The New ICGG Gaucher Disease Registry Platform
More Efficient, More Opportunity for Patient Involvement

Early Diagnosis of Type 1 Gaucher Disease Helps Patients Avoid Complications and Receive Appropriate Treatment

Type 1 Gaucher Disease and Diabetes: Patients Can Decrease Their Risk

Patient Profiles:
Andrea Scott
Marilyn Halsdorf

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Foreword

The International Collaborative Gaucher Group (ICGG) Gaucher Registry, built to promote the understanding of Gaucher disease and track its treatment worldwide, marked its 20th anniversary in 2011. This year, the ICGG Gaucher Registry has fully made the transition to a new web-based system. For physicians who treat patients with Gaucher disease, the new system will enable more efficient data collection and the opportunity to connect with their patients’ other health care providers. For patients with Gaucher disease, innovative features provide the opportunity for more involvement in the Registry. Learn how the ICGG Gaucher Registry has contributed to our understanding of the condition, and what the new features may mean for the treatment of the disease in the future.

Patients with Type 1 Gaucher disease may be at increased risk of developing Type 2 diabetes, and in this issue, David N. Finegold, MD, of the University of Pittsburgh School of Medicine, discusses what patients can do to reduce their risk. In our “Meet the Experts” profile, Maria D. Cappellini, MD, of Maggiore Hospital in Milan, Italy, talks about the importance of early diagnosis to avoid complications in Type 1 Gaucher disease. This issue of Horizons features the profiles of two patients with Type 1 Gaucher disease, Andrea Scott and Marilyn Halsdorf.

As always, we would love to hear your comments and feedback. Help shape your own Horizons by sending us a note.

—Your team at Genzyme

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 (low red blood cell count), thrombocytopenia (low blood platelet count), bone disease, hepatomegaly or splenomegaly (enlarged liver or spleen).

Important Safety Information
Approximately 15% of patients have developed immune responses (antibodies). These patients have a higher risk of an allergic reaction (hypersensitivity). Use Cerezyme® (imiglucerase for injection) carefully if you have had an allergic reaction to the product in the past. Symptoms suggestive of an allergic reaction happen in 6.6% of patients, and 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. Side effects related to Cerezyme 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, abdominal pain, vomiting, 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. Cerezyme is available by prescription only. For more information, consult your physician.

Please see accompanying full Prescribing Information on pages 9-10.

Patients are encouraged to report negative side effects of prescription drugs to the FDA. Visit FDA.gov/medwatch, or call 1-800-FDA-1088.
The New ICGG Gaucher Disease Registry Platform: More Efficient, More Opportunity for Patient Involvement

By Devera Pine

The year 2011 marked the 20th anniversary of the International Collaborative Gaucher Group (ICGG) Gaucher Registry—the first and largest database of its kind in the world, built to promote the understanding of Gaucher disease and to track outcomes of treatment worldwide. And now that 2012 is well under way, the ICGG Gaucher Registry has fully made the transition to a new web-based system, RegistryNXT!. RegistryNXT! allows for more efficient data collection and more opportunity for patients to access their information with the involvement of their physicians.

Impact of the Registry on Understanding Gaucher Disease
Few rare disease registries have the same breadth and depth of data, and, in fact, much of what we know about Gaucher and its treatment today is due to analyses and publications from the ICGG Gaucher Registry. To date, there have been more than 30 articles published on Gaucher disease from the Registry. Registry publications have increased knowledge about skeletal abnormalities in Gaucher patients, highlighting the need for early detection and treatment, with the ultimate goal of preventing bone complications. Registry publications have also increased knowledge about therapeutic goals, incidence of cancer in Gaucher patients, and neuronopathic involvement, among many other important topics.

The Launch of the Registry’s New Web-Based Platform
In a process that involved three years of development, the ICGG Gaucher Registry was transferred to an innovative web-based platform known as RegistryNXT!. The old platform, which was based on software that physicians downloaded to their computers, was outdated technology and deemed very inefficient by today’s standards. Because the new RegistryNXT! system is web-based, it can be easily accessed by participating health care providers around the world, making the collection of data easier. With the new RegistryNXT! system, Registry physicians can connect with their patients’ other health care providers through a new Registry directory and report-sharing features, promoting the exchange of information to help in making treatment decisions.

Gaining a Better Understanding of Gaucher Disease
The ICGG Gaucher Registry began in 1991 and is the most comprehensive database for monitoring Gaucher, with approximately 55,000 patient-years of data. The Registry has over 6000 patients enrolled from over 60 countries. More than 700 physicians participate. By collecting information on Gaucher, the Registry aims to advance the understanding of this rare disease and to improve quality of care for Gaucher patients worldwide. The more patients enrolled in the Registry with long-term data, the more robust the Registry data will be.

