



Center News

Emory Lysosomal Storage Disease Center

Emory LSDC News

The Emory Lysosomal Storage Disease Center is pleased to announce the opening of our new Genetics Infusion Center, concentrating on enzyme replacement therapy for patients with lysosomal storage diseases. Our patient-focused center is a cutting edge facility designed to provide patients with a level of personal and compassionate service unmatched by broader-focused infusion centers. The genetic infusion center provides a meeting place and stable medical home for patients who receive weekly, biweekly or monthly infusions.

Emory LSDC upcoming meetings

January 8, 2005 2-4 pm

The Emory Lysosomal Storage Disease Center's Open House for our New Genetic Infusion Center

January 29, 2005 1-4pm

The Annual Fabry Family Meeting
"Sick and Tired of Feeling Sick and Tired"
Maggiano's Little Italy-Buckhead
3368 Peachtree Road
Atlanta, GA

To RSVP for the Open House or Fabry Family Meeting, please call (800) 200-1524 or (404) 778-8565



Emory LSD team (left to right): Daniel Gruskin, MD, Karen Grinzaid, MS, Dawn Laney, MS, Eleanor Botha, MS, Sara Cooper MS, and Paul Fernhoff, MD

Welcome

This newsletter is designed by Healthcare Advocates specializing in lysosomal storage diseases as a resource for patients and families living with lysosomal storage disorders (LSDs). In particular, the newsletter will focus on issues of interest to individuals considering available therapy, those currently not on treatment and treatment related issues. The newsletter will feature scientific articles, general interest articles, family stories, upcoming national and local meetings as well as updates from the local LSD centers. 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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Patient Story

By Cecilia Fairley, MS, CGC UCSF - Stanford Lysosomal Disease Center

At our center, we have followed for many years a 35 year old Ashkenazi Jewish man with Gaucher disease, Type I. He has a long and complicated medical history and was originally misdiagnosed, which unfortunately is not uncommon in lysosomal storage diseases. His main concern throughout his care at our center has been the balance between adequately treating his Gaucher disease and trying to minimize its impact upon his life with regard to time and scheduling.

As a young child, he was diagnosed with a "blood disorder" while living in Poland and was treated with chemotherapy and a splenectomy. By the time he was a teenager, he had undergone 4 surgeries on his right femur. He moved to the US, was diagnosed with Gaucher disease, and began enzyme replacement therapy with the mid-level dose of 45 U/kg Ceredase shortly after it was approved in 1992. As a teenager, he began to voice concerns that Gaucher disease and enzyme replacement therapy were taking up too much time in his life. He was tired of being "sick". To try to compensate for this, we shortened the total time of his infusion, which he tolerated very well. Once he began college, he began to occasionally miss infusions. He stopped treatment entirely for nine months while in college due to his schedule. A few years later, he

resumed treatment at 60 U/kg, a high dose, after blood work revealed minor anemia (a low hemoglobin level) and possible bone disease progression. Four years later, his infusions stopped after he was found no longer able to be infused at home. At this time, he was enrolled in an advanced academic program and stated that he was "too busy" to take the time to receive treatment at an infusion center. He graduated from this program 18 months after stopping treatment. To celebrate his graduation, he took an extended trip and fractured both of his feet while walking around site-seeing. He resumed treatment at 60 U/kg at that time.

A consistent concern of this individual has been how much Gaucher disease intrudes upon his life and having to plan around an infusion schedule. He has stated several times that he is tired of being "sick" with Gaucher disease and needing treatment. Unfortunately, he has relatively severe disease and has had some blatant negative outcomes when stopping treatment, such as fractures and anemia. We are working with him to try to come up with a scheduling compromise. We want him to receive adequate treatment while still able to live his life as much as possible without feeling like it is dictated by Gaucher disease. Many individuals with Gaucher disease may feel this way and some of the alternatives that we have tried that have been helpful for this individual are a shorter infusion time and an infusion center that has extended hours including weekends. For someone who is able to do home infusions, who's insurance will pay for it, and who is comfortable with the infusion occurring in their home, this might also be a good alternative for scheduling.

Pharmacies Work With Patients to Simplify Home Infusion

By Lynette Washington, PharmD
Accredo Nova Factor

Since 1999, Lynette Washington, PharmD, has been working with Cerezyme® (imiglucerase for injection) and other lysosomal storage disorder therapies.

Chronically ill patients have unique needs and often require assistance to manage their therapies. Specialty pharmacies, like Nova Factor, help patients by meeting their specific needs and offering the coordination of home infusions.

