



**NEWBORN SCREENING
OFFICE OF HEALTH PROMOTION**
535 W. Jefferson St., 2nd Floor
Springfield, IL 62761
Phone: 217-785-8101
Fax: 217-557-5396

Fabry Disease

Information for Physicians and Other Health Care Professionals

Definition

Fabry disease is an inherited metabolic disorder in which harmful amounts of specific sphingolipids accumulate within lysosomes of cells. Individuals with Fabry disease do not produce enough of one of the enzymes (α -galactosidase) needed to metabolize these sphingolipids. Over time, this excessive storage of lipids in the lysosomes can cause permanent cellular and tissue damage, particularly in the autonomic nervous system, eyes, kidneys, and cardiovascular system.

Clinical Symptoms

Onset of symptoms is usually during childhood or adolescence. Symptoms include burning pain in the extremities, corneal clouding (but no change in vision), gastrointestinal problems such as diarrhea and abdominal pain, angiokeratomas on the lower part of the trunk, and decreased sweating. In adolescence or adult life, clinical findings include progressive renal impairment, cardiomyopathy and stroke. Individuals with milder variants of the disease have later-onset manifestations that are usually limited to the heart (cardiac variants).

Newborn Screening and Definitive Diagnosis

In Illinois, newborn screening for Fabry disease is performed by measuring the activity of α -galactosidase. **If newborn screening results indicate abnormal activity of α -galactosidase, referral should be made to a metabolic disease specialist.**

Treatment

Treatment for Fabry disease is not typically required in infancy or early childhood. Once clinical findings appear, treatment includes medications to treat pain and gastrointestinal distress. Enzyme replacement therapy is available and reduces the rate of progression of renal and cardiovascular disease. The optimal age for initiation of enzyme replacement therapy has not been determined.

Incidence

The precise incidence of Fabry disease is unknown; however, the incidence as determined by other newborn screening programs may be as high as one in 1,500 male births.

Inheritance Patterns

Fabry disease is an X-linked disorder. Males inheriting the X-linked gene mutation are always affected although the disorder is variable in age of onset and severity. Females who inherit the gene for Fabry disease also are affected, although clinical symptoms often develop at a later age and may be less severe than in affected males. Some affected females may remain asymptomatic. Affected females have a 50 percent chance to have a child with Fabry disease, whether male or female. Affected males will not pass the X-linked gene mutation to any of their sons but 100 percent of their daughters will be affected with Fabry disease. **Genetic counseling is recommended for families planning future pregnancies.**

It is anticipated that relatively few affected females will be detected through newborn screening since affected females commonly have higher α -galactosidase levels in blood than males. However, affected females may be detected through testing of family members, once a case is confirmed in a male infant.

Pathophysiology

In Fabry disease, an enzyme defect leads to an abnormal accumulation of sphingolipids within the lysosomes. The buildup of lipids in the lysosomes causes clinical findings of the disease. Much of the pathology of the disorder relates to the accumulation of lipids in the endothelial wall of blood vessels. This in turn leads to progressive renal disease, cardiomyopathy and an increased risk of stroke.

Key Points for Parents

Try to convey to parents that, although further testing is indicated, the child is not at risk of becoming seriously ill in early infancy. Even if the diagnosis of Fabry disease is confirmed, effective treatment is available. It is likely that treatment would not be required in infancy. If the child needs additional testing or diagnostic evaluation, make certain the parents understand the importance of following the pediatrician's and/or specialist's recommendations for additional testing and referrals.

Following Confirmation of Diagnosis

These guidelines should be followed after a diagnosis of Fabry disease has been confirmed:

- 1) Follow up with the child's metabolic disease specialist.
- 2) Recommend genetic counseling services to help the parents understand the complexity surrounding the carrier state and inheritance of this disease.
- 3) Provide parents information on support services, such as the National Fabry Disease Foundation and the local health department.
- 4) Additional information about newborn screening can be found at:
 - Baby's First Test: <http://www.babysfirsttest.org/>
Health Resource and Service Administration (HRSA), Grant no. U36MC16509, Quality Assessment of the Newborn Screening System.
 - National Center for Biotechnology Information: <http://www.ncbi.nlm.nih.gov/gtr/>
National Center for Biotechnology Information, U.S. National Library of Medicine, 8600 Rockville Pike, Bethesda MD, 20894 USA.