Any patient with Gaucher disease can be enrolled, regardless of treatment status or type. As a result, the Registry contains information on both treated and untreated patients, as well as on Types 1, 2, and 3 Gaucher disease. A group of international physician experts in Gaucher disease makes up the Registry’s Board of Advisors, which oversees the database, assists with the analyses, and establishes guidelines for disease monitoring and management. Genzyme, a Sanofi company, sponsors the Registry and operates a Registry team to assist Registry sites and board members with data collection, analyses, and publication of the Registry findings.
As part of the new Registry platform, physicians can access information on current monitoring and treatment guidelines. The current monitoring guidelines for Gaucher disease are based on information and publications from the ICGG Gaucher Registry, as well as feedback from the Registry’s Board of Advisors.

**Updates to the Patient Clinical Summary**

A key focus of the ICGG Gaucher Registry redesign project was the individualized summary of patient data, or Patient Clinical Summary (PCS) (formerly called the Patient Case Report). These reports now provide interactive, real-time patient data and allow a patient’s health care team to monitor changes in a patient’s disease and response to treatment. With the old Registry system, PCSs were only available in a monthly PDF format. Now, however, physicians can get an updated PCS within 5 to 15 minutes of entering new data. Physicians can view a summary of a patient’s clinical status, both now and over time, in easy-to-read graphs and tables. The PCS can be customized and shared with other care team members and with patients.

Although use of the RegistryNXT system is still relatively new, according to Julie Davis, Senior Global Project Manager for RegistryNXT, there are hundreds of physicians and health care professionals now using the system and so far their response has been positive.

**Opportunity for Increased Patient Involvement**

One innovative feature of the new Registry platform is the opportunity for more patient involvement. Registry physicians can choose to share the PCS with their patients by inviting them, via email, to create a patient Registry account. Once a patient creates an account and logs in, he or she can then view the shared PCS.

The hope is that by offering more opportunity for patient involvement, the new feature will provide patients with a better understanding of their disease and will assist patients with receiving more optimized care.

Physicians can customize the PCS that they share with a patient, displaying up to 10 key Gaucher parameters. Physicians can also add comments to the shared PCS. For instance, if a physician and patient are interested in looking at a specific parameter together, such as platelets or hemoglobin, the physician can create a customized PCS that includes only that parameter.

Unlike physicians, patients do not have “real time” access to their PCS and the Registry data. Instead, patients see a static version of the data that the physician has shared with them.

“Patients have never been able to create a Registry account before to see their PCS,” said Davis. “This is a way to enable patient participation while still retaining patient confidentiality.”

Although patients cannot directly access the Registry, the new feature will make the information in the Registry “more useful, valuable, and informative” for patients, said Nicole Robichaud, Principal Project Manager for the Registry.

**Patient Privacy and Confidentiality a Top Priority**

“Security and patient privacy are a top priority,” Davis emphasized. Patient names are not collected by the Registry. A patient whose Registry physician invites him or her to sign up for a RegistryNXT account will not be prompted to enter their real name when creating an account. Furthermore, when a Registry physician shares a PCS with a patient, that patient receives an email asking them to log in to their patient RegistryNXT account to view the report. No reports are ever sent via email.

Throughout the ICGG Gaucher Registry, patient privacy and confidentiality are strictly maintained in compliance with national privacy regulations and applicable state or local laws regarding medical data. Information submitted to the Registry references the patient only by his or her initials and Registry-issued ID number. Furthermore, all users transfer documents to the Registry by logging in to the website, and not by email.

**Moving Forward**

RegistryNXT is the patient-focused platform for all the Lysosomal Storage Disease Registries, which include the ICGG Gaucher Registry, as well as Pompe, Fabry, and Mucopolysaccharidosis I (MPS I) Registries. The ICGG Gaucher Registry was the first to be transitioned to the RegistryNXT platform. By 2014, all the LSD Registries will use the new platform, with the Pompe Registry scheduled to make the transition next. Moving forward, development of an iPad app for the Registry is also under way.

In the meantime, Gaucher patients can take an active role in the Registry by asking their physicians about reading and signing the latest version of the Patient Authorization and Informed Consent Form. Patients can ask their physicians if they can fill out the Quality of Life Survey (SF-36) to contribute information to the Registry. Patients can also speak with their physicians about the possibility of obtaining a RegistryNXT account or viewing their PCS. To learn more, visit the Registry website at www.gaucherregistry.com.
Early Diagnosis of Type 1 Gaucher Disease Helps Patients Avoid Complications and Receive Appropriate Treatment

By Neil Canavan

When it comes to Type 1 Gaucher disease, the earlier the diagnosis is made, the better. Early diagnosis means that the disease has had less time to progress. Furthermore, early diagnosis helps ensure that the patient receives appropriate treatment for symptoms.

