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The Gaucher Connection

GAUCHER connection

For people with Gaucher disease, their families and their health care providers.

In this issue:

The Gaucher Connection newsletter is part of the Gaucher Connection Program brought to you by Genzyme Canada. The Gaucher Connection Program is endorsed by the National Gaucher Foundation of Canada.

GAUCHER connection | A Lifeline for Patients Living with Gaucher Disease

www.gaucherconnection.ca

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Manifestations of Gaucher Disease

Dr. Neal Weinreb, Hematologist/Oncologist in Coral Springs, Florida and Chair of the North American Scientific Advisory Board of the International Cooperative Gaucher Group, outlines some of the most common manifestations of Gaucher disease.

Type 1 Gaucher disease is an inherited disorder caused by a mutation in a gene called GBA, which directs the body to make an essential chemical called glucocerebrosidase.[1] This mutation causes the body to produce defective glucocerebrosidase, an enzyme that catalyzes a chemical reaction by which glucose, a simple and very important sugar molecule, is split off from glucocerebroside, a complex fat-sugar molecule that is one of the building blocks of cell membranes.[1,2] Glucocerebrosidase deficiency causes progressive deposition of glucocerebroside within the cells of the body, especially within cells known as macrophages, which are found in large numbers in the spleen, liver and bone marrow.[2] For this reason, the most common manifestations of Gaucher disease occur in the blood, bone, spleen and liver.[1,2] However, the clinical manifestations of type 1 Gaucher disease can vary greatly from patient to patient, even differing between siblings.[2,3]

Hematological (Blood) Manifestations

The most common hematological manifestations are anemia and thrombocytopenia.[2]

Anemia means having too few of the red blood cells that carry oxygen from the lungs to all the tissues of the body.[4] The most common symptom of anemia is fatigue. As anemia worsens, patients may begin to complain of dizziness, limited exercise tolerance, shortness of breath or a rapid heart rate.[4]

Thrombocytopenia means having a low blood platelet count and can be associated with an increased risk of bleeding.[2,4] Signs of spontaneous bleeding include episodes of nose bleeding or gum bleeding, or a tendency to bruise easily.[2,4] Bleeding may sometimes be more serious, such as bleeding from the stomach or intestines, bleeding in the eye, or bleeding around or in the brain that can be life-threatening.[4] The risks associated with a low platelet count are greater in patients who suffer physical trauma, who have to undergo surgery, or in those who have taken aspirin or related medications. Additionally, some patients with Gaucher disease may have a risk of bleeding that is disproportionate to the degree of decrease in the platelet count.[5] This is of particular concern during pregnancy when patients with Gaucher disease have significant risk for bleeding at or after delivery.

Involvement of the **Spleen** and **Liver**

Nearly all patients with type 1 Gaucher disease have enlargement of the spleen, known as splenomegaly.[2] In half of patients, the spleen volume is more than 15 times normal, resulting in abdominal protrusion, bloating, inability to eat a normal sized meal, weight loss, and sometimes episodes of severe pain.[6]

Aside from taking up a lot of space in the abdomen, a big spleen also traps a large volume of blood, giving it an extraordinary opportunity to feed its appetite for red blood cells, white blood cells and platelets. This is the major reason why patients with type 1 Gaucher disease frequently have low blood counts.[2] Moreover, the increased volume of blood in the spleen can itself cause problems because most of that blood volume is

discharged directly into the blood vessels that supply the liver. This extra blood can add to the enlargement of the liver that often occurs in patients with Gaucher disease due to the presence of Gaucher cells and, in a small minority of patients, can lead to serious complications, such as inflammation and scarring in the liver and portal hypertension, an increased pressure in the veins that bring blood to the liver from the stomach and intestines.[1,2]

Bone Manifestations

More than 80% of patients have some evidence of bone involvement that can cause serious, even life-altering, skeletal and joint conditions.[6] Issues related to Gaucher disease and bones include growth retardation in children, increased risk of fracture and bone pain and bone crises.[3]

Fracture risk in patients with Gaucher disease is most commonly due to a generalized "thinning" of the bones known in its milder form as osteopenia and in its severe form as osteoporosis. This type of bone loss is common in all aging people, but may have more serious consequences in Gaucher patients who have lower levels of bone mass to begin with. Thus, doctors need to watch closely for evidence of low bone mineral density in all patients with Gaucher disease.[3]

