



## **Carrier Testing for Genetic Diseases**

The purpose of genetic screening tests is to determine the carrier status of common genetic abnormalities. These common inherited diseases can occur even without a family history. The tests do not detect all carriers of the diseases. If you screen positive as a carrier for any of the conditions, it is recommended that your partner be tested. If your partner is also a carrier, genetic counseling and further diagnostic testing is recommended. If you have already been screened, it is not necessary to test again. These tests are optional.

### **Cystic Fibrosis**

#### **What is cystic fibrosis?**

Cystic fibrosis (CF) is one of the most common genetic disorders in the Caucasian population, affecting approximately 1 in 3,000 people. The most common problems are chronic lung infection and poor absorption of nutrients due to the accumulation of thick mucus in the lungs and pancreas of patients with CF. While much progress has been made in the understanding and treatment of the disease, there is no cure. Symptoms of the disease range from mild to severe. Typical lifespan of an affected person is 37 years, though some may live longer.

#### **What causes cystic fibrosis?**

CF is an autosomal recessive disorder. If both parents are carriers, there is a 1 in 4 (25%) chance to have a child with cystic fibrosis. For an individual to be affected with CF, he or she must inherit one copy of the mutated CF gene from each parent. Individuals having one copy of the mutated gene and one copy of the normal gene are known as carriers. Carriers do not have any symptoms of the disorder. The CF carrier frequency differs among different ethnic groups. The frequency is approximately 1 in 25-30 in individuals of Northern European or Ashkenazi Jewish ancestry, 1 in 50 in Hispanics, 1 in 65 in African Americans and 1 in 50 in Asians.

#### **How can cystic fibrosis be detected?**

A DNA blood test for some of the mutations causing CF is available. The test can be performed on blood specimens or amniotic fluid to detect carriers or affected individuals. Since there are over 900 different mutations within the CF gene, this test cannot detect all the mutations. The detection rate varies among different ethnic groups, with 97% for Ashkenazi Jews, 90% for Caucasians, 68% for Hispanics, 45% for African Americans and 30% for Asians. If you are a carrier of CF and your partner has a negative test and no family history of CF, the chance that your baby will have CF is less than 1%.

#### **Who should be tested for cystic fibrosis?**

Because it is becoming increasingly difficult to assign a single ethnicity, it is reasonable to offer cystic fibrosis carrier screening to all pregnant patients, provided that women are aware of their carrier risk and of the test limitations. CF carrier testing is strongly

recommended for individuals with a family history of CF, spouses of CF carriers and pregnant couples who are of Northern European or Ashkenazi Jewish ancestry. Prenatal diagnosis is recommended when both parents have been found to be carriers, there is a family history of CF and one parent is found to be a carrier, a previous child has been diagnosed with CF or certain ultrasound abnormalities are seen in the fetus.

## **Thalassemia**

Thalassemia includes several different types of anemia. Alpha and beta thalassemias are named for the part of the oxygen carrying protein that is lacking in the hemoglobin of the red blood cells. Thalassemia occurs most frequently in people of Italian, Greek, Middle Eastern, Asian and African descent. The disease can cause the child to have frequent infections and an enlarged spleen, liver and heart. A hemoglobin electrophoresis to diagnose thalassemia is indicated if the MCV value on the routine blood count (CBC) is less than 80.

## **Ashkenazi Jewish Genetic Screening**

### **What is an Ashkenazi Jewish Disease?**

Ashkenazi is the term used to describe Jewish individuals who have ancestors from Eastern Europe. Roughly 90% of the six million Jewish individuals in the United States are of Ashkenazi descent. Similar to most ethnic populations, the Ashkenazi Jewish population has a higher prevalence of certain genetic disorders. Individuals of Jewish descent should be screened for Tay-Sachs disease, Canavan disease and Gaucher's disease.

### **What is Tay-Sachs disease?**

Tay-Sachs disease is a fatal genetic disorder that occurs more frequently in the Ashkenazi (Eastern European) Jewish population. Approximately 1 in 27 Ashkenazi Jewish individuals are carriers of this disease. A baby with Tay-Sachs disease appears normal at birth, but after six months of age, the child progressively develops mental retardation followed by paralysis, blindness, and seizures. Death usually occurs by the age of five. Tay-Sachs disease is caused by a deficiency of an enzyme called Hexaminodase-A. As a result of this deficiency, there is an accumulation of certain substances which damage the nervous system.

### **What is Canavan Disease?**

Canavan disease is a progressive disorder in which the brain and nervous system degenerate. Symptoms of Canavan disease include brain damage, mental retardation, feeding difficulties, blindness, and a large head. There is no treatment, and death usually occurs in the first decade of life.