Early diagnosis and appropriate treatment have not always been the case for patients with Type 1 Gaucher disease. “Splenectomy [removal of the spleen] was a procedure performed years ago in Gaucher patients, particularly when no treatments were available,” said Maria D. Cappellini, MD, professor of Internal Medicine, Maggiore Hospital, Milan, Italy. “Yet even today, some patients still undergo splenectomy before a Gaucher diagnosis.” However, in patients with Type 1 Gaucher disease, splenectomy may worsen the course of the disease, as well as cause additional complications, including an increased risk for cancer and infection.

Cappellini recalled one patient, a 64-year-old woman who had most of the symptoms of Type 1 Gaucher disease by the time that Cappellini diagnosed her condition. “She already had most of the known disease-related complications,” said Cappellini, including abnormal bruising, bleeding, and osteonecrosis (bone decay). The diagnosis of Type 1 Gaucher disease had been missed throughout the patient’s life, and at age 20, she had had a splenectomy.

Cappellini emphasized that multiple signposts for Type 1 Gaucher disease had been missed in this patient, and she stressed that splenectomy in such a case should be avoided until Type 1 Gaucher disease has been ruled out.

Because cases of Type 1 Gaucher disease are so rare, Cappellini acknowledged that many physicians, including hematologists, don’t think to look for it.

Type 1 Gaucher disease is a chronic, progressive, metabolic disorder, and, left untreated, can lead to complications such as low red blood cell count (anemia), low platelet count (thrombocytopenia), and bleeding, as well as thinning of bones and bone loss (osteopenia and osteoporosis).

Rare though it may be, Cappellini strongly encourages physicians to be aware of the symptoms of Type 1 Gaucher disease in order to ensure an early diagnosis. “As the disease goes its natural way without being diagnosed and treated,” she warns, “the result will be an incredible negative impact on the quality of the patient’s life.”

Indications and Usage
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 (low red blood cell count), thrombocytopenia (low blood platelet count), bone disease, hepatomegaly or splenomegaly (enlarged liver or spleen).

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Please see accompanying full Prescribing Information on pages 9-10.
Would you be interested in sharing your story of living with Gaucher disease?
If so, please fill in the following:

Name
Address
City               State                   Zip
Email
Phone

Do you feel you have been kept informed on the Cerezyme supply issue?
☐ Yes    ☐ No

How can Genzyme communicate better?

What channels are you using to keep informed?
☐ Your physician    ☐ Cerezyme supply website
☐ Your Genzyme Case Manager  ☐ Other
☐ National Gaucher Foundation

What different form of communication would you like to see used if any?

If you have enjoyed this issue of Horizons, please let us know by completing and returning the postage-paid Business Reply Card below.
DESCRIPTION

Cerezyme® (imiglucerase for injection) is an analogue of the human enzyme β-glucocerebrosidase, produced by recombinant DNA technology. β-Glucocerebrosidase (β-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® 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 (Mr = 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® 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:

<table>
<thead>
<tr>
<th>Ingredient</th>
<th>200 Unit Vial</th>
<th>400 Unit Vial</th>
</tr>
</thead>
<tbody>
<tr>
<td>Imiglucerase (total amount)</td>
<td>212 units</td>
<td>424 units</td>
</tr>
<tr>
<td>Mannitol</td>
<td>170 mg</td>
<td>340 mg</td>
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<tr>
<td>Sodium Citrates</td>
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<td></td>
</tr>
<tr>
<td>(Trisodium Citrate)</td>
<td>70 mg</td>
<td>140 mg</td>
</tr>
<tr>
<td>(Disodium Hydrogen Citrate)</td>
<td>(52 mg)</td>
<td>(104 mg)</td>
</tr>
<tr>
<td>Polysorbate 80, NF</td>
<td>0.53 mg</td>
<td>1.06 mg</td>
</tr>
<tr>
<td>Citric Acid and/or Sodium Hydroxide</td>
<td></td>
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</tbody>
</table>

*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-β-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 (Sodium Intravenous fluid) 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 β-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® (imiglucerase for injection) catalyzes the hydrolysis of glucocerebroside to glucose and ceramide. In clinical trials, Cerezyme® improved anemia and thrombocytopenia, reduced spleen and liver size, and decreased cachexia to a degree similar to that observed with Ceredase® (alglucerase injection).

