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# Horizons

A Newsletter for the Gaucher Community From the Genzyme Corporation



## Key Medical Research in Gaucher Disease

### *Also in this Issue:*

**The Journey to Diagnosis and Living with Type 1 Gaucher Disease:** Michelle's Story

**First Grader Who Chronicled His Experience with Gaucher Disease Now Headed to Medical School**  
Patient Update: Jeff Cohen

**Delicious Recipes,  
Holiday Tips,  
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What Concerns Patients with Type 1 Gaucher Disease and Their Families? ...	2
Key Medical Research into Gaucher Disease .....	4
Monitoring and Managing Bone Complications.....	6
The Genzyme Patient Advocacy Team...	7
The Journey to Diagnosis and Living with Type 1 Gaucher Disease .....	8
First Grader Who Chronicled His Experience with Gaucher Disease Now Headed to Medical School .....	10
Ask the Expert .....	13
Jewish Genetic Disease Consortium Continues to Evolve .....	14
Delicious Recipes.....	15
Holiday Tips .....	16

## From the Publisher

In the last two decades, tremendous strides have been made in the diagnosis and treatment of type 1 Gaucher disease, and we are pleased to share some of these new developments in the Winter 2008 issue of *HORIZONS*. Inside are highlights from recent articles from medical journals and interviews with two individuals with type 1 Gaucher who have learned to manage their disease successfully.

We also discuss concerns shared by patients with Gaucher disease and their families during recent Genzyme-sponsored focus groups; and Dr. Robert I. Parker answers your questions in our “Ask the Expert” column. On page 6, we explore Gaucher-related bone density loss and ways to identify it.

The Jewish Genetic Disease Consortium has helped increase awareness of lysosomal storage disorders like type 1 Gaucher disease. We cover their ongoing efforts, as well as Genzyme’s advocacy on behalf of the Gaucher community, through the Genzyme Patient Advocacy and Treatment Support teams.

In keeping with the holiday spirit, we include a few simple recipes and some tips on keeping safe and healthy this season. Please take a moment to complete and return the business reply card included in this issue and let us know your thoughts about this publication or submit a question for our “Ask the Expert” column.

**Wishing you a wonderful holiday season,**  
—Your team at Genzyme

# What Concerns Patients with Type 1 Gaucher Disease and Their Families?

**T**ype 1 Gaucher disease is a rare disorder, and individuals with this condition experience unique challenges related to diagnosis and treatment. To gain a better understanding of these patients’ concerns and attitudes about treatment, Genzyme hosted discussion groups for patients who have been receiving Cerezyme® (imiglucerase for injection) for at least 1 year and for parents of younger patients with type 1 Gaucher disease. Some of the groups’ participants had been undergoing treatment for more than 5 years.

The meetings produced many surprising findings. Some patients did not understand how the disorder affects other body functions and organs, particularly bones. Some did not know where to turn for supportive information and services to help them obtain medication and medication coverage. Others did not fully appreciate the impact that missed doses of medication could have in the treatment of type 1 Gaucher disease.

### Newly Diagnosed Patients Received Treatment Sooner Than Patients Diagnosed Years Ago

In the 1990s, few doctors were familiar with Gaucher disease; information on how to diagnose and treat the condition was just beginning to emerge. Only recently has awareness of type 1 Gaucher disease increased to the point where it is now recognized by physicians and other healthcare professionals. Thus, it is not surprising that type 1 Gaucher patients who have been undergoing enzyme replacement therapy for the longest period of time (more than 5 years) have generally experienced greater delays from symptom onset to diagnosis and treatment compared with new patients. This was borne out in the Genzyme discussion groups; patients who had been using Cerezyme the longest reported lengthier delays—and consequently more suffering—in getting a diagnosis and starting treatment than patients who received their diagnosis recently.

Some signs and symptoms associated with type 1 Gaucher disease are similar to those of other, more common disorders. Even today, it sometimes takes months or years for people with type 1 Gaucher disease to get an accurate diagnosis. In addition, the initial signs and

symptoms sometimes seem rather harmless, and it may be awhile before patients and their physicians suspect a progressive disease is at work. As a result, patients may not receive their first enzyme infusions until the illness is well underway.

### Missed Doses Are Missed Doses

Nearly everyone on any type of medication—antibiotics, pain relievers, a prescription for a chronic disease—occasionally misses a dose. It is no different for patients with type 1 Gaucher disease, although these patients are more likely to mischaracterize a missed dose as a “postponed” or “canceled” infusion session. Although patients in the focus groups acknowledged missing an infusion session on occasion, they rarely admitted to “missing a dose.”

To continue to benefit from treatment, it is important that patients receive regular intravenous infusions, even if they feel better. This is because once therapy stops, Gaucher cells may build up again and symptoms can return. Cerezyme is expected to be a long-term part of type 1 Gaucher disease therapy.

Half the patients in the focus groups said they received their infusions at home, but using home infusion does not guarantee that patients never miss a dose. The home health nurse may not show up, or a new nurse assigned to the

patient may not have the correct schedule.

Most parents participating in the groups expressed the view that home infusions worked best for children. They said that meeting the demands of treatment is more challenging when parents must leave work to transport their children to an infusion center or children are required to miss school or activities.

Home infusions are not for everyone. Every patient must be considered individually for home care. All patients start infusions as an outpatient under a doctor's supervision to monitor the safety and tolerability of the Cerezyme infusion. Once the physician determines that the patient has tolerated the drug and can move from an outpatient center to home infusion, insurance coverage must also be assessed.

Patients who cite appointment cancellations or postponements, home infusion nursing staff changes, or the inconvenience of a trip to the infusion center as reasons for missing doses need to be educated on the importance of adherence to their medication regimen. Adherence is essential to help avoid possible complications and ensure that patients derive the maximum benefit from their treatment. Patients should talk to their physician if they miss a dose.

### Securing Coverage for Treatment

Most health insurance plans place restrictions on how much the plan will spend on a person's medical care. Some designate annual limits, whereas others outline lifetime limits. Patients need to consult their individual plans to determine their coverage maximums.

Patients, the families of children with type 1 Gaucher disease, and providers may sometimes take coverage maximums into account when making initial treatment decisions. Determining a course of treatment based on coverage parameters may not represent the best approach to disease management in patients who need enzyme replacement. Treatment decisions should be made in conjunction with the patient's physician.

An insurance policy's maximum benefit limitation can present a challenge for patients seeking necessary treatment. Fortu-

nately, there are many ways to address this issue. Genzyme has established the Genzyme Treatment Support (GTS) team to help patients with type 1 Gaucher disease understand what their health plan offers in terms of benefits.

GTS is a free confidential service that supports patients in the United States who have a lysosomal storage disorder (LSD). For more than 15 years, GTS case managers have provided support to those living with an LSD and their families. GTS case managers are nurses, social workers, and other healthcare professionals employed by Genzyme. Case managers have extensive regional experience. They also have expertise in handling reimbursement issues, public and private health insurance, and healthcare delivery systems.

The GTS team can help patients determine how to use their coverage optimally and how to maintain existing coverage. GTS will work with the patient's health plan, seeking an exemption or trying to work out another solution so that the patient has access to essential treatment. For individuals who are having difficulty obtaining their medication, the National Gaucher Foundation ([www.gaucherdisease.org](http://www.gaucherdisease.org)) offers financial assistance programs.

### Maintaining Coverage for Older Children

Patients and the parents of patients who participated in the Genzyme focus groups shared another concern: Where can older children obtain health care coverage after they are no longer eligible under their parent's health plan? Options exist, but patients do not always know what they are or how to find them. This is another area where the GTS team can help. GTS case managers have experience working with patients to find alternate sources of funding. These might include state programs for adults with special needs or taking advantage of insurance options that allow patients to continue to access needed medications.

Educating patients on the availability of support services like the GTS team can ease some of the worry patients with type 1 Gaucher disease and their families feel, particularly in light of today's health insurance climate. Patients need to know that they are not alone; help and information are only a phone call away. For a detailed description on how the GTS team can help, patients can visit [www.gauchercare.com](http://www.gauchercare.com) or call (800) 745-4447, Option #3, or (617) 768-9000. Again, this resource is free and confidential for patients. ■

## Does Type 1 Gaucher Disease Damage Bones?

Gaucher cells accumulate in bone marrow and hasten the destruction of bone. This causes not only bone pain but also low bone density, which results in weak and brittle bones.

Nearly all patients in the discussion groups said they had bone disease, but few believed it was linked to Gaucher disease. Many patients said that even their physicians did not always attribute their bone disease to complications of type 1 Gaucher disease.

Current practice guidelines for patients with type 1 Gaucher disease recommend regular bone monitoring at least every 12 months, regardless of whether patients are undergoing treatment with enzyme replacement therapy. Monitoring might include radiography, magnetic resonance imaging, and tests to calculate bone mineral density.

# Key Medical Research into Gaucher Disease

## Introduction

**Darius Adams, MD**, Department of Pediatrics, Section of Genetics and Metabolism, Albany Medical Center, Albany, New York

This is an active and exciting time for Gaucher disease research. The International Collaborative Gaucher Group (ICGG) established the Gaucher Registry in 1991, to be a global resource to the medical and patient communities. The ICGG is a group of international experts in Gaucher disease and is the governing body of the Gaucher Registry.

