

# Report on Gaucher Disease

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**Abstract:** In This Research Paper issue you can find general information on the disease, some steps taken by the government for these rare diseases

**Keywords:** Gaucher disease—introduction---govt schemes

## 1. Introduction

### 1.1 Lysosomes : An Introduction

Lysosome was discovered by Christian de duve (1953) and were observed under electron microscope and named by novikoff, hence known as suicidal bags. These are formed when golgi bodies are pinched off from its tubules. These are single membrane bound organelles that contain hydrolytic enzyme 0.2µm to 0.8µm. lysosomes are polymorphic cell organelles existing in four forms namely primary lysosomes, secondary lysosomes, residual lysosomes, autophagic lysosomes. Lysosomes act as an waste disposal system of the cell by digesting unwanted materials. Synthesis of lysosomal enzymes is controlled by nuclear genes. And mutations in these genes for these enzymes are responsible for more than 30 different human genetic disorders, which are collectively known as lysosomal storage diseases. These diseases result from an accumulation of specific substrates, due to the inability to break them down. Lysosomal storage disorder (LSD) are a group of approximately 45 rare genetic disorder caused by the deficiency of certain enzymes in a cell. One such disease under this disorder is gaucher disease. It is a rare inherited disorder that causes too much of a substance called glucocerebroside to build up in spleen, liver, lungs, bones and sometimes in the brain. This prevents the organ from stops working due to the deposition in machrophage-monocyte system which results in from the deficiency of enzyme glucocerebrosidase.

## 2. Gaucher Disease

Gaucher disease results from not having enough glucocerebrosidase (GCCase), an important enzyme that breaks down a fatty chemical called glucocerebroside. Because due the lack of the enzyme body cannot break down this chemical, Gaucher cells build up in areas like the spleen, liver and bone marrow. Gaucher disease is more common among Jews of Ashkenazi (Eastern European), occurring in approximately 1 in 450 within this population.

### Types of Gaucher Disease

On presence or absence of early onset brain involvement, the disease is classified into:

**Gaucher disease type 1:** Gaucher disease type 1 is the most common in western countries. Symptoms include spleen and liver enlargement, bone problems and fatigue.

Gaucher disease type 2: This type of Gaucher disease is rare and involves severe neurological (brain stem) abnormalities.

Gaucher disease type 3: t is the most common form of the disease worldwide. causing the same symptoms as type 1 plus some neurological involvement. Patients have a short life.

## 3. Treatments of Gaucher Disease

Available treatments include enzyme replacement therapy (ERT) and substrate reduction therapy (SRT).

- 1) Enzyme replacement therapy (ERT) balances low levels of GCCase in patients with Gaucher disease so their bodies can break down glucocerebroside. ERT involves receiving intravenous (IV) infusions
- 2) **Substrate reduction therapy (SRT):** SRT is an oral medication that decreases the amount of glucocerebroside that the body makes, reducing excess buildup.

### Note

While you may experience severe symptoms & signs, it is also possible to have no symptoms or signs at all.

### a) Advantages and Disadvantages of Enzyme Replacement Therapy

Advantages of using ERT

- 1) Fewer side effects
- 2) Longer drug history: people prefer taking medications that have been on the market for a longer period of time.
- 3) Wider availability: available for children, adults, pregnant, breastfeeding women.

Disadvantages of taking ERT

- 1) Many people find taking an SRT pill is more convenient
- 2) More invasive: a device installed under the skin for repeat use in delivering IV medications. and the long-term safety of ports over many years of therapy is a potential concern.
- 3) Ups and downs: Some patients feel best right after an infusion and often feel fatigued when they are due for an infusion.

### b) Signs, Symptoms and Testing

Gaucher disease symptoms and signs include:

**Spleen and liver enlargement:** Gaucher cells build up in the spleen and/or liver, these organs become enlarged and painful.

**Low platelet count:** A spleen enlarged by Gaucher disease destroys blood cells too rapidly

**Bleeding and clotting problems:** With fewer platelets, patients with Gaucher disease can have bleeding issues. Low platelets can also result in particularly after dental work, surgery, trauma and delivering a baby.

**Anemia:** Gaucher cells in bone marrow reduce production of blood cells, and the spleen quickly destroys blood cells

**Lungs:** In some cases, glucocerebroside may accumulate in the lungs, causing respiratory problems.

**Bone infarction or avascular necrosis (AVN):** This condition occurs when parts of the bone don't get enough oxygen, causing bone tissue to deteriorate and die.

**Joint pain, arthritis and joint damage:** It is common for patients with Gaucher disease to experience joint pain. Gaucher disease can cause severe arthritis and joint damage, which can be permanent if the disease is untreated.

Testing for Gaucher disease involves a blood test called a beta-glucosidase leukocyte (BGL) test to determine enzyme levels in your body.

Patients with Gaucher disease may be at increased risk of developing other conditions later in life, usually after age 50. These include:

- a) Parkinson disease
- b) Osteoporosis
- c) Some cancer types, including liver cancer and myeloma (a blood cancer)

Gaucher disease is an autosomal recessive disorder. That means a person must receive the Gaucher gene from both parents in order to have the disease.

**c) If a Parent has Gaucher disease?**

If the partner is not having the Gaucher gene: Each child of them will be carriers of Gaucher disease

If carrier of Gaucher gene is the partner then : Each child will have a 50 percent chance of having Gaucher disease and a 50 percent chance of being a carrier.