Pharmacokinetics

During one-hour intravenous infusions of four doses (7.5, 15, 30, 60 U/kg) of Cerezyme® (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 9.4 minutes. Plasma clearance ranged from 9.8 to 20.3 mL/min/kg (mean ± S.D., 14.5 ± 4.0 mL/min/kg). The volume of distribution corrected for weight ranged from 0.09 to 0.15 L/kg (0.12 ± 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 do not appear to be different from placental-derived alglucerase (Ceredase®).

In patients who developed IgG antibody to Cerezyme, 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® (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:

- a. anemia
- b. thrombocytopenia
- c. bone disease
- d. hepatomegaly or splenomegaly

CONTRAINDICATIONS

There are no known contraindications to the use of Cerezyme® (imiglucerase for injection). Treatment with Cerezyme® 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® (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 after 12 months of therapy. Approximately 46% of patients with detectable IgG antibodies experienced symptoms of hypersensitivity.

Patients with antibody to Cerezyme® 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® 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® (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. No causal relationship with Cerezyme® has been established. Patients with respiratory symptoms in the absence of fever should be evaluated for the presence of pulmonary hypertension.

Therapy with Cerezyme® should be directed by physicians knowledgeable in the management of patients with Gaucher disease.

Caution may be advisable in administration of Cerezyme® to patients previously treated with Ceredase® (alglucerase injection) and who have developed antibody to Ceredase® or who have exhibited symptoms of hypersensitivity to Ceredase®.
ADVERSE REACTIONS
Since the approval of Cerezyme® (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 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 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® has revealed that approximately 13.8% of patients experienced adverse events which were judged to be related to Cerezyme 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.

Additional adverse reactions that have been reported in approximately 6.5% of patients treated with Cerezyme 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, pruritus, and rash.

In addition to the adverse reactions that have been observed in patients treated with Cerezyme, 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.
Type 1 Gaucher Disease and Diabetes: Patients Can Decrease Their Risk

People with Type 1 Gaucher disease may be at increased risk of developing Type 2 diabetes. Horizons interviewed David N. Finegold, MD, professor of medicine and pediatrics at the University of Pittsburgh School of Medicine, about the association between Type 1 Gaucher disease and diabetes, and about what can be done to reduce the risk of diabetes.

Why are patients with Type 1 Gaucher disease at risk for developing diabetes?

Finegold: Both Type 1 Gaucher disease and Type 2 diabetes are diseases that have an activated inflammatory state. This means that the body produces numerous chemicals in the blood, such as cytokines and chemokines, which are normally released by the immune system.

The release of these chemicals creates a state called insulin resistance, a condition in which the hormone insulin becomes less effective at processing and lowering blood sugar. Insulin resistance increases the risk of Type 2 diabetes.

The risk of Type 2 diabetes can also increase in people with Type 1 Gaucher disease as a result of weight gain; people with undiagnosed and untreated Type 1 Gaucher disease tend to be thin because of their untreated disease. Proper diagnosis and treatment may help patients start to eat more and weight gain can potentially contribute to Type 2 diabetes.

Does everyone with Type 1 Gaucher disease have this increased risk?

The risk seems to be most significant in adults with Type 1 Gaucher disease. There have not been many studies done on this problem with children. However, diabetes is not one of the main components of Type 1 Gaucher disease. The major components of Type 1 Gaucher disease continue to be enlarged liver and/or spleen, anemia, fatigue, easy bruising and bleeding, nosebleeds, osteoporosis, and bone pain. In addition, people with Type 1 Gaucher disease are generally diagnosed with Type 1 Gaucher disease before they develop diabetes. It is not that someone is diagnosed with diabetes, and the doctor says, “Oh, you also have Gaucher disease.”

The important thing to remember is that a risk has been identified, and it seems to contribute to a person’s overall risk of diabetes, but it is not such a large risk that a person should become overly concerned about it.

How can a person distinguish between Type 1 Gaucher disease symptoms and diabetes symptoms?

The symptoms for diabetes are quite distinctive. The hallmarks of diabetes are increased thirst, increased urination, weight loss, and fatigue. The major overlap with Type 1 Gaucher disease is fatigue, because many patients with Type 1 Gaucher disease have some level of fatigue. If a patient sees an unusual change in his or her level of fatigue, or has a significant increase in thirst or urination—for instance, he or she is getting up multiple times during the night—they should bring that information to the attention of their doctor.

Are most doctors familiar with these associations?

When doctors take a medical history, they certainly will ask about changes in thirst, weight, etc. The answers to any of these questions would tip them to test the patient’s fasting blood sugar to test for diabetes. In addition, many doctors check for diabetes in all their adult patients because it is so prevalent.

Is there anything that patients with Type 1 Gaucher disease can do to lower this risk?