The Gaucher Registry is sponsored by Genzyme Corporation and was developed for the purpose of collecting clinical information on patients with Gaucher disease, regardless of disease severity or treatment status. Data from the Gaucher Registry are retrospective and observational. These data have provided the medical community with important insights into the disease. The Gaucher Registry has more than 750 participating physicians in 60 countries contributing data. It is the largest database on patients with Gaucher disease.

Gaucher disease is a relatively rare disorder, and it is essential that we gather accurate and complete information on the disease and make it readily available. ICGG invites health care providers and researchers from around the world to provide and access clinical information about Gaucher disease through this centralized database. Sharing this information among medical professionals may facilitate earlier diagnosis, earlier intervention, and better disease management for people living with Gaucher disease.

For example, data indicate that individuals with type 1 Gaucher are at higher risk for multiple myeloma. This discovery has allowed

physicians to be more precise in targeting screening for individuals with Gaucher disease so that a potentially devastating condition can be detected earlier. Data also show that patients do not have an increased risk for several other cancers previously thought to be associated with type 1 Gaucher disease.

In addition, the Gaucher Registry offers vital information on treatments for type 1 Gaucher disease, such as data pointing to the benefit of long-term Cerezyme® (imiglucerase for injection) therapy in boosting bone density. Following are brief summaries of recent articles from medical journals reporting major research findings from studies on Gaucher disease that used data collected in the Gaucher Registry.

It is important to remember however, that there are some limitations associated with the use of the Gaucher Registry data common to most ob-

servational, non-randomized research. For example, the Registry is a collection of observational data and not a controlled clinical trial. The clinical data are voluntarily submitted into a database by physicians worldwide and have been collected and assessed by guidelines that may differ by region. Because of this, there is a potential for confounding factors or biases in the data. The following summaries are intended to help the broader Gaucher community understand the latest findings in Gaucher disease research.

As we move forward, we hope to continue this important work, illuminating other new discoveries on the pathophysiology of Gaucher disease. We also hope that our efforts continue to shed light on how therapies can be used to improve the lives of those afflicted with Gaucher disease.

If patients have questions about these topics or how they relate to their condition, they should consult their physician.



**Darius Adams, MD, with a patient**

Cerezyme® (imiglucerase for injection) is indicated for long-term enzyme replacement therapy for pediatric and adult patients with a confirmed diagnosis of type 1 Gaucher disease that results in one or more of the following conditions: anemia, thrombocytopenia, bone disease, hepatomegaly, splenomegaly.

### Important Safety Information

Side effects related to Cerezyme® (imiglucerase for injection) administration have been reported in less than 15% of patients. Each of the following events occurred in less than 2% of the total patient population. Reported side effects include nausea, vomiting, abdominal pain, diarrhea, rash, fatigue, headache, fever, dizziness, chills, backache, and rapid heart rate. Because Cerezyme® therapy is administered by intravenous infusion, reactions at the site of injection may occur: discomfort, itching, burning, swelling or uninfected abscess. Symptoms suggestive of allergic reaction include anaphylactoid reaction (a serious allergic reaction), itching, flushing, hives, an accumulation of fluid under the skin, chest discomfort, shortness of breath, coughing, cyanosis (a bluish discoloration of the skin due to diminished oxygen), and low blood pressure. Approximately 15% of patients have developed immune responses (antibodies); periodic monitoring by your physician is suggested. Patients should notify their physician immediately if they experience any side effects with treatment. For more information, consult your physician. To learn more, please see full product information; contact Genzyme at 800-745-4447, or visit [www.cerezyme.com](http://www.cerezyme.com). Cerezyme® is available by prescription only.

Patients are encouraged to report negative side effects of prescription drugs to the FDA. Visit [FDA.gov/medwatch](http://FDA.gov/medwatch), or call 1-800-FDA-1088.

## “Effect of Enzyme Replacement Therapy with Imiglucerase on BMD in Type 1 Gaucher Disease”

**Authors:** RJ Wenstrup, KA Kacena, P Kaplan, GM Pastores, A Prakash-Cheng, A Zimran, TN Hangartner  
Published in **The Journal of Bone and Mineral Research**, Volume 22, Number 1, 2007.

**E**nzyme replacement therapy with Cerezyme® (imiglucerase for injection) has been shown in numerous studies to improve a variety of signs and symptoms of type 1 Gaucher disease. Previously, little information was available about the treatment's effect on bone disease. People with type 1 Gaucher disease are frequently found to have reduced bone mineral density (BMD). Individuals with Gaucher disease lack sufficient amounts of an enzyme called glucocerebrosidase. Without this enzyme, a fatty substance called glucocerebroside builds up within cells (often called “Gaucher cells”) of various organs, including bone marrow. Reduction in BMD can occur as a result of this build up of “Gaucher cells” in the bone marrow. While it is believed that enzyme replacement therapy can help reduce the build up of glucocerebroside in certain cells, bones seem to take longer to show a response to treatment than do other signs of Gaucher disease, such as liver and spleen volume or platelet counts.

The authors of this study were interested in determining what effect treatment with Cerezyme has on BMD in patients with type 1 Gaucher disease. They used the Gaucher Registry to obtain anonymous medical information on more than 500 adults with type 1 Gaucher disease for whom results of an x-ray test to measure BMD, called dual energy x-ray Absorptiometry (DXA), were available. Women older than 50 years of age and children were not included in this study. People who had taken a type of medication for osteoporosis called bisphosphonates were also not included in this study. Researchers compared BMD scores in individuals who had received Cerezyme with those who had never received Cerezyme.

The researchers found that patients treated with Cerezyme showed significant improvements in BMD over time. Patients who had been treated for a longer time with Cerezyme showed greater improvement in BMD. After 8 years of treatment, some of these patients treated with Cerezyme had achieved BMD scores that approached average scores for the general population.

Tailoring therapy to meet the patient's individual therapeutic goals requires individualization of dosage. Responses to Cerezyme may vary, and the objective of individualized dosing is to enable the patient to achieve his or her therapeutic goals. Patients must be monitored after initiation of Cerezyme to assess drug tolerance and safety as well as whether their therapeutic goals have been met. Your physician will monitor your progress and determine if your dose should change based on your response. As with all therapeutic issues, patients should speak to their physicians about any questions or concerns they have regarding Cerezyme treatment.

The researchers also reported that patients with type 1 Gaucher disease had significantly lower BMD scores than are found in a reference population (people of the same height, weight, sex, and age who do not have Gaucher disease). The individuals in this study who were not treated with Cerezyme did not show any improvement in their BMD scores over time.

The researchers concluded that achieving and maintaining a normal BMD is an important therapeutic goal. Individuals with type 1 Gaucher disease may want to discuss BMD testing with their physician. ■

## “Gaucher Disease and Cancer Incidence: A Study from the Gaucher Registry”

**Authors:** BE Rosenbloom, NJ Weinreb, A Zimran, KA Kacena, J Charrow, E Ward  
Published in **Blood**, Volume 105, Number 12, 2005

**F**or many years, some physicians who treat patients with Gaucher disease have believed that individuals with Gaucher disease have a higher risk of developing cancer compared with the general population. While researchers cannot explain exactly why this might be true, some scientists believe that the way cells store excess glucocerebroside may interfere with the body's normal systems for preventing cancer. However, since Gaucher disease is so rare, it has been difficult to get enough information about enough patients with Gaucher disease to accurately measure the risk of cancer.

The authors of this study used data on almost 3000 patients from the Gaucher Registry. The majority of the patient population that was studied consisted of young or middle-aged adults. Only 14% of the population was older than 60 years of age. The researchers analyzed how often these patients were diagnosed with various forms of cancer. Then they compared those rates with cancer risk in the general population, adjusting for age (since cancer risk increases with age for all people). From the data that was reported, there appeared to be no overall increase

in the risk of developing cancer for people with Gaucher disease. The rates of relatively common cancers such as breast, prostate, and lung, were approximately the same in people with Gaucher disease and the population in general. However, the risk of one particular type of blood cancer, called multiple myeloma, appeared significantly higher in individuals with Gaucher disease. Data from the Gaucher Registry reported that people with Gaucher disease developed multiple myeloma approximately 6 times more often than would be expected. However, almost all the patients with multiple myeloma were older than 60 years of age, which is consistent with the general population.

The authors recommend that treating physicians be aware of the increased risk of multiple myeloma and monitor patients with Gaucher disease accordingly. Recently published guidelines recommend closely monitoring the immunoglobulin profile (a blood test that can indicate abnormalities in patients with blood cancer) in patients with type 1 Gaucher disease so that any warning signs of multiple myeloma

can be identified as early as possible.

Overall, these conclusions should reassure individuals with Gaucher disease and their families that their overall risk of cancer is no different from other people's risk, at least during early and middle age. As always, it is important to discuss your individual risk factors for cancer, including any family history of cancer, with your own physician. ■



Barry E.  
Rosenbloom, MD

# Monitoring and Managing Bone Complications

**M**ost people with type 1 Gaucher disease have some form of bone disease, which can be associated with pain and impairment of mobility. According to the Gaucher Registry, 83% of patients with type 1 Gaucher disease showed radiologic evidence of bone disease at the time of their diagnosis. Yet even though bone disease (or skeletal complications) is perhaps the most debilitating aspect of type 1 Gaucher disease, it is often not adequately assessed, managed, and monitored. Treatment with Cerezyme® (imiglucerase for injection) may improve some aspects of bone health over time (**Table I**).