More than 50% of patients with type 1 Gaucher disease have chronic bone pain, which may be difficult to reverse or control.[3] Patients may suffer also from bone crises, localized pain with acute onset sufficiently severe to require immobilization and strong painkillers.[3] Bone crises are often associated with another serious complication of Gaucher disease called osteonecrosis. Osteonecrosis is usually irreversible and can lead to bone deformities and joint destruction.[3] Patients with these complications can be helped with expert orthopedic management, including modern joint replacement techniques. Because osteonecrosis can sometimes occur in Gaucher disease patients without any acute symptoms such as a bone crisis, periodic serial skeletal evaluations using MRI are highly recommended.[3]

The key to the management of bone disease, as well as all other clinically significant complications of type 1 Gaucher disease, is vigilance and prevention. This is best achieved with a combination of serial comprehensive evaluations and prompt institution of treatment when indicated.[1]

Living Well, Staying Well:
Healthy Habits for People with Gaucher Disease

Balancing family, friends and work or school on top of the demands of managing a chronic condition like Gaucher disease can make it difficult to find the time and energy to pursue a healthy lifestyle – but the physical and emotional benefits make it well worthwhile.

According to Colleen McNeil, Nurse Clinician for Lysosomal Storage Disorders at the Alberta Children's Hospital in Calgary, the most important things people with Gaucher disease can do for their health are to listen to their Gaucher specialist physician and attend follow-up appointments and tests, including enzyme replacement infusions, MRI and X-ray bone scans, and routine blood work appointments. Ms. McNeil also highlights the importance of patients being fully educated on Gaucher disease. There are many ways to become more educated on Gaucher disease, including attending local or national patient meetings, reading up on research that is being done, and talking to other people with Gaucher disease. Becoming more knowledgeable not only allows people to make informed decisions about their health care, it means they can help educate family members and even other clinicians involved in their care about Gaucher disease and in doing so become advocates for their own health.

Of course, healthy living is not just about managing one condition. A healthy lifestyle should also incorporate a balanced diet, regular physical activity and a commitment to being tobacco-free.[7] Making the transition to a healthy lifestyle can seem daunting, but Ms. McNeil offers some practical advice on how to make changes you can live with.

"So many people start an exercise program… but they don't last. Part of the reason that may happen is they simply don't enjoy what the routine is," Ms. McNeil explains. She suggests incorporating activities you actually enjoy into your routine. She also recommends "mixing things up" to add variety and prevent yourself from getting bored. For instance, if walking is your regular exercise, you might want to consider adding an activity that focuses on your arms, such as a racquet sport. Whatever physical activity you choose to do, it is important for people with Gaucher disease, like anyone else starting an exercise regimen, to take small steps to begin with, modify the exercise to fit your level of fitness and set realistic expectations and timelines. It is also important to be realistic about your limitations. Someone with more severe bone disease, for example, might want to concentrate on lower impact activities like swimming, walking or yoga.

According to Ms. McNeil, variety is also the key to preventing a healthy diet from being a boring one. She suggests trying new recipes from newspapers, the internet or other sources, as well as keeping eating fun by incorporating mini-challenges like making sure to eat a red, yellow and green food every day. This kind of challenge will also help you include an appropriate amount of fruits and vegetables in your diet, something that is important for everyone. People with Gaucher disease should also make a special effort to eat foods that are high in vitamin D and calcium, nutrients that are important for bone health. Dairy products, like milk and yogurt, contain plenty of calcium and are also fortified with vitamin D, so Gaucher patients should aim to consume two to three servings of dairy every day.[8] Vitamin D can also be obtained from many kinds of fish, including salmon and tuna, as well as from exposure to sunlight.[9] However, it is not uncommon to need to take a vitamin D supplement, particularly during the winter.[9]

> **" Smoking isn't healthy for anybody. "**

One thing that remains the same regardless of season is the importance of staying smoke-free. "Smoking isn't healthy for anybody," says Ms. McNeil and adds it can be particularly harmful for Gaucher patients, as some rare patients can experience pulmonary involvement as part of the disease.[2] Additionally, smoking can make exercise difficult because it affects the lungs and this can have a negative impact on bone health.[10] For those people who are smoking, Ms. McNeil emphasizes there are many resources available to help them quit and suggests joining a support group as a good first step.

Ms. McNeil's final piece of advice for the Gaucher patient looking for a healthy lifestyle is to not neglect their emotional health. She advises people to include social time in their regular schedule, avoid worrying too much about things they cannot change and, above all, to get enough sleep. "I think all that plays an important role with regards to healthy living," she concludes.

Q&A

Dialogue: RegistryNXT!

Questions and answers from Chris Jones, RegistryNXT! program manager at Genzyme.

What is **RegistryNXT!**?