They can avoid excessive weight gain—they should have good eating habits, live a healthy lifestyle, and exercise regularly. In other words, do all the same things that any adult would do to prevent diabetes.

We know there are families that are more likely to be at risk for diabetes because they tend to be heavier. Patients from these families with Type 1 Gaucher disease have the overlap of a common condition (diabetes) and a rare condition (Type 1 Gaucher disease). So, if you are from a family that tends to be heavy, and everyone in the family tends to have Type 2 diabetes, hypertension, and heart disease, the fact that you have Type 1 Gaucher disease could increase your risk. However, I don’t think any of us really know how much of an increased risk there is.

Is diabetes managed differently in a person with Type 1 Gaucher disease?

No, it is managed the same. The most important thing a person with Type 1 Gaucher disease and diabetes can do is work with a nutritionist to get an appropriate diet to balance whatever medications their diabetes doctor is prescribing for them. One of the major hallmarks of treatment for Type 2 diabetes is weight loss. If you are overweight, and you are able to lose a significant amount of weight, you may stop having symptoms of diabetes.
with rubber stamps and scrapbooking material, Brooksville, Florida resident Andrea Scott finds inspiration in creating, selling, and sending greeting cards, from thank you notes to birthday cards and beyond.

Crafting is a way for her to focus on something other than her health—Scott, 48, has lived with the challenges of Type 1 Gaucher disease since early childhood. She had both her hips replaced by age 22, has a permanently fused left knee, and once spent 2 months in the hospital immediately after her honeymoon due to a bone crisis following a car accident.

“It’s funny how God may have allowed this terrible disease in my life but has gifted me with creativity,” she said. “I struggled with the ‘why me?’ stuff and ‘why do I have to look like this and others look normal,’” she said. But when a friend from church gave her a handmade card, it helped change her perspective.

The card featured a man who carried water jars on his shoulders down a path. He would fill the jars every day and haul the heavy vessels back home. But one day, the man noticed that one jar was empty when he returned home, despite filling it to the brim earlier.

The water had leaked out all the way on the path back to the house, unbeknownst to the man who had just hauled the jar home.

“But the thing is that it watered the flowers along the path, and they grew to be beautiful,” said Scott. The card became a turning point for her. “It was a neat way of looking at it,” she said. “Even if we think we are broken and not normal, we all have gifts to share with others, and ways we can reach out and help. Sometimes, we are not even aware of the help we can give.”

Finding Compassion
Type 1 Gaucher disease has had a profound impact on Scott’s life. She was diagnosed in kindergarten, after her legs hurt so much she couldn’t walk. For medical care to deal with Gaucher’s painful effects, Scott would travel with her family for care at Boston Children’s Hospital, about 50 miles from her Londonderry, New Hampshire childhood home. Ultimately, Scott would deal with a number of Type 1 Gaucher disease symptoms and many medical visits, including surgery to remove her enlarged spleen at age 6, an operation to remove a bone in her left knee to slow down its growth, a double hip replacement, and intense bone crisis, in which bone pain is accompanied by fever and joint swelling. The bone crisis affected her ability to walk.

“I would have a crisis late at night, and morphine was the only thing that would take the pain away,” she recalled. “It would start with horrible pain in the hips, over the course of one or two weeks, and it would almost feel like it was working its way out of the body. I had to be put in traction because the pain was so bad.”

“I have so many memories of being hospitalized and put in traction and strong pain medication and crying myself to sleep because I felt all alone,” she recalled. But through the pain, Scott remembers important glimmers of support.

“When I was little, I was sad about having to use crutches all the time. My doctor, Allen Crocker, would always tell me the same thing: ‘Andrea, the crutches are your friend,’ and that stuck with me,” she said. Scott’s mother, a former nurse, also tried to help her daughter whenever she was sad or discouraged while visiting the hospital. “My mom would always tell me, ‘Look around. There are so many other children struggling with things, too.’ It would help to see I was not alone.”

Scott particularly remembered one nurse who sat on the edge of her bed as she was hospitalized and alone as a young teenager. “A lot of it was just sitting there, listening to me, and saying it was going to be OK and rubbing my forehead,” said Scott. “It made such a difference. Compassion and empathy are

“Even if we think we are broken and not normal, we all have gifts to share with others, and ways we can reach out and help. Sometimes, we are not even aware of the help we can give.”
two wonderful gifts for a health care worker because it can make such a difference to take that extra moment to show you truly care for others.”