It is important to know that some bone complications related to type 1 Gaucher disease may be preventable or reversible if treated early and adequately. Early diagnosis and treatment may help to avoid more serious consequences. Advanced bone disease may not be alleviated with treatment. In this short primer, we provide some background on bone complications in type 1 Gaucher disease.

## Bone Evaluation

Assessing the bone health of patients with type 1 Gaucher disease involves many diagnostic tools. Obtaining the patient's history and conducting a physical examination are vital to assess the bones' health properly. This allows the doctor to evaluate growth patterns, family history, bone pain and cri-

**Table I: Treatable Signs and Symptoms of Bone Disease Associated with Type 1 Gaucher Disease**

Bone crises	Episodes of severe pain, along with swelling, tenderness, and fever.
Bone pain	Nonspecific, dull, and achy; or localized and intense.
Bone mineral density (BMD)	BMD is the measurement of calcium and other minerals in the bone.

ses, stature, deformities, range of motion, gait, and stability. Once these are recorded, more detailed assessment of the bones can be performed using x-rays, magnetic resonance imaging, and dual energy x-ray absorptiometry (**Table II**). Other tests may also be used, depending on the individual's needs and testing availability.

**Table III** outlines the treatment goals for bone health when taking Cerezyme.

## Summary

Bone disease is a common concern in patients with type 1 Gaucher disease. Once a diagnosis of type 1 Gaucher disease has been confirmed, it is important that the patient and the patient's family and clinicians develop a set of realistic treatment goals for the patient's

overall health and his or her bone health.

Each body organ affected by type 1 Gaucher disease should have its own treatment goals, its own time lines, and its own methods for measuring treatment success. For bone problems, the symptoms may not be noticeable, but they are still important. It is essential to continue monitoring bone health even after other organs appear to have reached their treatment goals.

The specific therapeutic goals for bone disease are to lessen or eliminate bone pain and bone crises within 1 to 2 years of treatment. The onset or development of bone pathology during treatment should prompt investigation for loss of mechanical bone integrity, indicating the need for changes in therapy and orthopedic intervention. ■

**Table II: Most Common Methods Used to Monitor Bone Health in Type 1 Gaucher Disease**

Method	Test Purpose	Recommended Time Line*
X-ray	Provides information on bone structure and abnormalities.	Every 12–24 months or when a significant clinical or treatment change occurs.
MRI (magnetic resonance imaging)	Tells the extent of Gaucher cells in bone marrow and shows local abnormalities.	Every 12–24 months or when a significant clinical or treatment change occurs.
DXA/DEXA (dual energy x-ray absorptiometry)	This is the “gold standard” for measuring bone mineral density.	Every 12–24 months or when a significant clinical or treatment change occurs.

\*Table II recommendations are from the Gaucher Registry.

**Table III: Treatment Goals for Bone Health**

Patient	Treatment Goals	Timeframe
All patients	Lessen or eliminate bone pain; prevent bone crises.	1-2 years
Adult patients	Improving and normalizing bone mineral density.	8+ years

# The Genzyme Patient Advocacy Team

**G**enzyme established its Patient Advocacy Team in August 2001 as a 1-person operation dedicated to supporting the Pompe disease program. In the span of 7 years, the Patient Advocacy Team has evolved into a global, multifaceted organization with 6 employees and several priorities. The team supports all of Genzyme's lysosomal storage disorder (LSD) programs worldwide, as well as some other disease programs within Genzyme. The team's 6 employees have more than 30 years' cumulative industry experience covering the entire spectrum of LSDs. Every team member has worked extensively with patients, healthcare providers, and Genzyme cross-functional teams.

## Goals and Priorities of the Patient Advocacy Team

The Patient Advocacy Team embodies Genzyme's commitment to patients by serving as an interface for patient communities to establish ongoing relationships with the company. The team's primary goals are to help facilitate optimal patient care and support the provision of sustainable healthcare systems for individuals with serious, unmet medical needs. The Patient Advocacy Team pursues its goals using programs designed to enhance the team/patient partnership.

The Patient Advocacy Team also encourages an ideal level of patient-centered thinking and dialogue within the company, helping to foster a true understanding of patient communities. Kathleen Coolidge, Associate Director, US Patient Advocacy, Genzyme Corporation, analyzed the totality of the team's efforts and activities and outlined the team's three greatest priorities.

### **Priority 1: Exposing the company's personnel to the real lives of LSD patients.**

The Patient Advocacy Team strives to be patient-focused, working to understand the needs of patients with LSDs and communicating patients' feedback to the organization. One of the program's main goals is to sensitize Genzyme at large to the unique

needs and challenges faced by patients with LSDs such as type 1 Gaucher disease. Ms. Coolidge described how patients meet with members of the Patient Advocacy Team and share information about the nature of their disease and its course. She remarked that "it is impactful for staff to meet a real patient and understand what it is to need chronic or life-long therapy, as well as understanding what it is to live with a chronic disease."

The interaction between patient and team member benefits both parties and the company as a whole. It serves to help the team advocate better on patients' behalf, which in turn helps Genzyme serve the LSD patient population more effectively.

### **Priority 2: Supporting patient community leaders.**

Through programs such as the Facilitative Leadership Workshops, the Genzyme Patient Advocacy Team seeks to create and support a network of patient leaders drawn from the community. "We hold workshops internationally with the goal of helping patient leaders build the capacity of their organizations to better meet the needs of the community they serve," Ms. Coolidge explained.

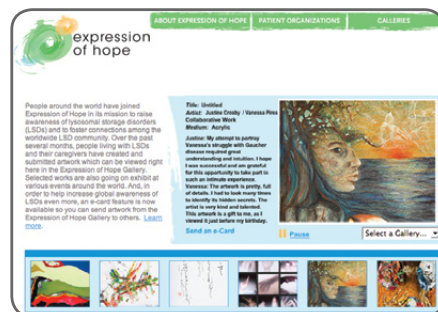
Genzyme started the Facilitative Leadership Workshops to help leaders of patient groups in the United States, Europe, and Latin America develop the skill sets needed to aid organizations in meeting their goals. Since the inception of Genzyme's workshops, more than 60 patient groups have participated. The Patient Advocacy Team facilitates and helps maintain Genzyme's relationships with these patient groups.

### **Priority 3: Expression of Hope.**

The Expression of Hope program is a major component of the Patient Advocacy Team's efforts. Patients and caregivers are encouraged to submit paintings inspired by their experiences with an LSD to Expression of Hope. Inspiration for the project came in part from the *also bin ich* (therefore I am) program in Germany. This artwork-based program was developed by the German Mucopolysaccharidoses (MPS) Society, an association of parents whose children have MPS, a rare metabolic disease.

The Expression of Hope Website ([www.expressionofhope.com](http://www.expressionofhope.com)) notes that "people

around the world have joined Expression of Hope in its mission to raise awareness of LSDs and to foster connections among the worldwide LSD community." According to the Website, more than 150 patients with an LSD and their caregivers submitted original artwork to Expression of Hope in 2006. The Website displays all submitted works in an online gallery and selects specific pieces of art for exhibition at various events worldwide. To increase global awareness of LSDs further, the Website includes an e-card feature that allows patients to send artwork from the gallery to friends and relatives.



Ms. Coolidge praised the Expression of Hope program as "a creative way [for Genzyme] to be engaged with the community," and she noted that through the program, patients have been able to share many inspiring stories. She relayed how moved she was by a painting of a dragon created by a child who had MPS. "When I asked about the choice of a dragon, the child stated that the dragon stood for the courage needed to face his disease." Ms. Coolidge said that the Patient Advocacy Team plans to launch the Expression of Hope 2 project in 2009.

## Patient-Focused Strategy Yields Results

The Patient Advocacy Team helps Genzyme optimize its service to patients with LSDs. It also provides tools patients can use to take charge of their disease, share their experiences with an LSD, and raise awareness in their communities. Ms. Coolidge expressed pride in the Patient Advocacy Team and its patient-focused mission. "We pay attention to what patients are saying, what it is that they emphasize...so we can incorporate their needs into our decisions," she concluded. ■

# The Journey to Diagnosis and Living with Type 1 Gaucher Disease

## Michelle's Story

**M**ichelle Pryor is a 30-year-old wife and mother of three children who was first diagnosed with type 1 Gaucher disease as a child. Like most individuals with type 1 Gaucher disease, her path to a diagnosis had many twists and turns.

When Michelle initially went to her physician as a child with an enlarged liver and spleen, her symptoms were dismissed as manifestations of baby fat. All in all, it took a couple of years for Michelle to get a final correct diagnosis of type 1 Gaucher disease. As distressing as this delay in diagnosis was, it could have been much worse if not for the consistently assertive involvement of Michelle's mother, who was very proactive and engaged in her daughter's care.

"My mom asked many questions of our doctors and always sought out a second opinion," recalled Michelle. "My mother also happened to know some clinical researchers, one of whom studied Gaucher disease." This researcher connected mother and daughter with experts at Mt. Sinai in New York City, where Michelle was officially diagnosed with type 1 Gaucher disease in 1985, at the age of seven.

### Waiting for Treatment

Although Michelle had the comfort of a definite diagnosis, effective treatment for her symptoms was still several years away. In the late 1980s, Michelle's persistent mother got her involved in one of the early clinical trials for enzyme replacement therapy.