Home infusions, when medically appropriate, may offer flexibility, convenience, and privacy for patients receiving enzyme replacement therapy (ERT). At first it may seem like there is a good amount of work involved in setting up the home infusion process, but once the initial coordination is done, home infusions may make it easier on the patient and the physician. For some patients, it permits infusions to occur in a familiar environment that increases comfort level and does not require travel.

The decision to transition to home care is a collaborative effort between the physician, patient, and (in most cases) the insurance company. The physician will evaluate each patient requesting home care and work with the home care agency and pharmacy to develop a treatment plan for the patient.

Patient Safety Is Important

The primary concern is always the patient's safety. The health care providers involved in patient treat-

ment take necessary precautions to help ensure that the patient is the appropriate candidate for home care, to ensure the nurse has proper training and to deliver the necessary supplies so that everything needed is on hand for a successful infusion and added peace of mind.

As a distributor partner to Genzyme, Nova Factor is a pharmacy experienced and trained in providing comprehensive services tailored to patients receiving Cerezyme® (imiglucerase for injection). The process for home care begins with Nova Factor's clinical coordinator, who is also a registered nurse. The clinical coordinator will credential and select a qualified and experienced agency based on the patient's geographical location, needs and preferences

As part of the Nova Factor credentialing process, the infusion nurse must attend an in-service training program on ERT infusion, dosage, proper storage, potential side effects and proper documentation. An educational reference manual is provided to each infusion nurse. Upon completion of the educational session, a competency test is required.

A pharmacist calls the patient prior to the initial visit to arrange the delivery of the medication and to validate the shipping address. During this call, the pharmacist will discuss the delivery process, the proper storage of the medication, and answer all questions the patient may have about ERT. A comprehensive drug history is obtained and documented to help ensure the safety of the patient. The clinical coordinator calls the patient and infusion nurse to schedule the initial visit. After the visit, the coordinator checks on the patient and the nurse to assess satisfaction. After the initial visit the pharmacist will call the patient to address additional questions. Once the initial visit has taken place the clinical coordinator monitors the infusion nurse/patient relationship on a quarterly basis, making adjustments as needed.

The infusion nurse documents each visit. A standardized visit report form is submitted to the pharmacy for communication, in part to assure timely changes to ship dates and supplies. Prior to each shipment, Nova Factor confirms the infusion date, doses on hand, address changes, and supply changes with the patient and/or caregiver. It is important that the patient or caregiver speak with a pharmacy representative before a shipment is sent to be sure someone is at home to receive the package. The pharmacy continues to monitor the safety and efficacy of the therapy administered at home during regular calls to arrange shipments. Information is submitted to the physician's office on an on-going basis to be sure the doctor is aware of the patient's progress.

The patient should notify the pharmacy and his or her doctor of all changes that may affect therapy, including vacations, illnesses, or hospitalizations. With advance notice, Nova Factor can partner with the physician and home care agency to help prevent missed or delayed infusions.

Flexibility Is Key

Flexibility of the infusion nurse, pharmacy, and the patient are key for successful home infusions. The patient can work with the infusion nurse to coordinate a date, time and/or place so the patient is comfortable. And, the patient can work with the pharmacy to coordinate ship dates and keep the pharmacy updated on changes so infusions and treatment plans are on track.

When medically appropriate, home infusions offer patients and physicians an opportunity to help make the management of their therapy more convenient. With the support of the pharmacy and other health care providers, the transition to home care can greatly enhance the convenience of the infusion process.

Monitoring Patients with type 1 Gaucher Disease: The Value of a Regular Schedule

By Neal J. Weinreb, MD

Living successfully with type 1 Gaucher disease is a lifelong challenge for patients and their families. Each patient has a unique complexion of symptoms and, therefore, management goals must be individually defined. Worldwide, most patients have symptoms, and treatment goals focus on the response to enzyme replacement therapy (ERT) as well as treatments for specific problems. Some patients, however, particularly North Americans and Israelis of Ashkenazic Jewish ethnicity, may not have symptoms when diagnosed, and do not require ERT (absent any signs of progressive or new manifestations). However, the ability to predict the future course of type 1 Gaucher disease in any given patient, even by referencing involved family members, is at best uncertain, as even apparently "healthy" patients may develop an unexpected complication such as a bone infarction. Therefore, regardless of whether or not

a patient presents with symptoms, the unpredictable, progressive, and sometimes clinically silent nature of the condition necessitates that all patients be regularly monitored.