That perspective would help her and her family as she dealt with the emotional aspects of living with an obvious chronic condition as a young child. She used a wheelchair off and on as a child and had leg braces as a teenager, both of which she still uses as an adult. “Kids can be awful,” she said, recalling the stares and taunts she experienced as a child. “It was having your crutches kicked out from under you and being told that you didn’t need them. There were all the times in school when I had to sit on the sidelines from any physical education activities. It makes you feel left out, and today, as an adult, I hate it when anyone is singled out for any reason. I like to include everyone.”

**Rough Starts**

Such memories help Scott appreciate the blessings of her family today.

She met her now husband, Andrew, at 19, when they were introduced through mutual friends. Friends first, they would talk while walking on a nearby beach at night, and she grew to appreciate his patience, helpfulness, and their shared sense of humor. They have been married for 24 years and Andrea said her health issues have only strengthened their bond.

“While we were dating, I had both my hips replaced, and I was able to walk down the aisle when we got married,” she said. The couple enjoyed a 10-day honeymoon in the US Virgin Islands, but Andrea returned not feeling well. She didn’t call the doctor, but instead focused on returning to work and settling into newlywed life. Less than a week later, just as Andrea was returning to her job in medical transcription at Elliot Hospital in Manchester, New Hampshire, she was involved in a car accident that totaled her vehicle.

“I bumped my knees in the accident and was taken to the emergency room,” she said. She was released from the hospital that day, but returned two days later in full bone crisis, with severe pain and swelling in both knees and a high fever. Scott learned that she had had food poisoning from her honeymoon that affected the bone or bone marrow of her knees and compounded her pain. She spent the next 60 days in the hospital.

“My parents took Andy to lunch after I was first admitted and they said to him, ‘We will understand if you want to get out of this marriage,’” Andrea said. “And he said ‘No, I love her and I’m staying with her.’” Once out of the hospital, Andrea couldn’t climb the stairs of the second-floor apartment the couple had rented, so they moved in with her parents in nearby Londonderry. The couple dealt with months of dressing changes, antibiotics, and physical therapy, all while continuing to pay $600 a month in rent for the now-unusable apartment because they had signed a lease.

“We had it rough from the beginning,” she said, but “if we can get through what we got through at the very beginning, we can get through anything.”

Andy, who today works as an assistant grocery department manager, was tested for Gaucher just before the couple decided to have a family, and the couple was thrilled when they learned he wasn’t a carrier. Their older daughter, Miranda, is now 20 and wants to go to school to be a nurse or a surgical technician, and their younger daughter, Tiffany, is now 15 and a high school freshman interested in law.

“We are often told what beautiful daughters we have inside and out, and I think that is due in part to growing up with a parent that is physically challenged,” said Andrea. “They haven’t known me any other way, but it has created in them great compassion and empathy for others.”

**Connections and Coping**

Humor, a strong independent streak, and thinking outside the box has helped the family thrive through the years. Scott also began taking Cerezyme® (imiglucerase for injection) treatment in 1993. She has had infusions every two weeks since then, except when she was pregnant with her daughters.

Through the years, she has learned to tailor a situation so that she can thrive. “In living with all this, you have to plan ahead for everything,” she said. “You don’t have a choice. It’s just thinking outside the box. I’m a very independent ‘I can do this myself’ kind of person.” Andrea learned how to sit in a wheelchair and push a shopping cart with her feet to grocery shop, and when her children were babies, she wore them in a sling while using her wheelchair.

“When the girls got a little older, I got a baby carriage with three wheels and had the handle of the carriage made lower so I could maneuver the carriage and the wheelchair at the same time.”

Andrea also credits her strong family ties—Andy has five siblings, and though her parents are now deceased, they were an important source of support, strength, and perseverance. She has other important people who make up her network of support, including her current doctor, Vikas Malhotra, MD, and his support and nursing staff. “He is a truly caring doctor who always asks how I am doing and wants to know about my entire family as well,” she said. She also relies on the online community on a Gaucher-themed Facebook page. “It’s nice to get feedback from other people,” she said.

Together, her network helps to keep her going. “My strong faith, a great supportive family, a great support system of doctors and nurses, perseverance and humor—I have been given it all over the years,” she said. “Giving up is certainly not an option for me.”
Patient Profile:
Marilyn Halsdorf
By Cheryl Alkon

I

f living with Type 1 Gaucher disease for more than 50 years has helped Marilyn Halsdorf learn anything, it’s compassion. Knowing how to sympathize with other people’s health issues has served the Schenectady, New York native well in her job as a team leader of member service representatives for MVP Health Care, a health maintenance organization.

“My most memorable member services call, which came to her randomly through the company’s telephone queue, was a real connection. The caller was asking about infusion therapy benefits, and Halsdorf, 57, quickly realized that the woman had Gaucher disease.

