GAUCHER DISEASE

BASIC ORIENTATIONS
to Patients and Families

PATIENT MANUAL – GAUCHER'S DISEASE REVISED EDITION 02/2009

HEMORIO
BLOOD CENTER OF RIO DE JANEIRO

Introduction

This manual aims to provide patients and their families with information on Gaucher's Disease.

We know that the medical information most times consists of technical terms difficult and incomprehensible by most users. Therefore, we expect this insert to clarify your doubts.

Any comment is highly welcomed, be it on the clarity of this manual or the omission of any information considered important and it can be sent through our HEMORIO suggestion box or by email ouvidoria@hemorio.rj.gov.br.

What is Gaucher Disease?

It is a hereditary disease transmitted from one generation to another, in which an important enzyme, glucocerebrosidase also called betaglucosidase, is deficient. This enzyme acts in the glucocerebroside, which is a type of fat, resulting from the decomposition of red blood cells and leucocytes. The lack of this enzyme results in the accumulation of undigested material in the macrophages. These cells are known as Gaucher cells, which are found in the bone marrow, spleen, liver and most rarely in the lungs, kidneys, skins, ganglia and perivascular spaces of the brain.

The disease is autosomal recessive. Autosomal because the genetic error is located in chromosome 1, which is an autosomal chromosome. Recessive because one person with Gaucher Disease inherited (gained) one mutation from the father and the other from the mother. Generally the fathers are carriers of the disease because they only carry a defective gene silently, without presenting symptoms. And patient with the disease has 2 defective genes.

There are three types of Gaucher Disease. Type 1, also called adult or chronic type, is the most common type and represents about 99% of all described cases, and there is no neurological manifestation; type 2, infantile form, acute, sudden, and extremely rare and rapid and severe neurological deterioration occurs; type 3, juvenile form, sub-acute, which presents neurological symptoms, with much broader evolution than type 2.

What are the symptoms?

Some patients with Gaucher Disease type 1 present few symptoms, others have more clinical symptoms. The most common complaints are paleness, tiredness, weakness due to anemia, bleeding, especially from the nose (epystaxis) due to reduced number of platelets, dark spots (ecchymosis and hematomas), pains on legs and bones. Some patients fracture their bones easily, that is, with minimum traumatism. Complaints of abdominal pain, abdominal distension, increased spleen and liver (hepatosplenomegaly) are also common. Types 2 and 3 present neurological impairment, which may be: strabismus, retroversion of the head, convulsion, motor paralysis, etc.

How is the diagnosis made?

The diagnosis of Gaucher Disease is confirmed through a simple blood collection drawn from the forearm. The dosing of the beta-glucosidase enzyme is taken from this specimen, which has values much lower than the normal values in Gaucher Disease carriers.

In some cases the hematologist has the urgent need to discard the possibility of more serious diseases and may therefore conduct a myelogram on the patient. The result of this test is ready in a few hours but it is a bit more painful and invasive. Myelogram analyses the cells of bone marrow, and it is conducted by drawing blood from the bone in the sternum region (which is the chest bone) or on the posterior iliac crest (which is the bladder bone) that can be performed on either adults or children. Local anesthetic is used in the execution of this procedure.

When the patient has Gaucher Disease, we find the Gaucher cells in the bone marrow, but it is compulsory to perform enzymatic dosing in order to confirm the diagnosis as other diseases with similar cells exist, such as the cells of Nieman-Pick's disease.

Study is also conducted on the DNA to identify the mutation involved. The most frequent mutations are researched, such as N370S, L444P, 84GG, IVS2+1, 55del. This test is important because patient that does not have the mutation N370S identified may develop a serious neurological condition. This may occur in these cases because there is the possibility of it being a Gaucher Disease type 3, which is treated with higher doses of the drug.