Based on data from the Gaucher Registry and advice from numerous experts of the International Collaborative Gaucher Group (ICGG), a monitoring schedule was developed and summarized in Table 1 (Please see the back cover for monitoring guideline chart). It is important that patients with type 1 Gaucher disease and their families be familiar with this recommended schedule. The following describes the ICGG monitoring guidelines in more detail.

Patients Not Requiring ERT

Some patients are not on enzyme replacement therapy (ERT) because they do not have symptoms or their symptoms are minimal. Provided there is no change in the patient's condition, a complete physical examination, including quality-of-life scores and blood work (hemoglobin, platelet counts), every 12 months is recommended. Other tests, such as bone assessments, should be performed every 24 months to be sure that disease progression is not occurring "under the surface." The annual check-up presents an excellent opportunity for patients to review their overall medical condition with their physicians and, depending on age and personal and family medical

(cont.)

history, to arrange for other health maintenance tests unrelated to type 1 Gaucher disease such as blood pressure measurement, checking for diabetes or cholesterol problems, and cancer screening (mammograms, PSA (prostate-specific antigen), stool hemoccult cards, colonoscopy, PAP smear, etc).

Patients Receiving ERT

Patients receiving ERT fall into three categories: 1) patients who have not yet attained all treatment goals; 2) patients who require treatment reevaluation for a possible dose change due to a recent clinical complication, and; 3) patients who have achieved their established treatment goals and are in a maintenance phase. Depending on the ERT dose and schedule of administration, patients on maintenance ERT may be candidates for a trial of dose reduction.

Patients receiving ERT who are symptomatic and have not reached treatment goals require frequent evaluation. A physician visit with blood tests is recommended at no less than three-month intervals and liver/spleen and bone assessments (x-rays, MRIs, and DXA bone density testing) are recommended every 12 months. Response to treatment varies greatly among patients, but a general rule of thumb is that improvements are first seen in the blood tests. Hemoglobin and platelet counts generally begin to improve within six months after ERT is begun and may normalize by 12 months. Reductions in liver and spleen size can be documented during the first six months to one year period, but maximum improvement may require 2-5 years of ERT. Prevention of bone crises and decreased bone pain may occur during the first one to two years of ERT.

Should routine monitoring indicate that treatment goals have not been achieved within the expected time frames, a dose adjustment may be necessary. It is important to emphasize that improvements in blood counts and in liver and spleen size are significant; however, continued monitoring is necessary to assess disease manifestations, such as bone involvement. Should patients receiving ERT have a significant clinical complication between scheduled monitoring appointments, it is recommended that the treatment plan be reevaluated starting with a new comprehensive assessment. In either case, prior to increasing ERT dose, the physician and the patient should both be certain that the therapeutic setback is not caused by poor patient compliance (missed treatments), other diseases or conditions, or by the development of antibodies that may block the effect of ERT.

Patients receiving ERT who have met their established treatment goals and are on maintenance treatment also require regular monitoring, although less frequently than patients with persistent symptoms. A history and physical examination, blood tests and a quality of life (QOL) survey should be performed

annually. Provided the patient has neither new complaints nor evidence of clinical relapse, X-ray and other imaging studies may be done at two-year intervals. Patients with other medical problems that are not directly related to Gaucher disease should consult their physicians about how frequently they need to be seen.

It is extremely important to remember that maintaining a good treatment response is dependent on continuing ERT in the dose and frequency of administration that the physician recommends. There is experience from all over the world showing that patients who frequently skip treatments or who try so-called “drug holidays” may have a recurrence of symptoms, and may even dramatically worsen within a surprisingly short period of time.

Gaucher Registry

Recommendations for evaluating and monitoring patients with type 1 Gaucher disease were designed by a panel of scientific directors of the ICGG and are briefly summarized in this article. It is anticipated that these treatment and monitoring guidelines will continue to be updated as scientific knowledge increases and more data become available through the Gaucher Registry.

The concept that “each patient is different” certainly applies to those with type 1 Gaucher disease. The diversity of this population makes it easy to understand why each patient is a potential source of valuable scientific information and how extensive collective information can be used to help optimize individual patient care. Patients and their families can strengthen the Gaucher Registry by requesting that physicians enter their clinical data, by asking to review their individual patient case reports, and by encouraging their physicians to participate in the many educational activities the Registry supports.