“When I told her I also had Gaucher, she could not believe it,” Halsdorf said. “It made things so much easier because I knew exactly what she needed. We had a nice chat and I will always remember that.”

Such random connections aren’t common for those living with Gaucher, a rare genetic disorder. The Type 1 form of the disease is the most common, but is typically only found in 1 in 45,000 to 60,000 people.

But when Halsdorf was first diagnosed with Type 1 Gaucher disease at age 5, her doctor didn’t know what was wrong with her. She remembered how she was always sick and missed a lot of school early on. “Before I was diagnosed, I got a lot of heavy nosebleeds and I wasn’t growing,” she said. Her pediatrician did many different tests, ultimately ruling out leukemia and cystic fibrosis, but didn’t stop there. “I had a very persistent and dedicated pediatrician who eventually found this disease, Gaucher, and sent me to a hematologist, who confirmed it with a bone marrow test.”

But this was in the early 1960s, long before there was any kind of treatment for Type 1 Gaucher disease. “They just didn’t know what to do with me,” Halsdorf said. “I was always sick and I just kind of lived with it.”

The High School Years
In that era, doctors would remove spleens enlarged by Gaucher’s effects, and at 12, Halsdorf’s spleen was taken out. However, after about a year, Halsdorf began experiencing bone crisis, or severe pain, in her hips.

Halsdorf was put in traction—lying flat in bed with weights and ACE bandages holding her legs and hips down—for several months as a way to try to help. Ultimately, she spent April of her freshman year in high school through the end of her sophomore year in traction, both at the Sunnyview Rehabilitation Center in Schenectady and later at Boston Children’s Hospital.

She watched a lot of television and colored, but there wasn’t much to do while in traction except keep up with her schoolwork. She earned top grades. “I guess I thought [traction] was helping—the pain was relieved, but for much of the time I was in Sunnyview, I was on a lot of painkillers,” she said. “I think that the real reason that the pain went away is that what is now known as a bone crisis had subsided.”

Halsdorf eagerly returned to school for her junior year. But in the summer between her sophomore and junior years, she was in a car accident. “My friend, who was driving the car, turned a corner, and said, ‘There’s something wrong with the gas pedal,’” Halsdorf remembered. The car cruised down the street, unable to stop, at about 45 miles per hour. Everyone in the car managed to fasten their seat belts, but Halsdorf, whose seat belts were tucked under her seat, could not. The driver steered the car into a gas station and the vehicle rammed through the garage door, which blocked the runaway car. Everyone had only minor injuries, except Halsdorf, who broke both legs.

The accident sent Halsdorf back to the hospital for another six weeks. She eventually returned to school that November, and ultimately, she graduated on time with her class in 1972. “I was so happy to be graduating,” she said. “Especially after such
a hard period in my life—I was glad it was over and I could move on. I earned high honors in high school and was especially proud of that.”

Hip Replacements
Although Halsdorf held several different brief jobs after high school, her hip pain remained constant. While working as a secretary in a local nursing home, she asked a staff physician for a shoe lift to counter her leg length discrepancy that had occurred because of the deterioration of her hip. He referred her to orthopedist Donald Paish, MD, who recommended a hip replacement instead. Ten days later, Paish replaced Halsdorf’s left hip—and she finally felt some relief from the crushing pain. For that, she said, “I owe my doctor my life.”

The first replacement lasted Halsdorf 11 years; she had a revision surgery on the left side in 1988, and again in 2007, while her right hip was replaced in 2006. The third procedure on her left side was the most intense, she said. Doctors inserted an 18-inch rod into her leg during a six-and-a-half-hour surgery, followed by a week of recovery at Massachusetts General Hospital and seven months of outpatient physical therapy.

Since that 2007 surgery, Halsdorf says she is nearly pain-free. “Knock on wood, it’s been great. Today, I use the treadmill and walk for an hour outside with my husband every day.”

Halsdorf also credits Cerezyme® (imiglucerase for injection) for helping her manage her Gaucher symptoms. “I was the first in the area to go on the drug, which was Ceredase, in 1991,” she said. Today, Halsdorf receives infusions every two weeks on her lunch break.

Social Ties
Halsdorf said an extended network of family and friends have helped her along the way. “Let me tell you about my wonderful husband, Jim,” she said. Married 32 years, the couple first dated at 19, but went their own ways for a few years. They reconnected when Halsdorf moved back in with her mother when her hip problems intensified when she was 22. “I had my hip done in November that year and he stuck around,” she said. He has continued to help her through the years as needed. “During my last surgery in 2007, he was unbelievable.” Jim, a machine operator for General Electric, cared for her when she couldn’t care for herself, making meals, doing the laundry and the housecleaning, and even visiting Marilyn’s sick mother in a nursing home, all while working full time. “I can’t say enough about him,” she said.

