EMORY UNIVERSITY SCHOOL OF MEDICINE

Department of Human Genetics

SUMMER 2004

WHAT'S IN STORE?

LYSOSOMAL STORAGE DISEASE CENTER NEWSLETTER

WELCOME

The Lysosomal Storage Disease Center of Emory University welcomes you to our first quarterly newsletter, What's In Store". Through this newsletter, we hope to keep you updated and informed about our clinical services, research endeavors, related activities and plans for the future. We will include articles about national programs, support organizations and new developments in the diagnosis and treatment of lysosomal storage diseases. In addition, we hope patients and family members will write in and submit their stories about how their lives are affected by these conditions and their treatment.

Please share this newsletter with your family, friends and health care providers. Feel free to contact us at 1-800-200-1524 with your comments, for additional copies of the newsletter, and/or any suggestions.

A FABRY FAMILY.
Infusions are a family event!

Trivia Question :

What was the source of the first enzyme used in enzyme replacement therapy for a lysosomal storage disease?

1) Chinese Hamsters
2) Human Placenta
3) Sea Cucumber Secretions
4) Echinacea

Answer: The first enzyme therapy developed to treat a lysosomal storage disease was made from human placenta. The medication, called Ceredase (alglucerase), served to replace the missing enzyme in Gaucher disease.

First Fridays

The Emory Lysosomal Storage Disease Center (LSDC) Clinic is now held on the first Friday of every month. This specialized clinic was created to serve the individual needs of patients and families with lysosomal storage diseases. Services provided in or through the clinic include: review of medical history, physical examination, laboratory studies, imaging studies, discussion of treatment options, assessment of ongoing treatment plans, genetic counseling, and other services as needed. Having a dedicated clinic for LSD's allows patients to meet other individuals with similar diagnoses who are dealing with some of the same health-related issues and concerns.

To schedule an appointment at the Emory LSDC Clinic, call (404) 727-3930 or 1-800-200-1524.

Our Newest Team Member

Daniel J. Gruskin, MD, FAAP

Dr. Daniel Gruskin is the newest faculty member of the Division of Medical Genetics, in the Department of Human Genetics at Emory University. He is an assistant professor of Human Genetics, with a joint appointment in the Department of Pediatrics. He has received specialized training in treating patients with inborn errors of metabolism, and is board eligible in both Clinical Genetics and Biochemical Genetics. He sees patients and families with metabolic disorders, including lysosomal storage diseases, as well as other genetic conditions.

WHAT ARE LYSOSOMAL DISEASES?

The Lysosomal Storage Diseases are a group of conditions in which certain substances (substrates) build up in compartments of the body's cells called lysosomes. These conditions are caused by missing or poorly functioning enzymes important in the breakdown of these substances. Over time, excessive amounts of the substrates accumulate and cause damage to involved systems and organs in the body.

NEW EMORY LSDC BROCHURE

Our Lysosomal Storage Disease Center Brochure is now ready for mailing. All of our families and referring physicians will receive copies of the brochure in the near future. Please contact us if you need additional copies or if you know of others who would be interested in learning more about our center.

OUR TREATMENT TEAM

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CONTACT US:
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GAUCHER DISEASE

MAJOR SIGNS & SYMPTOMS

Hematologic:
- Anemia / Thrombocytopenia

Visceral:
- Hepatosplenomegaly

Skeletal:
- Bone pain/bone crises
- Growth retardation
- Avascular necrosis
- Pathologic fractures
- Osteopenia

Child with enlarged liver & spleen

Erlenmeyer flask deformity (x-ray of femur)
(courtesy of Br J Radiol. 2002; 75(suppl 1) :A2-A12

RESOURCES

www.gaucher.com
www.gaucherregistry.com

WHAT'S NEW

Genzyme is currently recruiting patients with Type 1 Gaucher disease for an ongoing dose frequency clinical study of Cerezyme® (imiglucerase for injection).

Why should I decide to participate in this clinical study?

Your participation may help determine whether the health status of patients with Type 1 Gaucher disease can be maintained when they are given a 4-week dose of Cerezyme® in one infusion every four weeks instead of one infusion every two weeks.