If the partner has Gaucher disease: Each of children will have Gaucher disease.

**d) Genetic Mutations That Are Severe**

more than 400 genetic mutations are associated with Gaucher disease. Certain genetic mutations can cause more severe symptoms, Here are some factors about genetic mutations associated with Gaucher disease:

Having 2 copies of the L444P mutation causes neurological symptoms and is related to Gaucher disease types 2 and 3.

Patients with 1 copy of an N370S mutations plus another mutation almost certainly will have Gaucher disease type 1.

Patients with 2 copies of the N370S mutation may have a milder form of Gaucher disease

**e) The Note Introduction**

Facts about the govt replies for this disease and some policies implemented for the disease. Also the letters got from the government

**f) From Tamil Nadu Health And Family Welfare (H1) Department**

With reference to RTI, the Madras High court Ordered Formation of Committee Under J. Radhakrishnan (Principal Health Secretary to Government Of Tamil Nadu) and Edwin A. Joe (Chairman, Medical Education Department) To Formulate a policy for these rare diseases and funding for such diseases. We Requested The Details And Given The Information As Below

- 1) Centre For Rare Genetic Disorders was Set Up as per the National Health Policy For Genetic Disorders in March 2018 at Institute of Child Health( Egmore , Chennai) And Madras Medical Collage
- 2) At present three Patients confirmed with Lysosomal Storage Disorders Have Been Referred To Central Technical Committee , New Delhi For Enzyme Replacement Therapy

RTI Application No.: Government Letter no: 42086/H1/2018-1/2( Two Letters)

**g) To Maulana Azad Medical Collage( Government Of NCT of Delhi)**

The high court of Delhi Ordered The Government Of India To formulate a policy for such rare diseases and also formed a committee under Deepak K Tempe( Dean, Maulana Azad Medical Collage ) To give a report on lsd F. No: 150(2066)RTI/MAMC/2018-19

The main points are included in this report as follows :

**h) National Policy For Treatment of Rare Diseases  
Executive summary on rare diseases**

The rare diseases include genetic diseases and degenerative diseases and 80% of rare diseases are genetic in origin and hence disproportionately impact children. The common consideration in the definitions are primarily, disease prevalence and to varying extent-severity and existence of alternative therapeutic options.

**Need For A Policy**

The High Court of Delhi In W.P ( c ) no 4444/2016,7730/2016,7729/2013 directed the Ministry Of Health And Family Welfare to frame a national policy on Treatment of rare diseases

**Immediate Measures**

- 1) Constituting an inter-ministerial consultative committee to coordinate and steer the initiatives of different ministries
- 2) Management of corpus funds and developing technical guideline/criteria for— which rare diseases to fund, to what extent, review of treatment etc..
- 3) Creating a web based application for online application process to access the corpus funds
- 4) Constituting a rare diseases cell within Ministry of Health and Family Welfare, ICMR, and Departments in Ministry of Chemical And Fertilizers respectively

Long Term Measures that ought to be initiated now with deliberate, concrete steps towards their scale up and progressive realization:

- 1) Take measures, legislative or otherwise for encouraging local manufacturing of drugs for rare diseases
- 2) Take legal and other measures to control the prices of drugs for rare diseases

#### **Definitions of rare diseases across jurisdictions**

In the United States rare diseases are defined as a disease or condition that affects fewer than 2,00,000 patients in the country. European Union defines Rare diseases as a life threatening or chronically debilitating condition affecting no more than 5 in 10,000 people. In India we have 72 to 96 million people affected by rare diseases in the country which is a significant number. So far about 450 rare diseases have been recorded in India.

#### **Diagnosis**

According to a recent report it takes patients in the United States an average of 7.6 years and patients in United Kingdom an average of 5.6 years to receive an accurate diagnosis, typically involving as many as physicians

#### **Prohibitive cost**

At present very few pharmaceutical companies are manufacturing drugs for rare diseases globally and there are no domestic manufacturers in India. Due to high cost, the government has not been able to provide these drugs for free. It is estimated that for a child weighing 10 kg the annual cost of treatment for rare diseases is from Rupees 18 Lacks to 1crore 70lakhs .Several countries have through legislation provided incentives to drug manufactures to encourage them to manufacture drugs for rare diseases. The most powerful incentive for drug manufacturers for drug manufacture is the grant of 7 to 10 years of exclusive marketing rights including protection form imports. This means that that the pharmaceutical companies can rice their drugs without fear of competitor.

#### **Committees Appointed by Government of India**

- 1) Committee under Professor V.K Paul AIIMS, New Delhi
- 2) Sub Committee under Prof I . C . Verma Sir Ganga Ram Hospital
- 3) Interdisciplinary Committee under chairpersonship Dr Deepak K Tempe

#### **I C Verma Report**

The committee reviewed the burden and definitions of rare diseases globally as well as in India .it has evaluated the availability and efficiency of treatment and cost of rare disorders of immediate relevance in India

#### **Deepak K Tempe Report**

It stated that the Enzyme Replacement Therapy is very costly and life long and the public health system cannot support it in a cost effective way with its own funds. The annual recurring cost of 1.8-17.0 lacks per Kg of body weight. In Conclusion acknowledging the severity and impact of rare diseases on patients and their families ,the directions of the Hon'ble High Court Of Delhi and the consequent recommendation of the government sub-committee, there is a

need to chalk out a roadmap for facilitating access to treatment for rare diseases.

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