Participation in the trial generated new hope that, eventually, Michelle's disease could be managed. "During the trial, I don't know if I felt a lot of physical change; however, I felt excited and hopeful that a therapy would help me in the future," Michelle said.

Michelle recalled that in her childhood, she was frequently burdened with alienation and weariness. "I definitely remember often being fatigued," she related, "and I was in a lot of pain and not able to keep up with the other kids. Although, in retrospect, it's good that I wasn't running around too much, because I probably would have experienced a lot more pain. Overall, as a child I found it difficult to join in and be a part of normal childhood activities with other kids."

As Michelle moved through her school years, she found that "it was hard to participate in activities. For example, my doctor told me not to take gym class. I still liked to be involved in school, so I participated in activities such as drama club. I didn't play sports until I was a junior in high school."

### A Life-Changing Time

The year 1992 represented a sea change in Michelle's life. She explained, "I began receiving regular treatment with enzyme replacement therapy in 1992, and my health improved noticeably."

In 1991, Genzyme introduced Ceredase® (alglucerase injection) and the US Food and Drug Administration granted marketing approval for Ceredase as a treatment for type 1 Gaucher disease. In 1994, Cerezyme® (imiglucerase for

injection), a genetically engineered form of Ceredase, became available for patients with type 1 Gaucher disease.

According to Michelle, the impact that this treatment had on her health and life was profound. Many of her symptoms associated with type 1 Gaucher disease

improved after she began treatment. Her bone pain, spleen enlargement, anemia (resulting in general weakness and fatigue), and thrombocytopenia (low platelet levels resulting in easy bruising and bleeding) all improved, which helped Michelle feel better and become more active.

Still, challenges persisted. For the first year, Michelle obtained treatment at a children's hospital located over 100 miles away from her home. Living in a rural area, far from her point-of-treatment, turned therapy into a drawn-out, disruptive affair. "It was hard getting the treatment as a teenager," Michelle reported. "It was time-consuming—the entire process included back-and-forth travel, waiting, preparation, and the actual therapy—and took up the whole day."

"Treatments meant a lot of waiting. I had to get there by 8:00 in the morning," Michelle remembered. "Mid-to-late morning was consumed with preparation, and it wasn't until after lunch that hospital personnel would start the infusion." The infusion would be completed by late afternoon, which was followed by a long ride home.

Michelle's infusion experience during this time also offered her an unexpected—and sobering—perspective on her disease. When she arrived for treatments, Michelle explained, "I would have to go through the oncology ward on the way to receive my infusions and witness the life-or-death situations that other kids were experiencing." Seeing these courageous children battle health situations much more serious than her own gave Michelle a more practical understanding of her illness, which was not life-threatening and was being managed.

In addition to providing her impressionable, youthful mind with a degree of trauma, the ward also provided a valued life-lesson: "It's certainly easy to get stuck in one's own problems," Michelle stated, "[but] the oncology ward helped put things in perspective and taught me to be more empathetic."

*"I began receiving regular treatment with enzyme replacement therapy in 1992, and my health improved noticeably."*

Patient responses to treatment with Cerezyme may vary. Please see Important Safety Information on page 9.

In addition to her early experiences passing by patients in the oncology ward, Michelle explained that having the disease has radically broadened her horizons and the depth of her outlook. "Having type 1 Gaucher disease has helped me be more empathetic and turned me toward the profession that I have now (occupational therapist). Because of my experiences with type 1 Gaucher disease, I wanted to help people be independent and achieve their goals, to help them get stronger and help them take care of themselves. Although I am healthy and stable at this point, I know what its like to struggle with pain and not have the energy to do what you want to do," Michelle said.

Michelle's heightened level of compassion has also encouraged advocacy and activism on behalf of Gaucher awareness. "If I lived in a more urban area, I would be more involved with promoting Gaucher awareness," she noted, explaining that her rural Pennsylvania location limits the scope of her opportunities in this realm. Still, Michelle has been able to help facilitate Gaucher disease education among friends, family, and her immediate community. "In general, I'm open about what I go through. I have alerted my siblings and other members of my immediate family to the genetic risk factors. Thankfully, they've all been tested and none have the disease." In addition, Michelle has initiated various contacts with people of Jewish descent to make them aware of the risks of Gaucher disease and to spread the message that if they want to start a family, they should consider getting screened. Ironically, the majority of Michelle's informal outreach has been directed at the healthcare community. "A lot of doctors have never dealt with someone with type 1 Gaucher disease and have never had to treat it," she explained.

## Living with Type 1 Gaucher Disease Gets Easier

Eventually, Michelle's access to treatment facilities improved, as circumstances allowed for increased convenience and control. Michelle's family found a facility that was open on Saturdays, eliminating disruptions during the school week. Around this time, she also moved closer to a big hospital that was equipped to provide her with a more locally based point-of-treatment.

"Additionally, once my symptoms became more controlled," stated Michelle, "it got easier." Michelle's sense of ease, control, and convenience was further enhanced when her physician determined that she could move her therapy out of an institutional outpatient facility setting and into her home. Currently, Michelle receives her Cerezyme® (imiglucerase for injection) treatment via home infusion.

All patients receiving Cerezyme treatment are monitored for any side effects and tolerance to the drug. Michelle's physician believed that she was in stable condition, and because her insurance allowed for home infusion, her physician thought it would be beneficial as long as she had regular assessments and monitoring.

Staying involved in one's treatment is an important component of staying well. It is also important to have specific goals and targets, to help the patient and physician determine how well the treatment is working. All patients need to see their physicians on a regular basis and undergo periodic comprehensive evaluations to be sure that their response is optimal. This is particularly important for patients receiving home infusion therapy. Home infusion may not be appropriate for everyone, and patients need to consult with their treating physicians. It is also recommended that patients consult with

a Genzyme Treatment Support case manager to assess their insurance coverage.

"Getting treatment at home has many advantages," according to Michelle. "It's flexible, I can do things around the house, and I don't have to find care for my kids. Traveling to treatment was always a challenge. You don't know how long it's going to take and there is always the possibility of delays. It's a longer process at a clinic," she added

Overall, there have been many positive changes in Michelle's life, including the improvement of many of her symptoms associated with type 1 Gaucher disease. "Prior to Cerezyme treatment, I had trouble with bone pain and anemia (low red blood cell-count), which resulted in general weakness and fatigue.

I try to lead an active life that includes marriage, raising three kids, working part-time, and being active in church." In addition to teaching a ballet class at her church, Michelle likes to walk the shores of a nearby river and take backpacking trips. On the subject of being active, she quipped that "having three kids is pretty much exercise in and of itself."

## Conclusion: Reasons to Be Grateful

"I'm really grateful for the treatment and I'm interested in what the future holds for the treatment of type 1 Gaucher disease," Michelle concluded. "Genzyme has always been very supportive. When I've had struggles with insurance issues, Genzyme Treatment Support was there to assist me," she said.

Another person to whom Michelle feels she owes her present state of health and life-quality is her mother. "My mom was a strong person," remembered Michelle. "She wouldn't take the easy answer or way out, regardless of whether the issue was: diagnosis challenge, cost, or a struggle with insurance issues. I admire her for doing that." ■

Cerezyme® (imiglucerase for injection) is indicated for long-term enzyme replacement therapy for pediatric and adult patients with a confirmed diagnosis of type 1 Gaucher disease that results in one or more of the following conditions: anemia, thrombocytopenia, bone disease, hepatomegaly, splenomegaly.

### Important Safety Information

Side effects related to Cerezyme® (imiglucerase for injection) administration have been reported in less than 15% of patients. Each of the following events occurred in less than 2% of the total patient population. Reported side effects include nausea, vomiting, abdominal pain, diarrhea, rash, fatigue, headache, fever, dizziness, chills, backache, and rapid heart rate. Because Cerezyme® therapy is administered by intravenous infusion, reactions at the site of injection may occur: discomfort, itching, burning, swelling or uninfected abscess. Symptoms suggestive of allergic reaction include anaphylactoid reaction (a serious allergic reaction), itching, flushing, hives, an accumulation of fluid under the skin, chest discomfort, shortness of breath, coughing, cyanosis (a bluish discoloration of the skin due to diminished oxygen), and low blood pressure. Approximately 15% of patients have developed immune responses (antibodies); periodic monitoring by your physician is suggested. Patients should notify their physician immediately if they experience any side effects with treatment. For more information, consult your physician. To learn more, please see full product information; contact Genzyme at 800-745-4447, or visit [www.cerezyme.com](http://www.cerezyme.com). Cerezyme® is available by prescription only.

Patients are encouraged to report negative side effects of prescription drugs to the FDA. Visit [FDA.gov/medwatch](http://FDA.gov/medwatch), or call 1-800-FDA-1088.

# First Grader Who Chronicled His Experience with Gaucher Disease Now Headed to Medical School

## *Patient Update: Jeff Cohen*

**W**hen Jeff Cohen was 6 years old and in the first grade, he authored a memoir detailing his experiences with type 1 Gaucher disease. *Horizons* published this diary in 1997, when Jeff was a 10-year-old fourth grader. The article reflected Jeff's intelligence and upbeat attitude despite the disease's effects, and it largely glossed over the strain associated with the disease. Jeff looked back at his initial diagnosis and experience with type 1 Gaucher's disease over the years.