What will the benefit be for me and others if I decide to participate in this clinical study?

Study participation may help determine if a 4-week schedule of Cerezyme® is a safe and effective way for patients to receive Cerezyme® therapy.

Some Study Eligibility Requirements:

- You must have a confirmed diagnosis of Type 1 Gaucher disease.
- You must be at least 18 years old.
- You must have been on Cerezyme® for at least two years and on a stable dose of 20-60U/kg every two weeks for at least six months prior to study participation.

What will I be asked to do if I decide to participate in this clinical study?

You will undergo medical evaluations or tests at the beginning of the study and every three months for 2 years. Five of those evaluations are completed at a pre-determined clinical study center. The other four evaluations will be completed during your regularly scheduled infusion.
Additionally, you will be asked how you feel on the less frequent infusion schedule and whether or not this new schedule provides greater convenience for you and less disruption to your work schedules and personal lives.
These evaluations or tests are used not only to compare you with other participants involved in the study, but also to monitor any changes in your Gaucher disease while you are a participant in the study.

Who do I need to contact if I am interested in participating in this clinical study?

Please contact either your treating physician or:
Medical Information
Genzyme Corporation
500 Kendall Street
Cambridge, MA 02142
Phone: (800) 745-4447 (press Option #2).
Please refer to clinical study number: CZ-011-01

THE REGISTRY BENEFITS EVERYONE - DO YOUR PART!
www.gaucherregistry.com

WHAT'S NEW

Fabry disease is a progressive, destructive, and life threatening lysosomal storage disorder caused by the partial or complete deficiency of the enzyme a-galactosidase A.

Fabry disease is a rare inherited X-linked disorder which predominantly affects males, but carrier females can also be affected to a mild or severe degree because of X-chromosomal inactivation.

Deficiency of a-galactosidase A leads to accumulation of glycosphingolipids (particularly globotriaosylceramide (GL-3)) in visceral tissues and the vascular endothelium throughout the body, leading to episodic crisis of pain, acroparesthesia, angiokeratomas, corneal and lenticular opacities (generally not affecting vision), and eventually, by the third to fifth decade of life, to systemic diseases of the kidney, heart, and cerebrovascular system. Without treatment for uremia, the average lifespan for hemizygotes with classical Fabry disease is 41 years.

With the advent of renal dialysis or transplantation, the median survival is about 50 years.

Although Fabry disease usually presents in childhood or adolescence, it is often not diagnosed until adulthood.

Early diagnosis and intervention are critical, since organ system damage is progressive and can be irreversible or even life-threatening. Varied presentations and diffuse symptoms often hamper an accurate and timely diagnosis.

Although Fabry disease usually presents in childhood or adolescence, it is often not diagnosed until adulthood.

Diagnosis of Fabry disease is confirmed by low or absent a-galactosidase A activity in plasma or serum, leukocytes, tears, biopsied tissues, or cultured skin fibroblasts. Since female heterozygotes can have a wide range of enzymatic activity, mutation or DNA analysis may be necessary to establish carrier status.

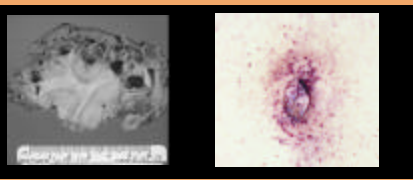
For additional information on Fabry disease call Genzyme Medical Information at 1 (800) 745-4447 to locate a Lysosomal Storage Disease Center nearest you.