The couple has one daughter, Courtney, whom they adopted as an infant from Korea and who is now 25 and a physician assistant in nearby Saratoga Springs. The couple chose to adopt when Halsdorf’s doctor discouraged her from trying to have a biological child due to her health history.

Marilyn also credits several friends, siblings, and her mother Florence, now deceased, as sources of support throughout her life. “My mom was great and she gave up a lot—not until I became a mom did I realize how hard it was,” Halsdorf said. “I really admire her strength—if she passed anything on to all of us, it was that.”

It’s that strength that helps keep Halsdorf going. “I think the best thing is to live each day to the fullest and don’t let [Gaucher] affect you,” she said. “You can do whatever you want as long as you pace yourself. Just take it one step at a time—for me, that’s been literally.”

Indications and Usage
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 (low red blood cell count), thrombocytopenia (low blood platelet count), bone disease, hepatomegaly or splenomegaly (enlarged liver or spleen).

Important Safety Information
Approximately 15% of patients have developed immune responses (antibodies). These patients have a higher risk of an allergic reaction (hypersensitivity). Use Cerezyme® (imiglucerase for injection) carefully if you have had an allergic reaction to the product in the past. Symptoms suggestive of allergic reaction happen in 6.6% of patients, and 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. Side effects related to Cerezyme 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, abdominal pain, vomiting, 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. Cerezyme is available by prescription only. For more information, consult your physician. To learn more, please see the enclosed full product information or contact Genzyme at 1-800-745-4447 (option 2).

Please see accompanying full Prescribing Information on pages 9-10.
Genzyme Co-Pay Assistance Program
Cerezyme® (imiglucerase for injection)

Get Started Today in

3 Easy Steps!

1. You complete the program application

For more information about the program and to complete the online application, please visit: www.cerezyme.com/copay.aspx

You can also call your Genzyme Case Manager directly to learn more about the program and application process at 1-800-745-4447, Option 3

2. Your Genzyme Case Manager verifies eligibility

Your Genzyme Case Manager will review your application to verify eligibility.

If you are eligible, you will be automatically enrolled in the program.

Enrollment in the program is subject to confirmation of eligibility.

3. You’re enrolled

Once approved, you will receive confirmation from your Genzyme Case Manager and an enrollment card will be mailed to you within 7-10 days.

Your doctor or specialty pharmacy will also receive a confirmation letter with instructions on how to submit claims for reimbursement through the program.

Your enrollment in the program is effective from the date of approval through the end of 2012.

Genzyme reserves the right to make eligibility determinations, to set program benefit maximums, to monitor participation, and to modify or discontinue the program at any time.

Genzyme Co-Pay Assistance Program

The Genzyme Co-Pay Assistance Program will help eligible individuals who are prescribed treatment with Cerezyme® (imiglucerase for injection) with their eligible drug related out-of-pocket expenses, including co-pays, co-insurance and deductibles, regardless of financial status.

Once enrolled in the Genzyme Co-Pay Assistance Program, Genzyme will pay 100% of your eligible out-of-pocket Cerezyme drug costs up to the program maximum. The 2012 Co-Pay Program runs from January 1, 2012 through December 31, 2012.

Who is eligible for this program?
Regardless of financial status, the program is open to individuals who are:
- U.S. citizens or legal residents who have primary commercial insurance
- Prescribed treatment with Cerezyme® (imiglucerase for injection)

Who is NOT eligible?
As required by law, the program is not available to individuals who:
- Are residents of Massachusetts
- Have coverage or prescriptions paid for in part or full under any state or federally funded healthcare program including:
  - Medicare
  - Medicare Advantage Plans (Example: FreedomBlue offered through Blue Cross Blue Shield)
  - Medicaid
  - Medigap
  - Veterans Affairs, Department of Defense or Tri Care
  - High Risk Pool or Pre-existing Condition Insurance Plan (PCIP)

Please call your Case Manager if you have any questions about your eligibility. If you are not eligible for our Co-Pay Assistance Program and need help with your out-of-pocket expenses, your Genzyme Case Manager is available to help review your coverage options and refer you to other financial assistance programs that may offer financial support for eligible individuals.

Genzyme reserves the right to make eligibility determinations, to set program benefit maximums, to monitor participation, and to modify or discontinue the program at any time. This program assists patients with their out-of-pocket Cerezyme drug costs only, not the cost of infusions, medical evaluations/appointments, testing, or other related services.

For full Prescribing Information for Cerezyme® (imiglucerase for injection) go to www.cerezyme.com