turn in response to sound is rewarded. The child will only continue to turn their head if they are reinforced to do so. This testing is called visual reinforcement audiometry. The child is reinforced by a brightly lighted animated toy for making a head turn in response to sound. This is a formal hearing test that has been well researched, and can lead to obtaining full auditory information in children.

For slightly older children, those no longer willing to be passively entertained, conditioned play audiometry works well. For conditioned play audiometry to be successful, a child must have the ability to wait until a sound is present to partake in a game. This takes some "impulse" control. Children younger than 2 ½ years might have difficulty with this procedure as they are not able to wait to play the game in response to the sound. These younger children just want to play the game without rules.

The tests that rely on the individual consistently responding to sound, with a hand raise, a head turn or a motor response, are "true" measures of hearing. All of the other tests described below are evaluating whether the anatomical structures are functioning normally. A normally functioning system allows sound to move effectively through the system. In order to be aware of a sound, the sound must be effectively transmitted to the inner ear.

### Tympanometry

Although part of the audiology test battery, tympanometry is not a hearing test. Tympanometry determines if sound is being transmitted through the outer and middle ear. The audiologist can determine if the ear canal is plugged with wax or debris, if the ear drum is intact, and if the ear drum is able to transfer sound. That is important for hearing to occur, but does not determine if hearing has occurred. Normal tympanometry suggests that the sound was delivered efficiently to the structures that process sound.



### Otoacoustic Emissions (OAE)

The otoacoustic emissions (OAE) test sends sound to the cochlea, the sensory organ of the ear. If the sound reaches the cochlea clearly, it causes the sensory units of the cochlea (the outer hair cells) to produce sound. If the hair cells can create sound, the test is 'normal' meaning that hair cells function is normal and hearing likely is as well. If otoacoustic emissions are absent, it suggests that the hair cells are not transferring sound OR that sound is not being efficiently delivered to the cochlea. The OAE is the test used in the newborn hearing screen.

### Auditory Brainstem Response (ABR):

Auditory Brainstem Response testing is used to determine if the auditory system transfers sound efficiently through the external, middle and inner ear and also what level of sound can make a neural response.

In MPS I and MPS II there are often problems with the transmission of sound through the external and middle ears. Ear canal drainage or debris can plug the ear causing a temporary conductive hearing loss. In addition, patients with MPS I and II sometimes have middle ear complications related to the upper airway congestion problems. Also it is not unusual for MPS I and II patients to have abnormalities of the ossicles- the bones in the middle ear. Other patients with MPS I or II have cochlear dysfunction. Finally, there are children and young adults with MPS I or II with normal hearing.

Fabry disease is not typically characterized by childhood hearing loss; however, hearing loss in adults with Fabry disease is characterized by a progressive high frequency sensorineural hearing loss. High frequency hearing loss is characterized by the loss of ability to hear consonants such as s, f, t, and z, even though vowels can be heard normally. Consequently, people can often hear sounds but may not be able to make out what is being said. This kind of hearing loss is common in aging individuals. But in Fabry disease, this loss occurs much earlier. The hearing loss identified in Fabry disease is often identified in the late teen years or in the second decade of life. Most people with high frequency hearing loss function well, without difficulty, in quiet situations.

All of the hearing loss examples described above may benefit from amplification to address the specific hearing loss identified. There is no one too young or too old to benefit from better hearing!

## National Gaucher Foundation Establishes Gaucher Mentor Program

The NGF established the Gaucher Mentor Program as a service to assist the Gaucher Community in navigating the maze of systems and programs which families and individuals face in dealing with Gaucher Disease.

The Mentors consist of individuals or family members who have Gaucher Disease. Collectively and individually, these volunteers share their knowledge, resources and personal experiences with others to help ease some of the stress and uncertainty that comes with being newly diagnosed. Whether previously diagnosed or newly diagnosed, Mentors can help individuals navigate the myriad issues that come with a diagnosis of Gaucher disease.

Individuals requiring a Gaucher Mentor may be referred to the Program through Gaucher treatment centers, the NGF at 800-GAUCHER, the NGF website or call Genzyme Treatment Support Services (GTS) at 800-745-4447. Interested persons may also call or email the NGF at [ngf@gaucherdisease.org](mailto:ngf@gaucherdisease.org) with a Mentor request.