THE REGISTRY BENEFITS EVERYONE - DO YOUR PART!
www.fabryregistry.com

FABRY DISEASE

MAJOR SIGNS & SYMPTOMS

- Acroparesthesia, episodic pain crises
- Hypohidrosis or anhidrosis
- Heat & cold intolerance
- Angiokeratomas
- Corneal & lenticular opacities
- Renal dysfunction
- Cardiovascular dysfunction
- Cerebrovascular complications
- Gastrointestinal manifestations
- Psychosocial manifestations



End-stage Fabry disease kidney
(courtesy of E. Gilbert-Barness and L. Barness, 2000)

Angiokeratomas
(courtesy of R. F. Desnick, PhD, MD)

RESOURCES

www.fabry.com
www.fabryregistry.com

OUR STORY

We are the parents of 2 children with mucopolysacchardosis (MPS I), more commonly referred to as Hurler, Hurler-Scheie, or Scheie syndrome. MPS I disease is a rare, inherited, lysosomal storage disorder caused by the deficiency of the lysosomal enzyme alpha-L-iduronidase. Deficiency of this enzyme results in the progressive accumulation of non-degraded material (called glycosaminoglycans, or GAG) in cells throughout the body. Here is our story….

"Mrs. Frix, did you know your son can't raise his arms above his head?"

In 1984, my wife Wanda and I were blessed with a baby boy, Michael, and with a baby girl named Ashley in 1987. For 5 years everything was normal in our family. One day in 1989, a daycare provider asked a question that would change our lives forever, "Mrs. Frix, did you know your son can't raise his arms above his head?" It was also brought to our attention that Michael couldn't do jumping jacks. The daycare provider thought he was just goofing around when in fact there was a problem far more serious then we could even imagine. Immediately, our first response was of course he can. We checked Michael that evening and his elbows would only come up to just under his eyes. There was something blocking his arms from going above his head.

Ashley turned 5 while we were stationed in Germany. She started limping and although,we noticed problems similar to Michael's, it never occurred to us that she could be affected with the same syndrome as Michael. Several doctors diagnosed her with "growing pains".

We returned to the United States where orthopedics diagnosed her with leg paresthesia. Ashley was then referred to the Shriner's Hospital in Greenville, S.C. and it was then that both children were diagnosed with Hurler-Scheie Syndrome by Dr. Curtis Rogers.

After learning about Michael and Ashley's syndrome, we started noticing more things that they were unable to do. We had been questioning why, why, why, after seeing so many doctors. Now all the puzzle pieces were beginning to fit together.

Michael was born with hernias which were identified at 2 weeks of age. He had surgery to repair the hernias when he was one month old. He also had 4 sets of tubes inserted in his ears as well as another hernia repair in his stomach area. We thought these were just normal problems, but Ashley had the same surgeries as well. Michael's joints progressively got stiffer. His arms, legs and fingers would no longer straighten. It seemed the older the children got, the stiffer their joints became. Michael's disease was most noticeable in his knees; he had a "space-walk" type of walk. Ashley's disease was most noticeable in her hands and fingers. She also had stiffness in her joints; her arms were as limited as Michael's and could not go above her head.

We noticed other limitations: our children loved to play ball however, they could not throw a ball up in the air. Their shoulder and arm rotation was such that they couldn't get any arc on anything they threw overhand. They loved playing in the band; however, their stiff joints and inability to get enough air in their lungs, led to them having to drop out of the band. Breathing, hearing, and vision were all affected. Michael wore hearing aids for some of his early years and his vision was affected with corneal clouding.

As Michael grew older, we needed to watch for other complications of Hurler-Scheie syndrome such as heart disease due to mucopolysaccharide storage in the heart valves. Michael started having seizures in 1998, and on August 22, 1998 he had his final seizure at the Atlanta Braves baseball game. Michael's heart got off rhythm. He died on August 22, 1998 of cardiac arrhythmias.

Ashley's disease had progressed, for the most part, as Michael's progressed. However, Ashley had mucopolysaccharide storage in areas different from Michael. In October 2001, Ashley was seen by her eye doctor and referred to a neurologist because of fluid collecting in her head. She had a VP Shunt placed to correct that problem. In March 2002, when she went to have braces put on her teeth, we were told her jaws had not developed normally. Her jaws were the size of a 5 year. She was 15 years old. Soon after, Ashley started losing her balance and falling for no apparent reason. After extensive testing by her neurosurgeon, she was diagnosed as having storage build up on her spinal cord; which was clamping down and causing her to lose her balance. In 2003, she had spine surgery to relieve this build up on her spine.

Her jaws were the size of a 5 year old, she was 15 years old.