### Getting a Diagnosis

In the first years of his life, Jeff was asymptomatic and never experienced any Gaucher-related difficulties or discomfort. "When I was 4 years old," Jeff recalled, "my mother realized that I was getting bruises in places kids shouldn't have bruises. The bruises weren't on my knees and elbows, but on the middle of my back." Jeff's mother suspected he might have a low platelet count and took him to his pediatrician's office.

The pediatrician noted that, in addition to the mysterious bruises, Jeff had a swollen abdomen. He ordered a series of diagnostic tests, including a sonogram, computed tomography scan, and blood tests. Doctors initially believed that 4-year-old Jeff might have acute lymphocytic leukemia (ALL), and he underwent a painful bone marrow biopsy. "It hurt severely," Jeff said. "I remember crying and gyrating; I was told that it took 5 nurses to hold me down."

Fortunately for Jeff, the proposed leukemia diagnosis turned out to be a false alarm. "The bone marrow and blood tests came back negative for leukemia. My pediatrician recognized the presence of Gaucher cells, and I was referred to Mt. Sinai," Jeff explained. At Mt. Sinai, Jeff received a definitive diagnosis of type 1 Gaucher disease, and his parents received an outline of treatment options.

### Lifelong Therapy

Jeff was lucky that doctors diagnosed his disease quickly and correctly. In 1992, he started enzyme replacement therapy.

Jeff receives Cerezyme® (imiglucerase for infusion) every 2 weeks, and he attributes strict adherence to his infusion schedule with successful disease management. Jeff credits proper planning and a willingness to be flexible with helping him adhere flawlessly to his medication schedule. "To this day I've never missed a single dose of Cerezyme," he said, adding, "I plan everything around my infusions, especially travel and vacations."



Jeff Cohen

### Disease Inspires Pursuit of Medical Career

For Jeff, the most profound impact of type 1 Gaucher disease has been on his future ambitions. Today he is a junior at the University of Rochester, in Rochester, New York. He reflected on his experiences with Gaucher disease in college admission essays, helping him gain acceptance into the competitive Bachelor-MD degree program at the University of Rochester. This program will allow Jeff to enter medical school automatically after graduation.

He credits his experience with type 1 Gaucher disease as inspiring him to follow this academic path because it made him want to give something back to the medical community. "At the root of my desire to practice medicine," related Jeff, "was the experience I had with treatment, seeing the good physicians and wanting to emulate them. Having personally been through the process, I can feel empathy for the patient." He believes that his experience as a chronic patient has given him a unique outlook on various aspects of the healthcare system. Jeff also feels that dealing with the rigors of type 1 Gaucher disease prepared him for the rigors of the program's demanding academic work and said it "helped me to be a strong student."

### Searching for the Optimal Specialty

Although Jeff has not decided which specific area of medicine he intends to practice, he said he is leaning against treating patients with type 1 Gaucher disease simply because "it hits a little too close to home." One of his mentors—Dr. Greg Pastores from the New York University Medical Center, a physician who treats patients with Gaucher disease—has urged him to reconsider.

In the 1990s, Dr. Pastores was affiliated with Mt. Sinai, and he is the clinician who first gave 4-year-old Jeff a diagnosis of type 1 Gaucher disease. "He was my doctor," explained Jeff, "and I was the youngest child that he ever diagnosed with type 1 Gaucher disease." Jeff has spent two summers conducting Gaucher-related research for Dr. Pastores in the neurological laboratory. "We've reviewed a lot of the latest Gaucher-related research papers together. It's nice to have that kind of relationship," Jeff noted.

Jeff said, "It's too early to tell," what area of medicine he will focus on. "I'll see where medical school takes me," he added. Currently, Jeff spends a lot of time contemplating the relationship between physician and patient, and he knows with certainty that he wants to work with children. "I want to get into pediatrics because I like the idea of helping children," Jeff stated.

Jeff believes that regardless of the specific clinical area he decides to pursue, entering the medical field will give him opportunities to exert a positive influence on individuals and society. "It may sound surprising," Jeff said, "but in some ways, I'm thankful that I have type 1 Gaucher disease." He described how having the disease led to unique experiences and relationships he otherwise would never have had. "The fact that I have type 1 Gaucher disease has turned me into who I am today," he concluded. ■

Results may not be typical. Patient experience with treatment may vary. Please see Important Safety Information on page 9.



**Cerezyme**<sup>®</sup>  
(imiglucerase for injection)

**200 UNITS**

**400 UNITS**

#### DESCRIPTION

**Cerezyme**<sup>®</sup> (imiglucerase for injection) is an analogue of the human enzyme  $\beta$ -glucocerebrosidase, produced by recombinant DNA technology.  $\beta$ -Glucocerebrosidase ( $\beta$ -D-glucosyl-N-acylsphingosine glucohydrolase, E.C. 3.2.1.45) is a lysosomal glycoprotein enzyme which catalyzes the hydrolysis of the glycolipid glucocerebroside to glucose and ceramide.

**Cerezyme**<sup>®</sup> is produced by recombinant DNA technology using mammalian cell culture (Chinese hamster ovary). Purified imiglucerase is a monomeric glycoprotein of 497 amino acids, containing 4 N-linked glycosylation sites ( $M_r = 60,430$ ). Imiglucerase differs from placental glucocerebrosidase by one amino acid at position 495, where histidine is substituted for arginine. The oligosaccharide chains at the glycosylation sites have been modified to terminate in mannose sugars. The modified carbohydrate structures on imiglucerase are somewhat different from those on placental glucocerebrosidase. These mannose-terminated oligosaccharide chains of imiglucerase are specifically recognized by endocytic carbohydrate receptors on macrophages, the cells that accumulate lipid in Gaucher disease.

**Cerezyme**<sup>®</sup> is supplied as a sterile, non-pyrogenic, white to off-white lyophilized product. The quantitative composition of the lyophilized drug is provided in the following table:

Ingredient	200 Unit Vial	400 Unit Vial
Imiglucerase (total amount)*	212 units	424 units
Mannitol	170 mg	340 mg
Sodium Citrates	70 mg	140 mg
(Trisodium Citrate)	(52 mg)	(104 mg)
(Disodium Hydrogen Citrate)	(18 mg)	(36 mg)
Polysorbate 80, NF	0.53 mg	1.06 mg
Citric Acid and/or Sodium Hydroxide may have been added at the time of manufacture to adjust pH.		

\*This provides a respective withdrawal dose of 200 and 400 units of imiglucerase.

An enzyme unit (U) is defined as the amount of enzyme that catalyzes the hydrolysis of 1 micromole of the synthetic substrate para-nitrophenyl- $\beta$ -D-glucopyranoside (pNP-Glc) per minute at 37°C. The product is stored at 2-8°C (36-46°F). After reconstitution with Sterile Water for Injection, USP, the imiglucerase concentration is 40 U/mL (see **DOSAGE AND ADMINISTRATION** for final concentrations and volumes). Reconstituted solutions have a pH of approximately 6.1.

#### CLINICAL PHARMACOLOGY

##### Mechanism of Action/Pharmacodynamics

Gaucher disease is characterized by a deficiency of  $\beta$ -glucocerebrosidase activity, resulting in accumulation of glucocerebroside in tissue macrophages which become engorged and are typically found in the liver, spleen, and bone marrow and occasionally in lung, kidney, and intestine. Secondary hematologic sequelae include severe anemia and thrombocytopenia in addition to the characteristic progressive hepatosplenomegaly, skeletal complications, including osteonecrosis and osteopenia with secondary pathological fractures. **Cerezyme**<sup>®</sup> (imiglucerase for injection) catalyzes

the hydrolysis of glucocerebroside to glucose and ceramide. In clinical trials, **Cerezyme**<sup>®</sup> improved anemia and thrombocytopenia, reduced spleen and liver size, and decreased cachexia to a degree similar to that observed with Ceredase<sup>®</sup> (alglucerase injection).

##### Pharmacokinetics

During one-hour intravenous infusions of four doses (7.5, 15, 30, 60 U/kg) of **Cerezyme**<sup>®</sup> (imiglucerase for injection), steady-state enzymatic activity was achieved by 30 minutes. Following infusion, plasma enzymatic activity declined rapidly with a half-life ranging from 3.6 to 10.4 minutes. Plasma clearance ranged from 9.8 to 20.3 mL/min/kg (mean  $\pm$  S.D., 14.5  $\pm$  4.0 mL/min/kg). The volume of distribution corrected for weight ranged from 0.09 to 0.15 L/kg (0.12  $\pm$  0.02 L/kg). These variables do not appear to be influenced by dose or duration of infusion. However, only one or two patients were studied at each dose level and infusion rate. The pharmacokinetics of **Cerezyme**<sup>®</sup> do not appear to be different from placental-derived alglucerase (Ceredase<sup>®</sup>).

In patients who developed IgG antibody to **Cerezyme**<sup>®</sup>, an apparent effect on serum enzyme levels resulted in diminished volume of distribution and clearance and increased elimination half-life compared to patients without antibody (see **WARNINGS**).

#### INDICATIONS AND USAGE

**Cerezyme**<sup>®</sup> (imiglucerase for injection) is indicated for long-term enzyme replacement therapy for pediatric and adult patients with a confirmed diagnosis of Type 1 Gaucher disease that results in one or more of the following conditions:

- anemia
- thrombocytopenia
- bone disease
- hepatomegaly or splenomegaly

#### CONTRAINDICATIONS

There are no known contraindications to the use of **Cerezyme**<sup>®</sup> (imiglucerase for injection). Treatment with **Cerezyme**<sup>®</sup> should be carefully re-evaluated if there is significant clinical evidence of hypersensitivity to the product.

