

# Genetic Testing

## Expanded AFP Test (Quad Marker Testing)

### What is the expanded AFP (Quad Marker Screening)?

The expanded AFP test is a screening test for pregnant women during the second trimester (between 15 and 20 weeks) of pregnancy who did not do a nuchal screening test. The test will help detect pregnancies at an increased risk for Down syndrome, Trisomy 18, and neural tube defects or abdominal wall defects. Occasionally, the test may also detect other chromosome abnormalities. This is not a diagnostic test; it simply indicates further testing may be advised. You will be asked to sign a consent stating your desire to take the test.

### What does the screening test measure?

This test measures four biochemical substances produced by fetal and placental tissues: AFP (alpha-fetoprotein), hCG (human chorionic gonadotropin), and uE3 (unconjugated estriol) and INH (dimeric inhibin-A).

### What is Down syndrome?

Down syndrome is a chromosome abnormality that causes mental retardation and certain types of birth defects. It is due to an extra copy of chromosome 21, so that, three copies (trisomy) versus the normal two copies of this particular chromosome are present. Down syndrome affects approximately one in every 800 newborns. The chance of having a pregnancy affected with Down syndrome increases with increased maternal age. Women age 35 years and older are more likely to have a child affected with Down syndrome.

### What is Trisomy 18?

Trisomy 18 is a fatal chromosome abnormality that causes multiple birth defects and profound mental retardation. Few Trisomy 18 infants survive into childhood. Trisomy 18 results when the fetus has three, instead of the normal two, copies of chromosome 18. Like Down syndrome, the chance of an increased risk for fetal abnormality is determined by the test and then genetic counseling, ultrasound examination, and when needed, amniocentesis will aid in the diagnosis. Having a pregnancy affected with Trisomy 18 increases with increased maternal age.

### What is a neural tube defect?

A neural tube defect, such as spina bifida or anencephaly, results from a failure of complete closure of the neural tube during early fetal development. Spina bifida is an opening on the spine that exposes nerve tissue and can lead to paralysis and mental retardation. Anencephaly is an incomplete development of the brain that usually results in death.

### What if the test result shows an increased risk?

A positive screening test result does not mean an abnormality is present in the fetus. Often, incorrect dating of fetal age is the reason for a positive result and invasive testing may not be necessary. However, when an increased risk for fetal abnormality is determined, genetic counseling, ultrasound examination, and when needed, amniocentesis will aid in the diagnosis. If this testing is necessary, your physician will contact you and ask you to schedule an appointment with Obstetrix Medical Group (371-7111).

### What does a negative test mean?

A negative result indicates the risk that the fetus has Down syndrome or Trisomy 18 is not greater than that of a 35-year-old woman, and the risk for neural tube defects is not increased compared to that of the general population. However, a negative result does not completely exclude the possibility that the fetus may have these abnormalities or other congenital abnormalities. The test detects approximately 75% of Down syndrome and trisomy 18 pregnancies, 80% of spina bifida, and 95% of anencephaly.

### **How accurate is the test?**

The test is not completely accurate. A baby may have a birth defect even though AFP levels are normal. A baby may be quite normal even though AFP levels are abnormal. For every 1,000 women tested, about 50 have an abnormal test result. Of these 50, only one or two with high AFP levels are carrying babies with a problem.

### **Who should have this test?**

All pregnant women should be offered AFP screening. If you are 35 and are having an amniocentesis, the blood test is not necessary as the amniotic fluid will be checked. If you did a nuchal screening test and are under 35, you should take the AFP only test which checks for spina bifida, and not the expanded AFP test (which again looks for chemical evidence of Down syndrome, but is less accurate than the NT test).

### **What are the benefits to taking the test?**

Most often, the test provides reassurance that your baby probably does not have a serious defect. Abnormal results can help you and your doctor manage your pregnancy more effectively. For example, if the test detects twins, your doctor can start providing the special prenatal care you need for a multiple pregnancy. When a brain or spinal defect is diagnosed, you and your partner can decide whether you want to continue the pregnancy. If you decide to continue the pregnancy, your doctor will be able to plan your delivery and optimize the outcome of the pregnancy for you and your baby.

## **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 food 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. At the present time, the median life expectancy is about 30 years.

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

CF is caused by mutations in the CFTR gene. CF is an autosomal recessive disorder. 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. When both parents are carriers for a mutation, there is a 1 in 4 chance that each pregnancy will be affected with CF.

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

A DNA laboratory test for the mutations causing CF is available. This is a blood test. Results are usually ready within a week. The test can be performed on blood specimens to detect carriers or affected individuals. It can also be performed on prenatal amniotic fluid specimens to detect affected

fetuses. 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.

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

CF carrier testing should be considered 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.

### **What if the test does not show a CF mutation?**

If your test does not show a mutation in the CFTR gene, the chance that you are a CF carrier is low. That chance will depend on your ethnic background and family history. However, no CF test can find all the mutations of the CFTR gene.

### **What if the test shows a CF mutation?**

If your test shows a mutation in the CFTR gene, then you are a CF carrier. The test has 99% accuracy. Being a CF carrier will not affect your own health. If your test is positive, your partner should then be tested. Special counseling and testing should be considered if both you and your partner are carriers of CF mutation.

## **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 Hex-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 Disease, there are 4 genetic mutations which account for 95% of the Gaucher's 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/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.

### **How do I get tested?**

A simple blood test can be performed from either parent to determine if he/she is a carrier of these diseases. If both parents are carriers, then prenatal testing can be performed to determine whether or not the fetus is affected.

## **Sickle Cell Anemia**

### **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 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, called sickle cell trait, is the presence of hemoglobin AS on the hemoglobin electrophoresis. This 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 can not 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.

### **How can I be tested?**

A simple blood test called the hemoglobin electrophoresis can be requested by your doctor. If you are found to have sickle cell trait, your partner should also be tested to determine if the baby is at risk for sickle cell disease.

## **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. 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. It is not currently recommended to test all women who are pregnant. For more information see:

<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).