Ashley had always had breathing problems due to mucopolysaccharide storage in her lung tissue. She was low on energy and felt bad much of the time.

In early 2003, while on a routine visit to Shriner's Hospital in Greenville SC, Dr. Rogers told us of a treatment he had heard about at an MPS I conference. He gave us contacts with Genzyme and through much work on both our parts Ashley started taking Aldurazyme, enzyme replacement therapy, in October 2003 at Emory University.

Ashley's progress, as a result of this treatment, is remarkable to say the least. Her breathing and lung capacity has increased. She is more limber, she doesn't hurt as much, and she feels all-around better than she has in so many years.

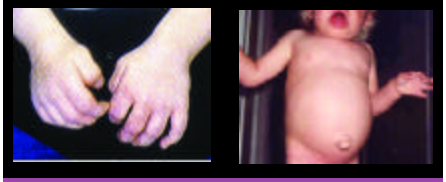
We thank all the folks that had a part in the development of Aldurazyme. While it isn't a cure for MPS I, it is a great help to the quality of life for Ashley. She can now brush the back of hair for the first time in her life, and she can go to the mall and shop from end to end.

We hope that after reading Michael and Ashley's story you are more aware of MPS I disease. For additional information regarding MPS I disease signs and symptoms, please call the Lysosomal Storage Disease Center at Emory University at 800-200-1524 or Genzyme Medical Information at 800-745-4447.

MPS I DISEASE

MAJOR SIGNS & SYMPTOMS

- Joint stiffness
- Skeletal deformities
- Coarse facial features
- Enlarged liver and spleen
- Corneal clouding
- Obstructive airway disease
- Recurrent ear and nose infections
- Valvular heart disease
- Inguinal/umbilical hernias



Joint deformity and organomegaly
(courtesy of Nat. MPS Soc., Inc.)

RESOURCES

www.mpsi.com
www.mpsiregistry.com

THE REGISTRY BENEFITS EVERYONE - DO YOUR PART!
www.mpsiregistry.com

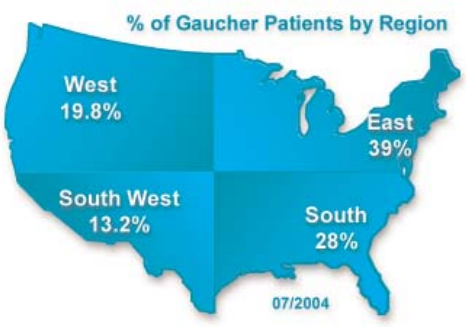
FACTS ABOUT THE REGISTRY

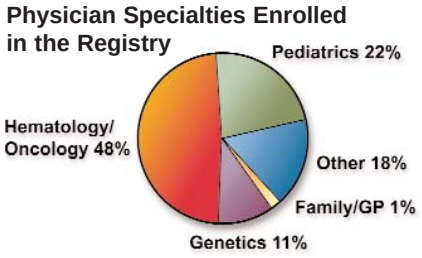
LYSOSOMAL STORAGE DISEASE REGISTRIES

A COLLECTIVE RESOURCE TO OPTIMIZE OUTCOMES

The Registry provides physicians access to a resource that can help better manage patients.

- Monitor disease progression through patient specific reports
- Exchange clinical data among participating physicians to facilitate clinical decision-making
- Access information on current treatment guidelines and practice patterns
- Potentially improve patient outcomes through information and collaboration





Examples of information available and made possible by the Lysosomal Storage Disease Registries Program.

THE REGISTRY BENEFITS EVERYONE - DO YOUR PART!

www.fabryregistry.com - www.gaucherregistry.com - www.mpsIregistry.com

COMING SOON

WHAT'S IN STORE

in Future Issues...

- You and the Registry
- Pompe Disease
- Clinical Trial Update
- Your Case Manager and You

Special thanks to the National Gaucher Foundation for making this newsletter possible.

HAVE YOU SEEN THESE?

Joint deformity and organomegaly: symptoms that can be found in MPS I disease.
(courtesy of Nat. MPS Soc., Inc.)

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Have you seen these lately?