RegistryNXT! is the name of the newly updated Genzyme-sponsored lysosomal storage disorder registry system. This web-based platform allows for high-quality data collection and the ability to transfer and store data, and incorporates a reporting system that allows registered sites and patients to view the data in near real time.

Why was a **new registry** system needed?

The registry was started as a paper-based system 20 years ago. With a life-long disorder like Gaucher disease, a great deal of information on any one patient can accumulate in 20 years and the registry has steadily been adding new patients since its inception. The registry moved to an electronic system nine years ago to help deal with this incredible amount of data, but the electronic technology platform had become outdated. Genzyme was faced with the question of whether to just replace the technology or to innovate, improving the registry system so it could better benefit researchers, physicians, nurses and patients.

What features does **RegistryNXT! offer**?

Typically, a registry is a way to collect and organize data for research, to better understand treatment and what happens to patients in the real world. However, involvement in the registry is voluntary and collecting these data requires interest on the part of physicians, nurses and patients. Data entry is a time-consuming process and patients can get lost to follow-up, making it difficult to know where the gaps in the data are. To help overcome this challenge, Genzyme wanted to design the registry system so that it would give something back to the Gaucher community, as well as to researchers.

With RegistryNXT!, nurses or physicians who take the time to enter patient information in the registry can immediately see near real-time reports on that patient. The registry provides a dashboard for each site so that members of the care team can view, download and share patient data in the form of customizable reports and tables. The care team can also decide to share some or all of this information with the patient through a secure portal. Patient privacy is protected by identifying patients by numbers rather than by name.

How will **RegistryNXT! benefit** Gaucher **patients**?

RegistryNXT! allows physicians to share data with patients, and also to add their own comments to help explain what the charts and tables mean. For the first time, with their physician's approval, patients will be able to view their own registry information. For instance, patients may be able to see a graph showing how their hemoglobin levels have changed over the past 15 years, or a report detailing the results of their most recent blood tests. Patients will also benefit indirectly from the research generated by the registry, which should help improve care for all patients with Gaucher disease.

How can Gaucher patients **join** the **registry**?

Patients who are not certain whether they are already part of the registry should discuss this with their physician. Access to the RegistryNXT! reports can also be obtained through the physician. Patients who are invited to join by their physician will receive an email from the registry system providing them with a link to set up their own secure password-protected access to RegistryNXT! This will allow patients to view the information and reports their physician decides to share with them. However, while RegistryNXT! began going online in April, all Canadian sites are not expected to be online until September 2011.

More information on **RegistryNXT!** can be found at **GaucherRegistry.com**.

Profile

Pierre Joly: Behind the Camera

An avid photographer, Pierre Joly is more used to being behind the camera than in the spotlight, but here he reveals how his twin passions of technology and photography have led him to some of the most remote spots in northern Ontario.

Being diagnosed with Gaucher disease at the age of 15 has not prevented Pierre Joly from being one of the busiest guys you might ever meet. By day, the 30-year-old is the assistant manager at Lucid Networks Corporation and travels across a territory covering more than 100,000 km^2 to set up and maintain servers, networks and other technology platforms for remote mining and power stations, as well as other small businesses and native communities in northern Ontario. In the evenings and on weekends, Pierre is an active member of both his hometown of Timmins, Ontario and the Canadian Gaucher community. He is not only a member of the executive committee for Science Timmins, a local organization that aims to make science fun, and an administration officer with the Timmins Navy League Cadets, but is on the board of directors for the National Gaucher Foundation of Canada and serves as its webmaster.

Joining **Art** and **Technology**

On top of his already busy schedule, Pierre also finds the time to indulge in his true passion, photography. Armed with one of his 1970s-vintage 35 mm SLR cameras, he frequently heads off into the wilderness of northern Ontario to capture his love of nature on film. He aims to take pictures from as far south as Sudbury up to the James Bay coast in order to showcase the beauty of northern Ontario for the rest of the world. "There are sights that most people have not seen and I would like to show it to everybody," he explains. To further this ambition, Pierre is currently in the process of starting up his own photography company, Joly Good Photography (http://www.jolygoodphotography.ca). He is also saving towards the purchase of an 18-plus megapixel digital SLR camera that will help him unite his loves of technology and photography – though he says 35 mm film will always have a place in his heart.