Bibliography

1. Pastores GM, Weinreb NJ, Aerts H, et al. Therapeutic goals in the treatment of Gaucher disease. *Semin Hematol* 2004; 41 (suppl 5):4-14.
2. Weinreb NJ, Aggio MC, Andersson HC, et al. Gaucher Disease Type 1: Revised Recommendations on evaluations and monitoring for adult patients. *Semin Hematol* 2004; 41 (suppl 5):15-22.
3. Andersson HC, Charrow J, Kaplan P et al. Individualization of long-term enzyme replacement therapy for Gaucher disease. *Genetics in Medicine* 2005; 7: 105-110.

The Gaucher Registry

One of the most important benefits of participation in the Gaucher Registry, a program sponsored by Genzyme Corporation, is the sharing of information by ICGG physicians and other health care professionals. The objective of this information is to assist practitioners in assessing a patient's overall clinical course and help optimize care. The Gaucher Registry is open to all Type 1 Gaucher patients regardless of treatment status.

One of the standard formats used to compile and summarize Registry data is the patient case report, which provides individualized clinical outcomes. Patient case reports enable the physician, nurse, and genetic counselor to monitor the patient's disease and if on treatment, his or her treatment response. The reports summarize the changes in clinical parameters over time and include the following data:

- Demographics
- Height and weight
- ERT history (if on therapy)
- Hematologic (blood) changes
- Visceral organ (liver, spleen) volume changes
- Skeletal (bone) involvement
- Quality of life

Visit the Gaucher Registry Website:
www.gaucherregistry.com

Monitoring Guidelines for Other LSDs

Gaucher

https://www.lsdregistry.net/gaucherregistry/hcp/pdfs/greg_Recommendations_for_Monitoring.pdf

Fabry

https://www.lsdregistry.net/fabryregistry/hcp/pdfs/freg_schedule_of_assessments.pdf

MPSI

https://www.lsdregistry.net/mpsiregistry/pdfs/mreg_Minimum_Schedule_Assessments.pdf

Pompe

http://www.lsdregistry.net/pomperegistry/hcp/partic/mater/peg_schedule_of_assessments.pdf

Table 1: Minimum Evaluations for Monitoring Type 1 Gaucher Disease

	Patients Not on Enzyme Therapy		Patients on Enzyme Therapy			
			Not Achieved Therapeutic Goals		Achieved Therapeutic Goals	At Time of Dose Change or Significant Clinical Complication
	Every 12 Mo	Every 12-24 Mo	Every 3 Mo	Every 12 Mo	Every 12-24 Mo	
Comprehensive physical examination	■			■	■ (Annual)	
SF-36 (QoL) Survey	■			■	■ (Annual)	■
Blood Tests						
Hemoglobin	■		■		■	■
Platelet count	■		■		■	■
Biochemical markers ¹ • Chitotriosidase • ACE • TRAP	■		■		■	■
Additional Blood Tests²						
Visceral³						
Spleen volume (Volumetric MRI or CT)		■		■	■	■
Liver volume (Volumetric MRI or CT)		■		■	■	■
Skeletal⁶						
MRI of entire femora (Coronal; T1- & T2-weighted) ⁴		■		■	■	■
X-ray ^{4, 7}		■		■	■	■
DEXA		■		■	■	■
Pulmonary⁵						
<ol style="list-style-type: none"> One or more of these biochemical markers should be consistently monitored every 12 months and in conjunction with other clinical assessments of disease activity and response to treatment. Of the three recommended markers, chitotriosidase, when available as a validated procedure from an experienced laboratory, may be the most sensitive indicator of changing disease activity, and is therefore preferred. These should be followed appropriately if abnormal based on each patient's age and clinical status. Obtain contiguous transaxial 10 mm-thick sections for sum of region of interest. AP view of the entire femora (optimally from hips to below knees), and lateral view of the spine. 			<ol style="list-style-type: none"> Pulmonary assessments are recommended every 12-24 months for patients with borderline or above normal pulmonary pressures at baseline. Anatomical sites not included here should be evaluated if symptoms develop in such locations. Optional in absence of new symptoms or evidence of disease progression. <p>ABBREVIATIONS: ACE, angiotensin-converting enzyme; ALT, alanine aminotransferase; AP, anteroposterior; AST, aspartate aminotransferase; CT, computed tomography; DEXA, dual-energy X-ray absorptiometry; ECG, electrocardiogram; MRI, magnetic resonance imaging; PT, prothrombin time; PTT, partial thromboplastin time; TRAP, tartrate-resistant acid phosphatase; WBC, white blood cell.</p>			

Upcoming Patient Meetings

June 29 - July 2, 2006

Venice - Lido, Italy

9th International Symposium on Mucopolysaccharide and Related Disease

July 27-29, 2006

The 21st Annual MPS Society Family Conference

www.mpssociety.org