

## GAUCHER DISEASE

### Mission Statement

- Increase community awareness and understanding of lysosomal storage disorders, their effects and potential solutions, through education and publicity;
- Increase political recognition and understanding of lysosomal storage disorders, their effects and potential solutions, particularly the cost-benefit advantages offered by therapies;
- Encourage research involved with the diagnosis, management and treatment of patients affected by lysosomal storage disorders;
- Maintain close links with family support groups;
- Promote and establish links with support associations for other, non-lysosomal, organelle diseases
- Promote and establish links with similar organisations internationally.

*Gaucher (pronounced go-shay) disease is the most common inherited lipid (fat) storage disorder in humans, and it is the most prevalent lysosomal storage disorder in persons of Ashkenazi Jewish ancestry. It is caused by a deficiency of the enzyme 'glucocerebrosidase', and is inherited in an autosomal recessive pattern.*

Some of the major aspects of this condition were first described in 1882 by the French physician C.P.E. Gaucher in his medical school thesis. He mistakenly believed that the patient he reported had a tumour of the spleen. In time, it was realised that the condition was an inherited lipid storage disorder. The metabolic abnormality in Gaucher disease was shown by Brady and coworkers in 1965 to be a deficiency of the enzyme glucocerebrosidase. In 1968, Weinreb and coworkers found that the highest activity of glucocerebrosidase was in cellular compartments called lysosomes, although the enzyme did not appear to be confined to these organelles. The gene that codes for glucocerebrosidase was shown to be on human chromosome 1 by Barneveld and coworkers in 1983. The gene was identified by Ginns and coworkers in 1984. Although there are some common mutations (mistakes) in the gene that cause Gaucher disease, more than 200 individual mutations have been described in patients with this disorder.

Glucocerebrosidase is required for the breakdown (degradation) of the sugar-lipid complex (glycolipid) called glucocerebroside. Glucocerebroside is composed of two

fatty materials linked together, to which a single molecule of the sugar, glucose, is also attached. Glucocerebrosidase plays an important role in the removal of glucose from this glycolipid, a reaction that is necessary for the breakdown of glucocerebroside. Glucocerebroside in the body arises from the turnover of normal cell membrane components. A particularly important source is red and white blood cells. When these become old, they are removed from the circulation and the materials in their membranes are degraded by a series of enzymes. If one of these enzymes, such as glucocerebrosidase, is less active than normal, some glucocerebroside accumulates every day in various organs and tissues in the patient's body. In Gaucher disease, the spleen, liver and bone marrow are primary sites of glucocerebroside accumulation. If enough glucocerebroside accumulates, it can damage the spleen, liver, bone marrow, and in a few patients, the lungs as well. In a small number of patients with Gaucher disease, glucocerebroside also accumulates in the brain and can severely impair its function.

### Classification of Gaucher disease

Patients with Gaucher disease have been divided into three principal groups, called Types 1, 2 and 3.

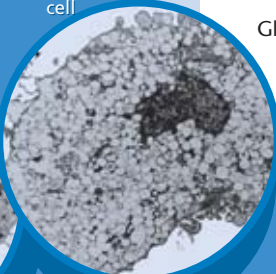
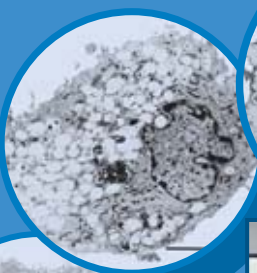
#### Type 1

patients are characterised by anaemia, low blood platelets, a tendency to easy bruising, enlargement of the spleen and liver, and weakening of their bones. Some patients may experience lung problems as well. The enlarged spleen can become massive and disfiguring (see pre-treatment photograph). The weakened bones are easily fractured. The hips and spine may be particularly involved, but evidence of widespread skeletal damage is often apparent in X-rays. The onset of these problems varies from patient to patient. In some patients, they may appear early in life, during childhood or adolescence, while in others not until they are adults. A principal characteristic of Type 1 Gaucher disease is the absence of brain involvement.

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Affected cells depicting the increase in number of lysosomes containing stored material.

Severely affected cell



Like the household kitchen, lysosomes can be described as 'recycling centres'. If waste material is not removed, it builds up and impairs normal functioning.

Normal cell



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