FABRY DISEASE

What is Fabry disease?

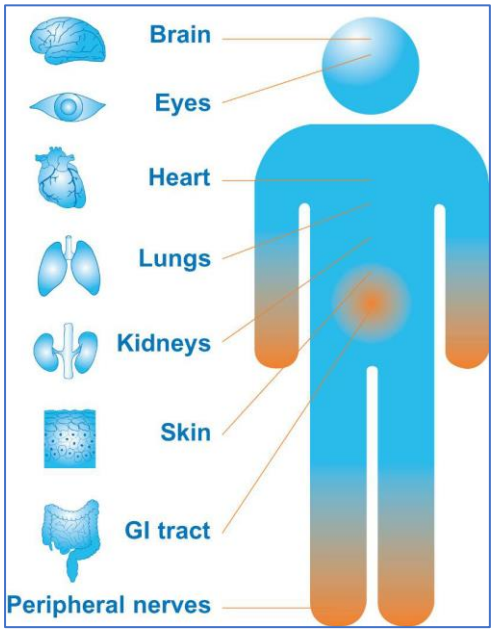
Fabry disease is an X-linked lysosomal disorder that results from a deficiency of the lysosomal enzyme alpha-galactosidase A. This leads to accumulation of harmful levels of glycosphingolipids in different organs of the body.

Why does it occur?

Fabry disease is caused by alterations (mutations) in the GLA gene located on the X-chromosome, which may be inherited from the parents. The GLA gene produces the alpha-galactosidase A enzyme that helps break down fatty substances (glycosphingolipids). This disorder is more commonly seen in boys than girls and males have more severe clinical presentation as compared to females.

What are the manifestations of Fabry disease? Symptoms of classic Fabry disease usually appear during childhood or adolescence. The usual clinical manifestations are shown in the figure & Box below.

Some people with late-onset Fabry disease may begin to manifest symptoms in 3rd-4th decade of life. The first indication of this problem may be kidney failure or heart disease.



1. Painful burning sensation in the hands and feet
2. Raised red or purplish skin lesions (angiokeratomas)
3. Numbness and tingling in the hands or feet
4. Heat or cold intolerance
5. Dizziness
6. Abdominal pain
7. Hearing loss
8. Decreased sweating (hypohidrosis)

How do we diagnose Fabry disease?

• Enzyme assay: This test measures alpha-galactosidase enzyme level in blood. Presence of 1% or lower level indicate Fabry disease.

• Genetic: Females with Fabry disease can have normal levels of alpha-Galactosidase A enzymes. So, the use of DNA testing to identify the variation in GLA gene is preferred.

What are the treatment options available for Fabry disease?

Fabry disease causes multi-organ dysfunction and patients need a comprehensive, multi-disciplinary treatment plan that is individually tailored.

Enzyme replacement therapy (ERT) is the cornerstone for treatment of Fabry disease and synthetic enzyme, produced by recombinant DNA technology, is infused intravenously. This treatment may slow down the build-up of fatty substances with the goal to prevent heart problems, kidney disease and other life-threatening problems.

An oral therapy, was approved in the EU (2017) and in the US (2018) to treat adults with Fabry disease. The drug is a can bind to, stabilize, and enhance the residual enzymatic activity. But only patients with certain specific genetic variations in the GLA gene are eligible for this treatment.

Other later complications (e.g., kidney failure or heart problems) are treated symptomatically after consultation with a physician who is experienced in the care of patients with Fabry disease. Haemodialysis and kidney transplantation may be necessary in cases that have progressed to kidney failure.

Therapeutic product	**Manufacturer**	**Route of Administration**
Agalsidase alpha (Replagal®)	Takeda India	Intravenous
Agalsidase beta (Fabrazyme®)	Sanofi Genzyme	Intravenous
Galafold (Migalastat)	Amicus Therapeutics	Oral

What is the annual cost of therapy?

Does the treatment of Fabry disease affect survival?

Yes! Enzyme replacement therapy (ERT) in patients with Fabry disease may help normalize kidney function, heart function, and blood supply to the brain. Quality of life of patients receiving ERT is improved. Enzyme replacement stabilizes or slows the decline in renal function and reduces heart enlargement

What happens to patients with Fabry disease who remain untreated?

As Fabry disease is a progressive disease, symptoms, and the risk of serious complications, worsen with age in untreated patients. Years of accumulation of fatty substance in Fabry disease can damage blood vessels and lead to life-threatening problems, such as: arrhythmia , heart attacks, enlarged heart, heart failure, kidney failure, nerve damage (peripheral neuropathy) and Strokes, that can shorten life expectancy.

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

Links to patient videos: Dr Shubha's patient