Going the **Distance**

Given Pierre's busy schedule and extensive travelling, it seems like having Gaucher disease has not slowed him down. However, as Pierre explains, managing his condition has not been without its challenges. Both his work with Lucid Networks and his photography hobby require him to travel to some fairly remote locations. On one occasion, Pierre was scheduled to set up the computer and communications system at a mining outpost, accessible only by air. However, the planned dates of the visit overlapped with Pierre's scheduled Cerezyme® infusion. Unfortunately, despite everyone's best efforts, it proved impossible to guarantee the cold chain to perform the infusion at the mining site. The trip was eventually cancelled when the client changed his mind about the proposed computer system. Since that time, however, Pierre has entered the Eliglustat clinical trial program. According to Pierre, the convenience of the twice a day Eliglustat oral tablet as compared to the biweekly Cerezyme infusion has really expanded his ability to take extended leave and to venture to more remote locations.

Given all that Pierre has accomplished so far, it will be interesting to see where this newfound freedom takes him. ■

"There are sights that most people have not seen and I would like to show it to everybody."

References

1. Harmanci O, Bayraktar Y. Gaucher disease: new developments in treatment and etiology. *World J Gastroenterol* 2008; 14(25):3968-73.
2. de Fost M *et al.* Gaucher disease: from fundamental research to effective therapeutic interventions. *Neth J Med* 2003; 61(1):3-8.
3. Wenstrup R *et al.* Skeletal aspects of Gaucher disease: a review. *Br J Radiol* 2002; 75(Suppl 1):A2-12.
4. Merck & Co., Inc. *The Merck Manuals Online Medical Library.* Available at: http://www.merckmanuals.com. Accessed: June 7, 2011.
5. Spectre G *et al.* Platelet adhesion defect in type I Gaucher disease is associated with a risk of mucosal bleeding. *Br J Haematol* 2011; 153(3):372-8.
6. Charrow J *et al.* The Gaucher registry: demographics and disease characteristics of 1698 patients with Gaucher disease. *Arch Intern Med* 2000; 160(18):2835-43.
7. Health Canada. *Healthy Living.* Available at: http://www.hc-sc.gc.ca/hl-vs/index-eng.php. Accessed: June 7, 2011.
8. Health Canada. *Vitamin D and Calcium: Updated Dietary Reference Intakes.* Available at: http://www.hc-sc.gc.ca/fn-an/nutrition/vitamin/vita-d-eng.php. Accessed: June 7, 2011.
9. Hanley DA *et al.* Vitamin D in adult health and disease: a review and guideline statement from Osteoporosis Canada (summary). *CMAJ* 2010; 182(12):1315-9.
10. National Institutes of Health. *Smoking and Bone Health.* Available at: http://www.niams.nih.gov/Health_Info/Bone/Osteoporosis/Conditions_Behaviors/bone_smoking.asp. Accessed: June 7, 2011.

Consumer Information

CEREZYME® (IMIGLUCERASE FOR INJECTION)

This leaflet is part III of a three-part "Product Monograph" published when CEREZYME® was approved for sale in Canada and is designed specifically for consumers. This leaflet is a summary and will not tell you everything about CEREZYME®. Contact your doctor or pharmacist if you have any questions about the drug.

ABOUT THIS MEDICATION

What the medication is used for:

CEREZYME® is used to treat patients with a confirmed diagnosis of non-neuronopathic (Type 1) or chronic neuronopathic (Type 3) Gaucher disease resulting in one or more of the following conditions:

- Anaemia after exclusion of other causes, such as iron deficiency
- Thrombocytopenia
- Bone disease after exclusion of other causes such as Vitamin D deficiency
- Hepatomegaly or splenomegaly

What it does:

Gaucher disease is a genetic disorder resulting in deficient ß-glucocerebrosidase activity. Therefore, glucocerebroside accumulates in the lysosomes of tissue macrophages in the liver, spleen, bone marrow and occasionally in lung and kidney. CEREZYME® is a form of β-glucocerebrosidase produced by recombinant DNA technology. CEREZYME® can help to treat some of the symptoms of Gaucher disease by replacing the deficient enzyme.

When it should not be used:

Do not use CEREZYME® if you are hypersensitive to imiglucerase or to any ingredient in the formulation or component of the container.

What the medicinal ingredient is:

Imiglucerase

What the important nonmedicinal ingredients are:

Mannitol, Polysorbate 80, Sodium citrates

For a full listing of nonmedicinal ingredients see Part 1 of the product monograph.

What dosage forms it comes in:

CEREZYME® is supplied as a sterile lyophilized powder for intravenous infusion.

CEREZYME® is supplied in a 20 mL vial containing either 200U (aqua label) or 400U (red label) of imiglucerase.

