Inheritest℠
CARRIER SCREEN

What is Gaucher Disease?
Gaucher disease is an inherited disease characterized by bone disease, enlargement of the spleen and liver, anemia, and bleeding problems, along with nervous system involvement in a subset of individuals. It involves a deficiency of an enzyme that breaks down a fatty component of cells called glucocerebroside (which is also known as glucosylceramidase). Many of the symptoms associated with Gaucher disease are attributed to the accumulation of glucocerebroside in the liver, spleen, bone marrow, and other organs.[1]

What are the symptoms of Gaucher Disease and what treatment is available?
Gaucher disease is most often classified into three major types that are distinguished by the presence (or absence) and severity of primary neurological symptoms. The disease varies in severity and age of onset, even within types [1,2]:

Type	Typical Age of Onset	Primary Neurological Symptoms?	Severity
Type 1	Childhood to adulthood*	No	Variable
Type 2	Infancy	Yes, severe	Often fatal by early childhood
Type 3	Childhood to early adulthood	Yes, chronic and progressive	Reduced life expectancy; childhood to the 30s

*Symptoms in a subset of individuals can be so mild as to go undetected for many years.

Two additional subtypes are a perinatal-lethal form, which is associated with prenatal complications, skin manifestations, and death before or during infancy, and a cardiovascular form, which is associated with heart and eye issues.[1]

Symptoms of Gaucher disease may include: [2, 3]

- Hepatosplenomegaly (enlargement of the liver and spleen)
- Bone disease, including bone pain, decreased bone density and tendency to fracture
- Anemia and easy bruising or bleeding
- Fatigue
- Lung disease, which may include pulmonary hypertension (high blood pressure in the lungs)
- Primary neurological problems, such as seizures, swallowing problems, eye problems, and difficulties with movement (types 2 or 3)
- Increased risk of Parkinson's disease or parkinsonism (type 1)

Additional symptoms of type 2 may also include[4]:

- Dry, scaly skin or other skin problems
- Limited mental and motor development
- Failure to thrive (poor growth and weight gain)

Treatment for nonneurological symptoms of Gaucher disease may include enzyme replacement therapy or other medications to reduce the amount of glucocerebroside that accumulates in the body. Bone marrow transplantation may benefit individuals with chronic neurological symptoms. Removal of part (or all) of the

spleen may be performed due to the severity of spleen enlargement or bleeding issues. Supportive care for the various types may include blood transfusions for anemia and bleeding, pain control for bone disease, and calcium supplementation to maintain bone density.[2]

Gaucher disease is expected to be included in newborn screening panels in a few states in the US starting in 2012.[5]

How is Gaucher Disease inherited?
Gaucher disease is an autosomal recessive disease caused by mutations in the *GBA* gene.[1] An individual who inherits one gene mutation in the *GBA* gene is a "carrier" and is typically not expected to have related health problems. An individual who inherits two mutations in the *GBA* gene, one from each parent, is expected to be affected with Gaucher disease.

If both members of a couple are carriers, the risk for an affected child is 25% in each pregnancy; therefore, it is especially important that the reproductive partner of a carrier be offered testing.

Who is at risk for Gaucher Disease?
Gaucher disease can occur in individuals of all races and ethnicities. In the Ashkenazi (Eastern European) Jewish population, type 1 occurs more frequently with an estimated carrier frequency of 1 in 15[6] and a calculated disease incidence of approximately 1 in 900.

Having a relative who is a carrier or who is affected can also increase an individual's chance of being a carrier. Consultation with a genetics health professional may be helpful in determining carrier risk and appropriate testing.

What does a positive test result mean?
If a gene mutation is identified, an individual should speak to a physician or genetics health professional about the implications of the result and appropriate testing for the reproductive partner and at-risk family members.

What does a negative test result mean?
A negative result reduces, but does not eliminate, the possibility that an individual carries a gene mutation. The likelihood of being a carrier is also influenced by family history, medical symptoms, and other relevant test results.

Where can I get more information?
- National Gaucher Foundation: www.gaucherdisease.org
- Childrens Gauchers Disease Research Fund: www.childrensgaucher.org
- Gaucher Care: www.gauchercare.com/en/

References
1. Gaucher disease. Genetics Home Reference. Available at: http://ghr.nlm.nih.gov/condition/gaucher-disease Accessed May 9, 2012.
2. Pagon, RA, et al. GeneReviews. Available at: http://www.ncbi.nlm.nih.gov/books/NBK1269/. Accessed February 24, 2012.
3. Bultron G, et al. The risk of Parkinson's disease in type 1 Gaucher disease. *J Inherit Metab Dis*. 2010; 33(2): 167-173.

4. Gupta N, et al. Type 2 Gaucher disease: phenotypic variation and genotypic heterogeneity. *Blood Cells Mol Dis*. 2011; 46(1):75-84.
5. National Newborn Screening report: http://genes-r-s.uthscsa.edu/nbsdisorders.pdf). Accessed March 31, 2012.
6. Scott SA, et al. Experience with Carrier Screening and Prenatal Diagnosis for 16 Ashkenazi Jewish Disease. *Hum Mut*. 2010; 31: 1-11.