For Program information, or to apply to become a mentor, go to [www.gaucherdisease.org](http://www.gaucherdisease.org) and click on "Programs" or call/email Megan Kirby at 1-800-GAUCHER (428-2437) email: [megan@gaucherdisease.org](mailto:megan@gaucherdisease.org).

## Clinical Trials: Is Research for Me?

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Emory Lysosomal Storage Disease Center

Medical geneticists, genetic counselors, and other health care professionals involved in the care of people with lysosomal storage diseases (LSDs) are always looking for better and more effective ways to keep their patients informed about the latest research and newest developments. Recently, the Emory Lysosomal Storage Disease Center (ELSDC), a center in Georgia that follows over 200 patients, tried a new tactic by holding an exciting and informative meeting for patients and families which was specifically focused on research. The meeting, called "Behind the Scenes: The Inside Scoop on LSD Research," was an all day event held on May 17, 2008 at the Emory Conference Center in Atlanta, Georgia. The meeting was jointly sponsored by Actelion Pharmaceuticals, Amicus Therapeutics, BioMarin, Genzyme Therapeutics, and Shire Human Genetic Therapies.



The fascinating variety of speakers and their excellent presentations on research-related topics made the meeting a great success. In the morning, individuals with all different types of LSDs gathered in one amphitheatre to learn about LSD research in general. After a warm welcome by Dr. Paul Fernhoff, medical director of the Division of Medical Genetics at Emory, the keynote lecture was given by Dr. Roscoe Brady, an internationally acclaimed scientist who has dedicated most of his research career to unveiling the mysteries surrounding lysosomal storage disorders. Dr. Brady reviewed the history of the development of enzyme replacement therapies and then talked about future prospects for treatment of Gaucher disease and possibly other LSDs. Dr. Fernhoff then presented Dr. Brady with a "friend of Emory" award in recognition of his expertise, determination and vision for families with LSDs.

Next, the Emory LSDC staff gave a quick series of lectures discussing broad topics including: an overview of clinical research, the role of the Institutional Review Board, the best way to look for appropriate research opportunities and the top ten questions a person should ask themselves before joining a research trial. After these lectures, a diverse patient panel provided a fascinating look at the reality of participating in clinical trials. The members of the panel provided candid and honest recounting of their research experiences (both positive and negative) and then discussion was opened to the audience. As many in the audience had also enrolled in clinical research trials, the session was lively and informative. For a summary of the session on questions to ask before deciding to participate in a trial, see Eleanor Botha's article in this issue.

In the afternoon, meeting participants attended disease-specific groups (Gaucher, Fabry, Pompe and MPS) to learn more about research and developments that applied to them directly. In each of these breakout sessions, a speaker from that disease support group (such as the Fabry Support and Information Group, the National Gaucher Foundation and the National MPS Society) spoke about the need for continued research to improve current treatment options. They also discussed their groups' goals in working with patients and in promoting research opportunities. All of the groups affirmed their commitment to working together. They invited patients to use their websites as resources about research trials and for general information and support.

Next, for each group, one of the Emory genetic counselors gave a lecture that focused on current and future technologies and on available research trials for that disease. Specifically, they reviewed technologies being explored by other academic centers and by companies such as Actelion, Amicus Therapeutics, Armagen, Biomarin, Genzyme, PTC Therapeutics, Protalix Biotherapeutics, and Shire HGT. Each of the technologies was put in the context of their research status or "phase". The speakers also touched upon disease-related issues that are under study at Emory, such as optimal methods for monitoring response to therapy and prospects for newborn screening.

Following the counselors' talks, speakers from the pharmaceutical companies presented information on their emerging technologies and explained the mechanisms of the new approaches. The breakout session attendees had many questions about these technologies. After a long, information packed day, the meeting attendees headed out to digest everything they had learned and to distribute this knowledge to others family members. Based on the very positive feedback from all participants, the Emory group plans to hold a similar research meeting every two to three years. Emory will also continue to hold their annual disease-specific family meetings. If you are interested in attending any of these meetings, please contact the Emory LSDC by phone at 404-778-8565 or 800-200-1524 or email Dawn Laney at [dlaney@genetics.emory.edu](mailto:dlaney@genetics.emory.edu) and ask to be added to the Emory mailing list. For more information about current LSD-related clinical trials, visit the National Institutes of Health clinical trials website at <http://www.clinicaltrials.gov> and search for specific trials using your/your child's diagnosis as the keyword.