#### WARNINGS

Approximately 15% of patients treated and tested to date have developed IgG antibody to **Cerezyme**<sup>®</sup> (imiglucerase for injection) during the first year of therapy. Patients who developed IgG antibody did so largely within 6 months of treatment and rarely developed antibodies to **Cerezyme**<sup>®</sup> after 12 months of therapy. Approximately 46% of patients with detectable IgG antibodies experienced symptoms of hypersensitivity.

Patients with antibody to **Cerezyme**<sup>®</sup> have a higher risk of hypersensitivity reaction. Conversely, not all patients with symptoms of hypersensitivity have detectable IgG antibody. It is suggested that patients be monitored periodically for IgG antibody formation during the first year of treatment.

Treatment with **Cerezyme**<sup>®</sup> should be approached with caution in patients who have exhibited symptoms of hypersensitivity to the product.

Anaphylactoid reaction has been reported in less than 1% of the patient population. Further treatment with imiglucerase should be conducted with caution. Most patients have successfully continued therapy after a reduction in rate of infusion and pretreatment with antihistamines and/or corticosteroids.

#### PRECAUTIONS

##### General

In less than 1% of the patient population, pulmonary hypertension and pneumonia have also been observed during treatment with **Cerezyme**<sup>®</sup> (imiglucerase for injection). Pulmonary hypertension and pneumonia are known complications of Gaucher disease and have been observed both in patients receiving and not receiving **Cerezyme**<sup>®</sup>. No causal relationship with **Cerezyme**<sup>®</sup> has been established. Patients with respiratory symptoms in the absence of fever should be evaluated for the presence of pulmonary hypertension.

Therapy with **Cerezyme**<sup>®</sup> should be directed by physicians knowledgeable in the management of patients with Gaucher disease.

Caution may be advisable in administration of **Cerezyme**<sup>®</sup> to patients previously treated with Ceredase<sup>®</sup> (alglucerase injection) and who have developed antibody to Ceredase<sup>®</sup> or who have exhibited symptoms of hypersensitivity to Ceredase<sup>®</sup>.

FPO

# FPO

### Carcinogenesis, Mutagenesis, Impairment of Fertility

Studies have not been conducted in either animals or humans to assess the potential effects of **Cerezyme**<sup>®</sup> (imiglucerase for injection) on carcinogenesis, mutagenesis, or impairment of fertility.

### Teratogenic Effects: Pregnancy Category C

Animal reproduction studies have not been conducted with **Cerezyme**<sup>®</sup> (imiglucerase for injection). It is also not known whether **Cerezyme**<sup>®</sup> can cause fetal harm when administered to a pregnant woman or can affect reproductive capacity. **Cerezyme**<sup>®</sup> should not be administered during pregnancy except when the indication and need are clear and the potential benefit is judged by the physician to substantially justify the risk.

### Nursing Mothers

It is not known whether this drug is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when **Cerezyme**<sup>®</sup> (imiglucerase for injection) is administered to a nursing woman.

### Pediatric Use

The safety and effectiveness of **Cerezyme**<sup>®</sup> (imiglucerase for injection) have been established in patients between 2 and 16 years of age. Use of **Cerezyme**<sup>®</sup> in this age group is supported by evidence from adequate and well-controlled studies of **Cerezyme**<sup>®</sup> and **Ceredase**<sup>®</sup> (alglucerase injection) in adults and pediatric patients, with additional data obtained from the medical literature and from long-term post-marketing experience. **Cerezyme**<sup>®</sup> has been administered to patients younger than 2 years of age, however the safety and effectiveness in patients younger than 2 have not been established.

### ADVERSE REACTIONS

Since the approval of **Cerezyme**<sup>®</sup> (imiglucerase for injection) in May 1994, Genzyme has maintained a worldwide post-marketing database of spontaneously reported adverse events and adverse events discussed in the medical literature. The percentage of events for each reported adverse reaction term has been calculated using the number of patients from these sources as the denominator for total patient exposure to **Cerezyme**<sup>®</sup> since 1994. Actual patient exposure is difficult to obtain due to the voluntary nature of the database and the continuous accrual and loss of patients over that span of time. The actual number of patients exposed to **Cerezyme**<sup>®</sup> since 1994 is likely to be greater than estimated from these voluntary sources and, therefore, the percentages calculated for the frequencies of adverse reactions are most likely greater than the actual incidences.

Experience in patients treated with **Cerezyme**<sup>®</sup> has revealed that approximately 13.8% of patients experienced adverse events which were judged to be related to **Cerezyme**<sup>®</sup> administration and which occurred with an increase in frequency. Some of the adverse events were related to the route of administration. These include discomfort, pruritus, burning, swelling or sterile abscess at the site of venipuncture. Each of these events was found to occur in < 1% of the total patient population.

Symptoms suggestive of hypersensitivity have been noted in approximately 6.6% of patients. Onset of such symptoms has occurred during or shortly after infusions; these symptoms include pruritus, flushing, urticaria, angioedema, chest discomfort, dyspnea, coughing, cyanosis, and hypotension. Anaphylactoid reaction has also been reported (see **WARNINGS**). Each of these events was found to occur in < 1.5% of the total patient population. Pre-treatment with antihistamines and/or corticosteroids and reduced rate of infusion have allowed continued use of **Cerezyme**<sup>®</sup> in most patients.

Additional adverse reactions that have been reported in approximately 6.5% of patients treated with **Cerezyme**<sup>®</sup> include: nausea, abdominal pain, vomiting, diarrhea, rash, fatigue, headache, fever, dizziness, chills, backache, and tachycardia. Each of these events was found to occur in < 1.5% of the total patient population.

Incidence rates cannot be calculated from the spontaneously reported adverse events in the post-marketing database. From this database, the most commonly reported adverse events in children (defined as ages 2 – 12 years) included dyspnea, fever, nausea, flushing, vomiting, and coughing, whereas in adolescents (>12 – 16 years) and in adults (>16 years) the most commonly reported events included headache, pruritis, and rash.

In addition to the adverse reactions that have been observed in patients treated with **Cerezyme**<sup>®</sup>, transient peripheral edema has been reported for this therapeutic class of drug.

### OVERDOSE

Experience with doses up to 240 U/kg every 2 weeks have been reported. At that dose there have been no reports of obvious toxicity.

### DOSAGE AND ADMINISTRATION

**Cerezyme**<sup>®</sup> (imiglucerase for injection) is administered by intravenous infusion over 1-2 hours. Dosage should be individualized to each patient. Initial dosages range from 2.5 U/kg of body weight 3 times a week to 60 U/kg once every 2 weeks. 60 U/kg every 2 weeks is the dosage for which the most data are available. Disease severity may dictate that treatment be initiated at a relatively high dose or relatively frequent administration. Dosage adjustments should be made on an individual basis and may increase or decrease, based on achievement of therapeutic goals as assessed by routine comprehensive evaluations of the patient's clinical manifestations.

**Cerezyme**<sup>®</sup> should be stored at 2-8°C (36-46°F). After reconstitution, **Cerezyme**<sup>®</sup> should be inspected visually before use. Because this is a protein solution, slight flocculation (described as thin translucent fibers) occurs occasionally after dilution. The diluted solution may be filtered through an in-line low protein-binding 0.2 µm filter during administration. Any vials exhibiting opaque particles or discoloration should not be used. DO NOT USE **Cerezyme**<sup>®</sup> after the expiration date on the vial.

On the day of use, after the correct amount of **Cerezyme**<sup>®</sup> to be administered to the patient has been determined, the appropriate number of vials are each reconstituted with Sterile Water for Injection, USP. The final concentrations and administration volumes are provided in the following table:

	200 Unit Vial	400 Unit Vial
Sterile water for reconstitution	5.1 mL	10.2 mL
Final volume of reconstituted product	5.3 mL	10.6 mL
Concentration after reconstitution	40 U/mL	40 U/mL
Withdrawal volume	5.0 mL	10.0 mL
Units of enzyme within final volume	200 units	400 units

A nominal 5.0 mL for the 200 unit vial (10.0 mL for the 400 unit vial) is withdrawn from each vial. The appropriate amount of **Cerezyme**<sup>®</sup> for each patient is diluted with 0.9% Sodium Chloride Injection, USP, to a final volume of 100 – 200 mL. **Cerezyme**<sup>®</sup> is administered by intravenous infusion over 1-2 hours. Aseptic techniques should be used when diluting the dose. Since **Cerezyme**<sup>®</sup> does not contain any preservative, after reconstitution, vials should be promptly diluted and not stored for subsequent use. **Cerezyme**<sup>®</sup>, after reconstitution, has been shown to be stable for up to 12 hours when stored at room temperature (25°C) and at 2-8°C. **Cerezyme**<sup>®</sup>, when diluted, has been shown to be stable for up to 24 hours when stored at 2-8°C.

Relatively low toxicity, combined with the extended time course of response, allows small dosage adjustments to be made occasionally to avoid discarding partially used bottles. Thus, the dosage administered in individual infusions may be slightly increased or decreased to utilize fully each vial as long as the monthly administered dosage remains substantially unaltered.

