



## Fabry Disease

### Alternative Names

Angiokeratoma, Diffuse  
Anderson-Fabry Disease  
Hereditary Dystopic Lipidosis  
Alpha-Galactosidase A Deficiency  
GLA Deficiency  
Ceramide Trihexosidase Deficiency  
Galactosidase, Alpha  
GLA  
Alpha-Galactosidase A

### WHO International Classification of Diseases

Endocrine, nutritional and metabolic diseases

### OMIM Number

301500

### Mode of Inheritance

X-linked recessive

### Gene Map Locus

Xq22

### Description

Fabry disease is a rare, X-linked lysosomal storage disorder, caused by an inborn deficiency of alpha-galactosidase A. The resulting inability to catabolize glycosphingolipids causes progressive accumulation of globotriasylceramide (Gb3) in endothelial cells, vascular smooth muscle, erector pilori muscles in the skin, myocardium, corneal epithelial cells, and in organs such as the kidney, pancreas, bowel and lung. The resulting symptoms usually appear during childhood and adolescence, followed by disease progression and premature death. The disease manifests primarily in affected homizygous males and to some extent in heterozygous (carrier) females with a mild or severe degree because of random X-chromosomal inactivation.

The clinical features of Fabry disease include corneal and lenticular opacities, acroparesthesias, angiokeratomas, hypohidrosis,

and major end organ disease (with involvement of the kidneys, heart, and brain). Acroparesthesia constitutes the earliest major source of morbidity during the first two decades of life and often remains undiagnosed unless other manifestations or a positive family history provide diagnostic clues. Most affected males have proteinuria and ultimately develop renal failure. The clinical course can also be complicated by cardiac and cerebrovascular disease, which combined with renal failure, lead to early mortality.

### Molecular Genetics

Fabry disease is caused by mutations in the alpha-galactosidase A (GLA) gene. The GLA gene is a 12-kb gene mapped to the long arm (Xq22.1 region) of the X chromosome, and is comprised of seven exons. The native GLA enzyme is a glycoprotein of approximately 101 kD with a homodimeric structure.

Molecular analyses have demonstrated that a wide variety of molecular lesions can cause Fabry disease; approximately 57% of disease alleles are missense mutations, 11% nonsense mutations, 18% partial gene deletions, 6% insertion, and 6% RNA processing defects due to aberrant splicing. Mutations are found in all seven exons, and are mostly confined to a single Fabry disease family.

### Epidemiology in the Arab World

#### United Arab Emirates

Al Talabani et al. (1998) studied the pattern of major congenital malformations in 24,233 consecutive live and stillbirth at Corniche hospital, which is the only maternity hospital in Abu Dhabi, between January 1992 and January 1995. A total of 401 babies (16.6/1,000), including 289 Arabs, were seen with major malformation. Single gene disorders accounted for 24% of the cases of which 3% were due to



sex linked disorders. In their study, Al Talabani et al. (1998) observed a microcephalic baby with ceramide trihexosidase deficiency in a family from the United Arab Emirates. Recurrence was not reported in the family. Al Talabani et al. (1998) concluded that their study was very close to representing the true incidence of congenital abnormalities in the whole United Arab Emirates, as they investigated over 98% of deliveries in Abu Dhabi, the capital of United Arab Emirates.

#### **References**

Al Talabani J, Shubbar AI, Mustafa KE. Major congenital malformations in United Arab Emirates (UAE): need for genetic counselling. *Ann Hum Genet.* 1998; 62 (Pt 5):411-8.

#### **Contributors**

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