The diagnosis can be performed at any moment of the patient's life, from the first months to the adult phase. Not all patients with diagnosis of Gaucher Disease are indicated to begin treatment but the earlier the symptoms the more serious the disease. Therefore, diagnosed children should begin treatment immediately. Adults, on the other hand, should be evaluated with several tests to decide the best moment to begin or not begin treatment.

Therefore, brothers of patients should always be investigated to search for an early diagnosis even before the appearance of any symptom.

How is the treatment performed?

Only patients diagnosed with Gaucher Disease type 1 and 3 are indicated to receive treatment. Type 2 does not respond to any known treatment.

The first drug for the Gaucher Disease was developed in the beginning of the 90s. This drug is the enzyme that is deficient, which is initially extracted from human placenta and is currently developed by recombinant DNA technology. This enzyme is administered endovenously with infusions scheduled for every 14 days for the rest of one's life. This medication is administered as outpatient and does not require hospitalization, and it takes approximately 90 minutes. Therefore, studies show that treatment lead to the resurgence of the symptoms after some months.

The enzyme currently used is IMIGLUCERASE (cerezyme 200u/bottle), and the administered dose is calculated based on the severity criteria and patient weight. There are other oral and venous drugs, such as velaglucerase alfa, taliglucerase alfa and miglustat.

The objective of the treatment is to improve the quality of life of the patient by reducing the size of the spleen, liver, correcting the laboratory examinations and solving the bone pains, allowing the patient to have a normal social life, to be able to study and work normally.

Can patients with Gaucher Disease practice sports?

It depends on the treatment phase and degree of the disease. Patients with very large spleen or liver or with serious bone disease require more attention and care in order not to get hurt. Sometimes they have to wait a bit for clinical improvement before practicing sports.

Patients are encouraged to swim, which is a sport that does not stress the bones. It is also recommended to stay in the sun until 10 am and after 3 pm. Physical exercise and sunlight exposure, together with a good meal (based on milk and cheese) strengthens the bones.

It is worth emphasizing that all patients should ask their physicians about physical exercise before practicing because only the physician can consider the patient's clinical conditions.

However, one thing is certain: if we begin to treat the patient as soon as the symptoms begin (normally at childhood), the patient should be able to practice sports soon after some months of regular use.

Patients with Gaucher Disease can marry and have children?

Since the disease is hereditary, it passes on to the next generation. This does not mean that your children will have the disease. We have to know the partner, know if it has the gene for

