GAUCHER DISEASE

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What is Gaucher disease?

Gaucher disease is a rare genetic disorder affecting fat metabolism. It belongs to a family of diseases called Lysosomal Storage disorders (LSDs). In affected individuals, a protein (enzyme) called Beta-glucosidase is not made by the body because of a gene error. Beta glucosidase is important for the breakdown and metabolism of certain types of fat in the body. In its absence, the precursors get progressively accumulated in different parts of the body causing signs of this disease.

Clinically GD is classified into three types:

Type I: Mostly affecting spleen, liver, blood and bone with no neurological signs

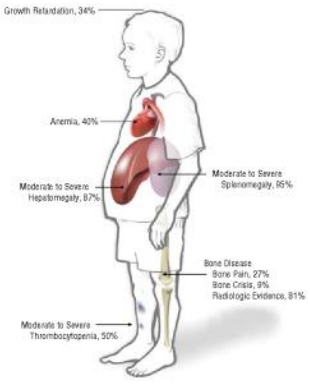
Type II: Early onset with severe neurological problems. Many do not survive beyond infancy

Type III: Like Type I but also have some neurological and eye problems

What are the commonest signs and symptoms of Gaucher disease?

Children with Gaucher disease appear normal at birth. As a child grows the following symptoms develop:

- Poor growth
- Progressive abdominal distension
- Progressive and massive enlargement of the spleen and liver
- Abnormalities of blood cells causing anaemia and low platelet counts which can cause bleeding from the nose, gums and other sites
- Weakness of bone with poor growth, fractures and deformities
- Eye abnormalities such as a squint or gaze palsy
- Occasionally they may develop learning difficulties or fits
- Rarely the heart or lungs may also be affected.



Signs and symptoms in Gaucher disease
Image Credit: Archives of pediatrics & adolescent medicine, 2006

Affected children may develop some or many of these symptoms and these usually get worse with age.

What happens if an affected child is not treated in time?

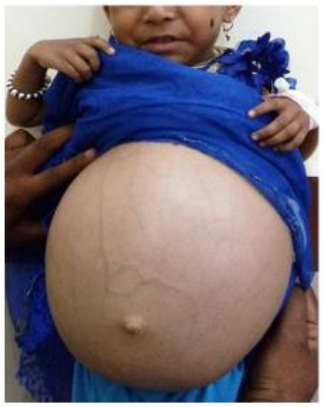
Growth failure, a progressive increase in spleen and liver size and many blood complications may occur over a period of time. Untreated children develop serious complications and may not survive childhood.

How is Gaucher disease inherited?

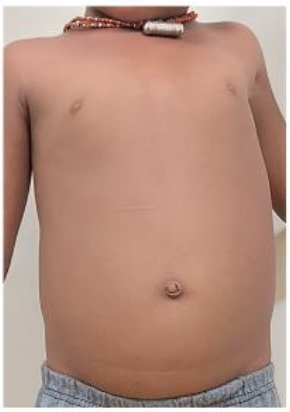
Gaucher disease is inherited in an autosomal recessive pattern. All individuals have two copies of GBA gene. In carriers, one of the pair is faulty. Carriers do not usually have any problems. When both parents are carriers, the chance of their child inheriting the gene fault (mutation) from both parents is 1 in 4 (25%) in each pregnancy. Children with Gaucher disease have mutations in both copies of the GBA gene and the normal synthesis of beta-glucosidase enzyme does not happen in them.

What is the treatment of choice for Gaucher disease?

Enzyme replacement therapy: For affected children, a specific treatment called Enzyme Replacement Therapy (ERT) is available for the treatment of GD Type I and most cases of Type III. The missing enzyme is given as an intravenous injection every fifteen days. This treatment needs to be given lifelong. The best results are seen when a child is begun on treatment early. The majority of affected children respond well to ERT and improvement is seen within six months of starting treatment. Many children who have been treated appropriately grow up to be able, working individuals and may even become professionals like engineers, doctors etc. They can also get married and have healthy children of their own.



Gaucher disease: untreated



Gaucher disease: after 2yrs of ERT

What are the limitations of ERT? The limitations of ERT is that it does not cross the blood brain barrier or penetrate into bones. For children who have neurological or intellectual problems, these problems may not improve with ERT.

Substrate reduction therapy (SRT): these are oral medicines which can be used in cases of GD where ERT is contra-indicated, in specific types of GD such as Saposin C deficiency and in milder types of GD with residual enzyme function. SRT does not cross the blood-brain barrier and is also very expensive.

Newer treatments are in research to improve neurological and bony problems in Gaucher disease and to develop more medicines that can be taken orally instead of by injection.

What is the cost of therapy?

ERT is very expensive and costs approximately INR 30 lakhs/ year to treat a 10kg child. These costs are beyond the reach of most families.

Products available in India:

Product	**Indication**	**Frequency**	**Duration of therapy**
Cerezyme® (Imigucerase) Sanofi-Genzyme, India	Approved for use in Type I and Type III GD	60mg/kg/dose given as an IV infusion every fortnight	Life-long
VPRIV® (Velaglucerase alfa) Takeda, India	Approved for use in Type I GD	60mg/kg/dose given as an IV infusion every fortnight	Life-long

Prevention

Families having affected children are encouraged to consult a clinical geneticist for counselling and prevention of recurrence in future pregnancies.

For further information:

Link to videos