WARNINGS AND PRECAUTIONS

Serious Warnings and Precautions

Do not use CEREZYME® if you are severely hypersensitive to imiglucerase or to any ingredient in the formulation or if you have experienced severe hypersensitivity to imiglucerase.

Anaphylactoid reaction has been reported in less than 1% of the patient population. Further treatment with CEREZYME® should be conducted with caution.

In rare cases, pulmonary hypertension has also been observed during treatment with CEREZYME®. Pulmonary hypertension is a known complication of Gaucher disease, and has been observed both in patients receiving and not receiving CEREZYME®. No causal relationship with CEREZYME® has been established. Patients with respiratory symptoms should be evaluated for the presence of pulmonary hypertension. But, if you suffer with any shortness of breath you should tell your doctor.

BEFORE you use CEREZYME® talk to your doctor or pharmacist if:

- You have been treated with placental-derived ß-glucocerebrosidase (CEREDASE®, alglucerase injection) and have developed antibody or exhibited symptoms of hypersensitivity to placental-derived ß-glucocerebrosidase (CEREDASE®, alglucerase injection)
- You have had a severe hypersensitivity or anaphylactic reaction to administration of CEREZYME®
- You have any allergies to this drug or its ingredients or components of the container
- You are pregnant or plan to become pregnant or are breast-feeding

INTERACTIONS WITH THIS MEDICATION

No formal interaction studies have been conducted. Please inform your doctor if you are using any other medicinal products, due to the potential risk of interference with the uptake of imiglucerase.

PROPER USE OF THIS MEDICATION

Usual dose:

Dosage should be individualized to each patient.

Treatment may be initiated from 2.5 units/kg of body weight 3 times a week up to 60 U/kg administered as frequently as once every two weeks. If CEREZYME® is to be administered in a home care environment, it is suggested that the health care professional be trained and prepared for the possibility of an allergic-type reaction.

Overdose:

There have been no reports of obvious toxicity for doses up to 240 U/kg (every two weeks).

Missed dose:

If you have missed a CEREZYME® infusion, please contact your doctor. It is important to have your infusion on a regular basis to avoid the accumulation of glucocerebroside. The total dose administered each month should remain substantially unchanged.

SIDE EFFECTS AND WHAT TO DO ABOUT THEM

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, 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 reactions (antibodies); periodic monitoring by your physician is suggested.

If you exhibit such a reaction following the administration of CEREZYME®, you should immediately contact your doctor.

Pre-treatment with antihistamines and/or corticosteroids and reduced rate of infusion has allowed continued use of CEREZYME® in most patients.

This is not a complete list of side effects. For any unexpected effects while taking CEREZYME®, contact your doctor or pharmacist.

HOW TO STORE IT

Keep out of reach and sight of children. Store under refrigeration at 2 °C to 8 °C. Do not use after the expiration date on the vial.

Since CEREZYME® does not contain any preservative, after reconstitution, vials should be promptly diluted and not stored for subsequent use.

International Collaborative Gaucher Group (ICGG) Registry

The ICGG Registry is a longitudinal prospective study that includes over 4,936 patients (as of March 7, 2008), with Gaucher disease from around the world. The Registry was established to assist physicians in the treatment and management of patients with Gaucher disease.

Treatment centres involved with Registry enrolled patients are required to collect data on a regular basis.

In Canada, the ICGG Annual Report is made available at the beginning of each year. This report details the data collected in the seven provinces with Gaucher patients. The Canadian Annual Report is available upon request through Genzyme Canada.

Information regarding the registry program may be found by calling (800) 745-4447. If you are interested in participating, please contact your doctor.

REPORTING SUSPECTED SIDE EFFECTS

You can report any suspected adverse reactions associated with the use of health products to the Canada Vigilance Program by one of the following three ways:

- Report online at www.healthcanada.gc.ca/medeffect
- Call toll-free at 1-866-234-2345
- Complete a Canada Vigilance Reporting Form and fax toll-free to 1-866-678-6789, or mail to:

  Canada Vigilance Program
  Health Canada
  Postal Locator 0701D
  Ottawa, Ontario
  K1A 0K9

Postage paid labels, Canada Vigilance Reporting Form and the adverse reaction reporting guidelines are available on the MedEffect™ Canada Web site at **www.healthcanada.gc.ca/medeffect**.

NOTE: Should you require information related to the management of side effects, contact your health professional. The Canada Vigilance Program does not provide medical advice.

MORE INFORMATION

This document plus the full product monograph, prepared for health professionals, can be found at: http://www.genzyme.ca or by contacting the sponsor, Genzyme Canada Inc., at: 1-877-220-8918.

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