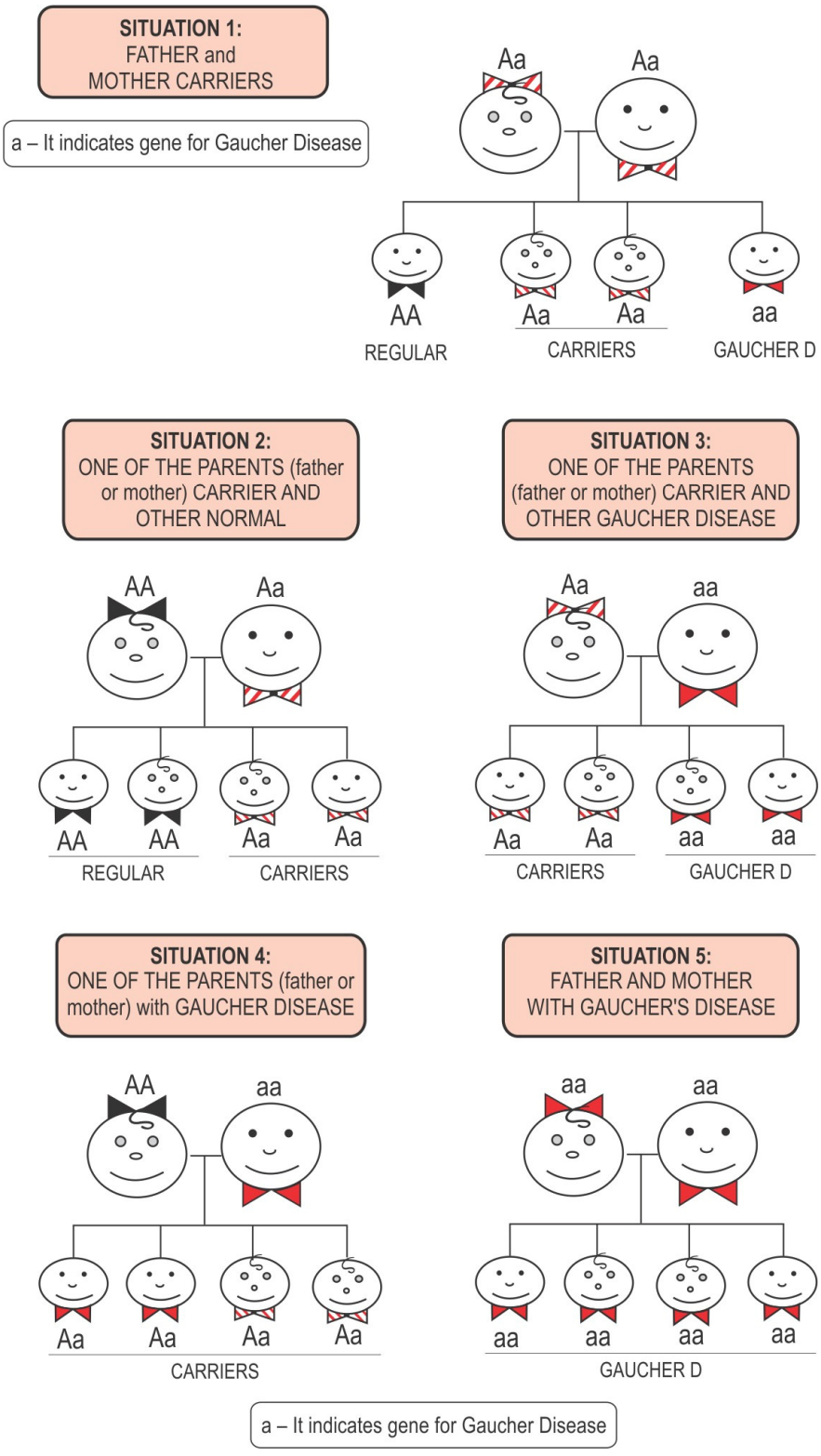
the disease, before planning a baby. This is because if you marry someone who has the same disease 100% of the children will also have it. If it is with a carrier, the chances are 50%. But if the partner does not have any of the genes for Gaucher Disease, then none of the children will have the disease, but all will become carriers, that is, all will have one gene of the disease. See the diagrams below.

How can I identify similar cases in other families?

We have to study the entire families of patients with Gaucher Disease, especially those that can have children because they have to be oriented since it is a genetic disease.

The diagram below aims to enable you to understand the transmission process of Gaucher Disease. It is a simplified heredogram. Talk to your physician.

Heredogram of Gaucher Disease



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TAKE NOTE:

Associação Brasileira dos Portadores da Doença de Gaucher

[Brazilian Association of Gaucher Patients]
www.gaucherbrasil.org.br

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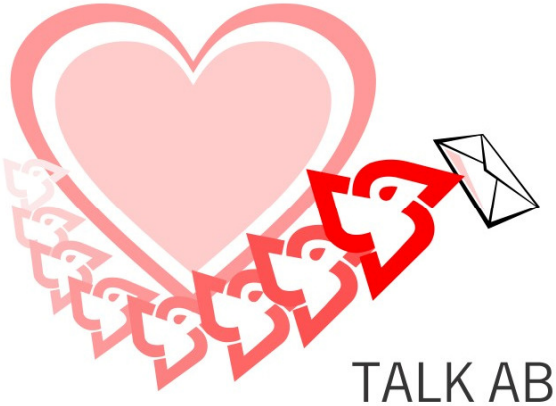

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