### HOW SUPPLIED

**Cerezyme**<sup>®</sup> (imiglucerase for injection) is supplied as a sterile, non-pyrogenic, lyophilized product. It is available as follows:

200 Units per Vial NDC 58468-1983-1

400 Units per Vial NDC 58468-4663-1

Store at 2-8°C (36-46°F).

### Rx only

U.S. Patent Numbers: 5,236,838

5,549,892

**Cerezyme**<sup>®</sup> (imiglucerase for injection) is manufactured by:

**Genzyme Corporation**  
500 Kendall Street  
Cambridge, MA 02142 USA

Certain manufacturing operations may have been performed by other firms.

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## Ask the Expert

In this month's column, **Robert I. Parker, MD**, answers patient's questions about *Gaucher disease*.



**Robert I. Parker, MD, FAAP**, is a professor and vice chair of Pediatrics for Academic Affairs and director of Pediatric Hematology/Oncology. He is also an associate director of the Stony Brook University Cancer Center, SUNY, Stony Brook, New York.

**Q: Is there any way to replace the enzyme I am missing?**

**A:** Gaucher disease is caused by an inherited genetic defect. People with Gaucher disease are deficient in the enzyme glucocerebrosidase, which is responsible for breaking down a certain fat molecule called glucocerebroside. This enzyme deficiency causes a buildup of glucocerebroside in cells. When these cells are filled with glucocerebroside, they are called "Gaucher cells." It is possible to replace the missing enzyme in type 1 Gaucher disease with Cerezyme® (imiglucerase for injection), a modified form of glucocerebrosidase, or by undergoing a bone marrow transplant. However, for most patients, the risks and side effects of a bone marrow transplant are not justified because treatment with Cerezyme is sufficient to control the disease with fewer risks to the patient.

The goal of Cerezyme therapy is to provide the appropriate amount of enzyme to allow glucocerebroside to be processed. Cerezyme works by supplementing or replacing the Gaucher patient's missing or deficient enzyme in an infusion lasting 1 to 2 hours.

**Q: What are the possible side effects of Cerezyme therapy?**

**A:** Side effects related to Cerezyme® (imiglucerase for injection) administration have been reported in less than 15% of patients.

Each of the following events occurred in less than 2% of the total patient population. Reported side effects include nausea, vomiting, abdominal pain, diarrhea, rash, fatigue, headache, fever, dizziness, chills, backache, and rapid heart rate. Because Cerezyme therapy is administered by intravenous infusion, reactions at the site of injection may occur: discomfort, itching, burning, swelling or uninfected abscess. Symptoms suggestive of allergic reaction include anaphylactoid reaction (a serious allergic reaction), itching, flushing, hives, an accumulation of fluid under the skin, chest discomfort, shortness of breath, coughing, cy-

anosis (a bluish discoloration of the skin due to diminished oxygen), and low blood pressure.

Approximately 15% of patients have developed immune responses (antibodies). Patients with antibody to Cerezyme have a higher risk of developing an allergic reaction, therefore, periodic monitoring by your physician is suggested.

The incidence of these events varies according to age group.

**Q: How can I find out if my bones are affected by Gaucher disease?**

**A:** Bones are actually two organs. The first is "structural" bones—what most people think of when they see a skeleton. This is the outer part of the bones that we see on x-rays. This outer part of bone, or cortex, is composed of minerals, with the most abundant being calcium. The second organ is the bone marrow. This is the inner core of bone where blood cells (red cells, white cells, and platelets) are made. This part of bone is spongy rather than hard.

As you get older, the formation of new bone slows down. Your bones lose minerals from the cortex and become more delicate. In addition, your active blood-forming bone marrow is increasingly replaced with fat, and production of blood cells decreases. Gaucher disease can speed up both processes. Accumulation of Gaucher cells in the marrow takes over the space typically occupied by the normal blood-forming cells. This hampers the bone marrow's ability to make blood cells (causing lower blood counts) and impairs the process by which new bone is formed and minerals are incorporated into new and existing bone. Normal aging and certain diseases put you at risk of developing a condition called osteoporosis, a reduction in bone mass that increases your susceptibility to fractures.

Individuals with Gaucher disease need to work with their physicians to check the health of their bones on a regular basis by undergoing certain tests. There are several tests your doctor can order to determine whether your bones are affected by Gaucher disease:

**X-ray.** A regular x-ray will detect any bone deformities or fractures. X-rays are also an excellent means of measuring the thickness of your outer bone layer. However, regular x-rays are relatively insensitive, only showing measurable abnormalities when there are severe changes in bone. Nor do they allow your physician to accurately determine bone density (a marker of the amount of

calcium and other minerals in the bone), which can be used to assess your risk of bone fracture.

**Magnetic resonance imaging (MRI).** This imaging modality allows a noninvasive view of the internal organs. An MRI can determine the health of the innermost part of your bone: the bone marrow. This is the best noninvasive test to assess the degree of Gaucher cell accumulation in the bone marrow.

**Dual-energy x-ray absorptiometry (DXA or DEXA).** A DXA (pronounced "dexa") test is the best way to measure the density or hardness of your bones. At the end of a DXA test, you will know how your bone health compares to other men or women who are the same age as you.

If you are concerned about the health of your bones, ask your doctor which of these medical tests are appropriate for you, when and how frequently you should check on your bones, and how your treatment is working.

**Q: I'm always reluctant to travel because of my disease. How can I manage travel and other schedule changes?**

**A:** Type 1 Gaucher disease does not need to stop you from traveling for work or pleasure. If you are going on vacation, just remember that your type 1 Gaucher disease is not on holiday. This does not mean it has to be an inconvenience. If an individual with type 1 Gaucher disease is going to be away from home for an extended period of time, it may be appropriate to continue Cerezyme infusions. For most individuals with type 1 Gaucher disease, a brief interruption in treatment while traveling will not compromise their overall care and health. A decision as to whether to continue or interrupt infusion therapy while traveling should be made in conjunction with your physician. People with type 1 Gaucher disease can find treatment centers all over the world to receive Cerezyme treatment if continued therapy is deemed prudent by their physician. If you need to travel, it may be easier to have treatment before and after you go if you will not be away for more than a few weeks. If you need treatment while you are away, talk with your doctor or Genzyme Treatment Support about receiving Cerezyme where you are going. Genzyme Treatment Support can be reached by calling (800) 745-4447, option 3. ■

# Jewish Genetic Disease Consortium Continues to Evolve

**J**ewish people of Eastern European or Ashkenazi descent are predisposed to a range of hereditary diseases, such as Gaucher disease, Bloom's syndrome, Canavan disease, and familial dysautonomia. In 2005, advocacy groups dedicated to combating various lysosomal storage disorders (LSDs) and other Jewish genetic diseases (JGDs) recognized a pressing need to increase awareness of these conditions in and outside the Jewish community. In collaboration with LSD patients and their families, the advocacy groups established the Jewish Genetic Disease Consortium (JGDC; [www.Jewishgeneticdiseases.org](http://www.Jewishgeneticdiseases.org)). The JGDC promotes and facilitates genetic testing for people of Jewish descent, with the ultimate goal of reducing the number of children born with these serious conditions.

Dr. Stuart Ditchek, medical director at the JGDC, explained, "There is a lack of awareness in both the Jewish and medical communities concerning JGDs and LSDs." He noted that many individuals are not even aware that they may be carriers of a JGD. He summarized the consortium's primary mission as educating communities and physicians on the need for "appropriate and thorough" screening to determine the carrier status of at-risk individuals.

### Beyond Awareness

Increasing general knowledge about genetic conditions such as Gaucher disease has tremendous value, according to Dr. Ditchek, but he cautioned that "just creating awareness is not enough." He stressed the JGDC's commitment to developing or coordinating screening initiatives. The JGDC also serves as a resource where individuals can access information about where and how to receive screening.

The JGDC recently established an innovative screening program targeting college-aged Jewish adults. The organization operates this program in partnership with the New York University Molecular Genetics Laboratory at NYU Medical Center, under the supervision of Dr. Harry Ostrer, Professor of Pediatrics, Pathology, and Medicine. Incorporating several novel techniques, the program reaches out to at-risk students with the goal of identifying those who have or are carriers of a genetic disease. Students can then apprise their physicians and future spouses of their carrier status and "prevent the transmission of these terrible diseases to future generations," said Dr. Ditchek.

One of the unique aspects of the program is its use of the Internet to reach this Web-savvy demographic. The JGDC maintains a Webpage on Facebook, a social networking site popular with college students. The JGDC Facebook page includes links to the JGDC Website and to an online registration form. The JGDC still employs traditional avenues of outreach and enrollment, such as a Jewish Community Center, but the Internet broadens

its reach to include students who are less active in the Jewish community. Once a student enrolls and completes an informed consent form, those determined to be at risk for a JGDC receive a salivary kit for DNA collection, which includes instructions and a return envelope.

In an effort to increase student participation, the JGDC simplified the screening process for its college-aged program, instituting a one-step testing method using salivary DNA. The program is the first to rely exclusively on salivary DNA testing, according to Dr. Ditchek, and

he described it as "an accepted way to diagnose actual [LSD] disease or carrier states." Dr. Ditchek explained that college students were less receptive to the conventional screening process, which "entails a pre-testing counseling session, the attainment of informed consent from the subject, a blood test, and then another session with the genetic counselor once results are in."

A few weeks after the salivary kit is received, the JGDC contacts the student with the test results. Students whose results were negative are notified by mail and via a secure online message; those with positive test results are contacted by telephone and instructed on how to obtain counseling or medical care.