### **What is Gaucher's Disease?**

Gaucher's Disease is an inborn error of metabolism that results from a specific malfunction in one of the body's individual chemical processes. Although there are at least 34 mutations known to cause Gaucher's Disease, there are 4 genetic mutations, which account for 95% of the Gaucher Disease in the Ashkenazi Jewish population. The carrier rate is 1 in 14 Jewish people of Eastern European ancestry and 1 in 100 of the general population.

### **How are these diseases inherited?**

All three diseases are inherited in an autosomal recessive pattern. For an individual to be affected, he or she must inherit one copy of the abnormal (mutated) gene from each parent. Individuals having one copy of the particular disease-causing gene and one copy of the normal gene are known as carriers. Carriers usually do not have any symptoms of the disorder. If both parents carry the same mutated gene, their child has a 25% chance of having the disease. If only one parent carries the disease gene, their child is not at risk for having that disease but has a 50% chance of being a carrier. If both parents are carriers, the couple should undergo prenatal genetic counseling.

## **Fragile X Syndrome**

### **What is Fragile X Syndrome?**

It is the most common form of inherited mental retardation and accounts for approximately 40% of cases with X-linked mental retardation. Clinical characteristics include mild learning disabilities to severe mental retardation. Approximately one-third of all children diagnosed with fragile X syndrome also have autism and hyperactivity. Almost all males with full mutations have developmental delay or mental retardation. Approximately 50% of females with a full mutation have IQs in the borderline or mentally retarded range; of the remaining 50%, half have learning disabilities.

### **Who should be tested?**

It is recommended that any person with unexplained mental retardation, developmental delay or autism be tested. The American College of Medical Genetics also recommended carrier testing on the basis of a family history of unexplained mental retardation.

### **How common is Fragile X Syndrome?**

The incidence is 1 in 4,000 males and 1 in 8,000 females. The carrier frequency is 1 in 260 and occurs in all ethnic backgrounds. If the test shows that you are a carrier of fragile X, your partner does not need testing because this disease is inherited only through the woman. If a mother is a carrier, there is a 50% chance to have a child with fragile X syndrome. Therefore, the next step is for you to consider diagnostic testing by amniocentesis or chorionic villi sampling (CVS) to determine if your baby is affected.

### **Where can I find out more information?**

For more information see: [www.fragilex.org/](http://www.fragilex.org/) or [http://www.cdc.gov/genomics/hugenet/factsheets/FS\\_FragileX.htm](http://www.cdc.gov/genomics/hugenet/factsheets/FS_FragileX.htm)

## **Spinal Muscular Atrophy (SMA)**

### **What is Spinal Muscular Atrophy (SMA)?**

SMA is an autosomal recessive condition that causes progressive degeneration of the lower motor neurons, muscle weakness and, in the most common type, respiratory failure by age two. Muscles responsible for crawling, walking, swallowing and head and neck control are the most severely affected. It is variable in severity and age of onset and does not affect intelligence. There is no cure or treatment.

### **What is the carrier frequency?**

The frequency varies by ethnicity and ranges from 1 in 35 to 1 in 117 in the United States. The incidence is 1 in 6,000 to 10,000

**What is the carrier detection rate?**

Caucasian: 95%, Ashkenazi Jewish: 90%, African American: 71%, Hispanic: 91%, Asian: 93%.

**Sickle Cell Disease****What is sickle cell anemia?**

Sickle cell anemia is an inherited disorder that affects hemoglobin, a protein that enables red blood cells to carry oxygen to all parts of the body. The disorder produces abnormal hemoglobin, which causes the red blood cells to become crescent or sickle shaped.

Normal red blood cells are round and move through blood vessels in the body to deliver oxygen. Sickle red blood cells become hard, sticky and have difficulty passing through the small blood vessels. When these hard, pointed red cells go through capillaries, they clog the flow and break apart. This causes pain, damage and anemia.

**What is sickle cell trait?**

Sickle cell trait is seen in a person who carries one sickle hemoglobin producing gene inherited from their parents and one normal hemoglobin gene. Normal hemoglobin is called type A. Sickle hemoglobin is called hemoglobin AS on the hemoglobin electrophoresis. This combination of one normal and one abnormal gene will NOT cause sickle cell disease.

**How do you get sickle cell anemia or trait?**

You inherit the abnormal hemoglobin from your parents, who may be carriers with sickle cell trait or parents with sickle cell disease. You cannot catch it. You are born with the sickle cell hemoglobin and it is present for life. If you inherit only one sickle gene, you have sickle cell trait. If you inherit two sickle cell genes you have sickle cell disease.

**How common is sickle cell anemia?**

It is most common in people whose ancestors come from sub-Saharan Africa, Spanish-speaking regions of Central and South America, Saudi Arabia, India and the Mediterranean. The disease occurs in approximately 1 in every 500 African American births and 1 in every 1,200 Hispanic-American births. One in 12 African Americans carries the sickle cell trait.