Gaucher Disease
Information for Physicians and Other Health Care Professionals

Definition
Gaucher disease is an inherited metabolic disorder in which harmful amounts of a sphingolipid called glucocerebroside accumulate within lysosomes of cells. Individuals with Gaucher disease do not produce enough of one of the enzymes (β-glucosidase or glucocerebrosidase) needed to metabolize glucocerebroside. Over time, this excessive storage in the lysosomes can cause permanent cellular and tissue damage, particularly in the spleen, liver, bone marrow, and rarely, the brain.

Clinical Symptoms
The three forms of Gaucher disease include type I (attenuated, non-neuroneupathic), type II (acute, neuronopathic), and type III (chronic, neuronopathic). The vast majority of patients have type I disease.

In Gaucher type I, the brain is not affected; symptoms are variable in severity and age of onset and may include hepatosplenomegaly, easy bruising due to thrombocytopenia, and fatigue secondary to anemia. Chronic bone pain or acute bone crises also may occur.

Gaucher type II, a very rare disorder, is more severe due to involvement of the nervous system; infants with this type typically have a life expectancy of less than two years. Symptoms include enlarged spleen and liver, which are often present at birth; liver malfunction; bone deformities, pain or crises; severe neurologic complications; and failure to thrive.

Gaucher type III is not as severe as type II; however, the nervous system is involved and lifespan can be significantly decreased.

Newborn Screening and Definitive Diagnosis
In Illinois, newborn screening for Gaucher is performed by determination of the activity of β-glucosidase. If **newborn screening results indicate an abnormal activity of β-glucosidase, referral should be made to a metabolic disease specialist.**

Treatment
Individuals with Gaucher disease are best treated by a team of specialists knowledgeable about the disease, who can offer supportive and symptomatic care. Enzyme replacement therapy is available for Gaucher disease type I. It is not typically instituted until clinical symptoms appear, which may be at any age. Due to the involvement of the brain, individuals with Gaucher disease types II and III may not benefit in the long-term from enzyme replacement therapy. Stem cell transplantation has been accomplished with variable results in patients with type III disease.

Incidence
The incidence of type I Gaucher disease is approximately one in 50,000 births. The incidence in the Ashkenazi Jewish population is one in 1,000 births. Type II Gaucher is a very rare panethnic disease and type III occurs most often in the Northern Swedish population.
Inheritance Patterns
Gaucher disease is inherited in an autosomal recessive pattern. Parents of a child with Gaucher disease are unaffected, healthy carriers of the condition, and have one normal gene and one abnormal gene. With each pregnancy, carrier parents have a 25 percent chance of having a child with Gaucher disease (inheriting two copies of the abnormal gene). Carrier parents have a 50 percent chance of having a child who is an unaffected carrier, and a 25 percent chance of having an unaffected, non-carrier child. These risks would hold true for each pregnancy. Genetic counseling is recommended for families planning future pregnancies.

Pathophysiology
In Gaucher disease, an enzyme defect leads to sphingolipid storage in the lysosomes, primarily in cells of the reticuloendothelial system. The build-up of sphingolipids in the lysosomes causes clinical findings of the disease.

Key Points for Parents
Not all infants identified as having low enzyme activity by newborn screening will turn out to have Gaucher disease. Parents should be reassured that most infants with Gaucher disease will have type I disease, and that effective treatment is available for this disorder. Treatment is rarely required in early childhood. 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 Gaucher 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 Gaucher 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, U.S. National Library of Medicine, 8600 Rockville Pike, Bethesda MD, 20894 USA.