Dr. Ditchek reported that the JGDC recently tested its college-aged program in select populations with "dramatically good results." The program officially launches in the fall, focusing on students in the Los Angeles area throughout the fall and winter months.

### Reaching Physicians

Raising patient awareness of LSDs and JGDs is only part of the equation. Dr. Ditchek emphasized that physician education is a critical component of any screening program. He reported that the JGDC uses a grand rounds program to educate physicians on LSDs, the importance of screening, who needs to be screened, and screening options.

The JGDC recruits physicians into the grand rounds program through mail and direct contact. Dr. Ditchek praised Genzyme for furthering this effort by reaching out to obstetricians/gynecologists and internal medicine physicians all over the country. He relayed the JGDC's willingness to visit any hospital that welcomes its services.

### Getting the Word Out

To further JGDC's goals of improving screening rates and facilitate better treatment of patients with JGDs, the organization works to remove barriers to screening. In addition

**"Just creating awareness is not enough."** —Dr. Stuart Ditchek

to the lack of awareness of LSDs and JGDs among physicians and the at-risk population, Dr. Ditchek identified an individual's "self-concept" as another barrier. "Many at-risk patients are of mixed ancestry so they don't identify themselves as Jewish and therefore don't identify themselves as being at risk for a JGD," he explained.

Dr. Ditchek's vision is to see the JGDC expand from a regional testing organization into a national, coordinated, cohesive testing network. "We are reaching out to anybody who can help us get the word out and get everybody that is at risk tested so we can get rid of these horrific diseases that are unfortunately still out there," he concluded. ■

# Delicious Recipes

## For Holiday Gatherings

### Jam Thumbprint Cookies

- 1 ½ cups all-purpose flour
- ¼ teaspoon salt
- ¾ cup butter or margarine
- ½ cup granulated sugar
- 2 egg yolks
- 1 teaspoon vanilla
- 2 slightly beaten egg whites
- ¾ cup finely chopped walnuts
- ½ cup cherry or strawberry preserves

Stir flour and salt together in a small bowl. In a large bowl, beat butter for 30 seconds. Add sugar, and beat until fluffy. Separate eggs, reserving whites. Add yolks and vanilla to sugar mixture and mix thoroughly. Blend in flour mixture. Cover and refrigerate dough for 1 hour. Preheat oven to 350°. Shape dough into 1" balls; roll balls in egg white, then walnuts. Place 1" apart on an ungreased cookie sheet and depress centers with thumb. Bake 15 to 17 minutes and cool. Before serving, fill centers with preserves. Makes 3 dozen.

### Kugel

- 1 bag egg noodles
- 1 cup sour cream
- 2 sticks butter (melted)
- 2 large eggs
- 8 oz cream cheese
- ½ cup granulated sugar
- 1 teaspoon cinnamon

Preheat oven to 350°. Bring a large pot of lightly salted water to a boil. Add egg noodles and boil 10-12 minutes or until al dente; drain. Beat eggs in a large bowl. Add sour cream and cream cheese, beating after each addition. Add cooked noodles and stir. Stir in most of the melted butter, reserving small amount to coat a 13" x 9" pan. Stir in cinnamon and sugar, reserving some to sprinkle on top before baking. Bake 1 hour or until a knife inserted in the center comes out clean.

### Pumpkin Bread Pudding

- 5 cups (8 oz) challah or brioche bread, torn into small pieces
- 2 cups half and half
- 3 large eggs
- ¾ cup granulated sugar
- ¾ cup packed brown sugar
- 1 can (15 oz) pumpkin puree
- 3 tablespoons butter (melted)
- 1 teaspoon ground cinnamon
- ½ teaspoon ground nutmeg
- 1 teaspoon vanilla
- 1 cup dried cranberries or raisins
- ½ cup toasted pecans (optional)

Place bread cubes in a bowl and cover with half-and-half. In another bowl, blend eggs, sugars, pumpkin, butter, spices, and vanilla. Fold in dried fruit and nuts. Pour mixture over milk-soaked bread and stir. Spoon contents into a greased 11" x 7" baking dish. Refrigerate for 2 hours. Preheat oven to 350°. Bake for 45 to 60 minutes, or until set. Serves 8.

Serve warm with brown sugar sauce (below), whipped cream, or vanilla ice cream.

#### Brown sugar sauce

- ½ cup packed brown sugar
- 2 tablespoons corn syrup
- ¼ cup butter
- ½ cup heavy cream
- 1 ½ teaspoon vanilla

Combine ingredients in a saucepan and bring to a boil over low heat, stirring frequently. Reduce heat to medium-low and boil for 5 minutes, stirring often. Remove from heat and allow sauce to cool and thicken.



### Crumb Cake

- 1 cup granulated sugar
- ½ cup shortening
- 2 cups all-purpose flour
- 1 teaspoon cinnamon
- ½ teaspoon baking soda
- 1 teaspoon baking powder
- 1 cup sour milk (add 1 tablespoon vinegar or lemon juice plus milk to equal 1 cup, let stand for 5-10 minutes) or 1 cup buttermilk

Preheat oven to 350°. Cream sugar and shortening together in a large bowl. Mix in flour until crumb-like consistency. Set aside ½ cup crumb mixture for topping. Mix in remaining dry ingredients one at a time, alternating with milk. Pour batter into a greased and floured 8" cake pan and sprinkle topping evenly over batter. Bake for 40 minutes.

# Happy Holidays

## Tips for Enjoying This Season's Festivities

**T**he holidays are a time when friends and families get together not only to enjoy themselves, but also to promote love, hope, and goodwill for those who are less fortunate. The holiday season helps renew our sense of faith and heritage. No matter what celebration your family rejoices in during the holiday season, there are a few things you can do to help make it enjoyable and safe.

### Plan Ahead

Effective planning is one of the keys to having a truly enjoyable holiday. Begin planning your holiday well before the season arrives. This may include drawing up your gift list or outlining travel arrangements. The more you can accomplish in advance, the less stress you will feel later and the more time you will have to enjoy the festivities.

### Make Time for Family and Friends

Holidays are a great time to get the whole family together. Plan to spend quality time with your spouse, children, parents, or friends. Invite friends and loved ones for din-

ner, or arrange a time for everyone to take in a concert together or participate in some other group activity. Remember to leave yourself time to focus on whatever special meaning the holiday holds for you.

### Think of Others

Although we should think of those who are less fortunate all year round, it is easy to overlook them during the hustle and bustle of daily life. Let the holidays serve as a reminder to reach out to those in need, such as the poor and the elderly. Visit nursing home residents, donate items to Toys for Tots, or contribute time or money to the Salvation Army, the Red Cross, and other religious and civic organizations dedicated to helping the poor. In addition to bringing joy to someone in need, giving to those less fortunate adds joy and satisfaction to your life, as well.

### Some Things Should Be Enjoyed in Moderation

It is easy to overindulge during the holiday season. Remember to do everything in moderation, like eating and drinking. It is important to take care of your health. Get



enough rest and stay within the limits of your dietary restrictions to avoid unnecessary health emergencies. A trip to the hospital is a quick way to dampen holiday spirits.

### Create a Festive Mood

There are many exciting ways to create a festive atmosphere. Make or buy gifts for family and friends; decorate your home, perhaps with the help of family and friends; play holiday music; send out holiday cards; or make holiday treats. Then, find time to relax and enjoy the season.

### Reflect

Take time to reflect on your life and remember those who are most important to you. Think about the past year's achievements and disappointments. Discuss family goals with your spouse and children.

*Most importantly, have a happy holiday season. ❄️*

## Tips for Adhering to Treatment During the Holiday Season

**P**lanning ahead during the holiday season is essential for patients being treated with Cerezyme® (imiglucerase for injection). For those about to begin treatment, it is important to understand the disease and determine how best to fit treatment into your life. Before initiating treatment, patients and family members may want to receive counseling on infusion therapy, treatment-associated risks, possible therapeutic outcomes, and the need to keep infusion appointments. Some patients may find it more challenging to stick to their treatment schedule during the holidays, but this is not the time to let things slide. Adhering to a treatment schedule is an essential component of taking control of one's health. The following tips can help patients stay positive about sticking with their treatment regimen throughout the holiday season.

- Keep dialogue open with your doctor and other healthcare providers.
- Plan ahead for appointments, and avoid scheduling conflicts.
- Talk with others who are dealing with type 1 Gaucher disease about how they handle treatment during the holidays.
- Talk with a counselor.
- Reward yourself for sticking with treatment.
- Make treatment more enjoyable for your children with type 1 Gaucher disease by reading to them or playing games during infusions.
- Monitor changes in your health and record them in a diary.
- Follow your medical progress for improvements over treatment sessions and therapy maintenance.
- Plan trips as far in advance as possible, working with your Genzyme case managers to help ensure uninterrupted treatment. ■

# Horizons

If you have enjoyed this issue of *Horizons*, please let us know by completing and returning the postage-paid Business Reply Card that follows page 12.

You can submit a question for our "Ask the Expert" column, volunteer to share your story of living with type 1 Gaucher disease, or provide us with your comments and suggestions for improving this publication.

Horizons

## Comments:

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## Do you have a question for our "Ask the Expert" column?

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## Are you interested in being a speaker (provide information below)?

Yes     No

## Would you be interested in sharing your story of living with Gaucher disease?

If so, please fill in the following:

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