

IF YOU HAVE QUESTIONS ABOUT PRENATAL SCREENING or would like more information, contact your obstetrician or one of our genetic counselors. Please note that not all genetic screening tests are covered by insurance. Be sure to check with your insurance carrier about your coverage for first trimester screening and other tests. To make a prenatal or genetic counseling appointment with a Penn Ob/Gyn Care physician, please call, 1-800-789-PENN.

LOCATIONS

Hospital of the University of Pennsylvania
Division of Reproductive Genetics
3400 Spruce Street
Philadelphia, PA 19104

Chestnut Hill Hospital
Department of Obstetrics and Gynecology
8811 Germantown Avenue
Philadelphia, PA 19118

Pennsylvania Hospital
Prenatal Diagnosis at Pennsylvania Hospital
800 Spruce Street
Philadelphia, PA 19107

The Pavilion of Voorhees
2301 Evesham Road
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Voorhees, NJ 08043

Our physicians and counselors provide evaluation and consultation at various other locations throughout the Philadelphia region and New Jersey. For more information or to schedule an appointment, please call 1-800-789-PENN (7366) or visit pennhealth.com.

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Penn Ob/Gyn Care

PRENATAL Genetic Testing Program at Penn



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ABOUT PRENATAL GENETIC SCREENING

Pregnancy and childbirth can be one of the most exciting times in a woman's life, but potential parents often have concerns about the health of their unborn child. Genetic counseling and prenatal diagnosis can help answer some key questions and provide expectant parents with information about their pregnancy.

Couples who are thinking about having a child may consider genetic counseling before conception to determine if they have an increased risk for having a child with a birth defect, Down syndrome, or other inherited genetic conditions. Genetic counseling is also recommended for individuals or couples when there is a family history of birth defects, mental retardation, or genetic disorders such as muscular dystrophy, cystic fibrosis or hemophilia. Others may use genetic counseling and prenatal diagnosis after they conceive to evaluate the condition of the fetus.

While screening tests can determine if your risk is low or high, they cannot be 100 percent accurate. On the other hand, diagnostic tests are designed to detect a particular problem with a high degree of accuracy.

What is a genetic counselor?

Genetic counselors work closely with physicians. They are health care professionals with master's degrees and are certified by the American Board of Genetic Counseling.

A counselor will ask you detailed questions about your family history to determine if your child is at risk for inheriting a genetic condition or birth defect. A genetic counselor coordinates prenatal screening tests and will help you interpret the results of the testing so that you can make educated decisions about your pregnancy.

Before you decide to have or not have genetic counseling and testing, you should read the information within this brochure. If you think that you may have a special risk for having a child with birth defects or a genetic disorder, tell your doctor or call one of our genetic counselors.



Prenatal Genetic Screening Tests

Screening tests can be performed prior to conception or early in pregnancy to determine whether you and your partner have an increased risk of having a child with a genetic disorder. For example, testing for Down syndrome and neural tube defects can only be done during pregnancy. Many other genetic tests are available before or during pregnancy to couples who have a family history of an inherited disorder, mental retardation or birth defects.

The decision to have a screening test is personal and voluntary. A number of prenatal genetic screening tests are available (see table below). Your health care provider may offer all or some of the following tests based upon your health history, ancestry/race, and/or age.

GENETIC SCREENING TESTS

Timeline	Condition
PRECONCEPTION OR LESS THAN 20 WEEKS GESTATION	<i>Canavan Disease Cystic Fibrosis Familial Dysautonomia Sickle Cell Tay Sachs* Thalassemia</i>
10 TO 13 WEEKS GESTATION	<i>Down Syndrome Trisomy 18</i>
15 TO 20 WEEKS GESTATION	<i>Down Syndrome Trisomy 18 Neural Tube Defects</i>

**Testing is also available for Gaucher disease, Bloom syndrome, Niemann-Pick disease, Fanconi Anemia and Mucopolidosis Type IV. See the glossary on page 11 for further details on these conditions.*



PRENATAL DIAGNOSTIC TESTS

In contrast to screening tests that determine a level of risk that problems *may* occur, diagnostic tests are designed to determine if a problem is present. Amniocentesis and chorionic villus sampling (CVS) are diagnostic tests. Some parents choose amniocentesis or CVS to determine if a specific inherited or genetic disorder is present in their baby. These tests are also performed to ascertain whether the fetus has a chromosome abnormality such as Down syndrome.

A diagnostic test may be offered to you after the screening test or as part of the evaluation of suspected problems such as a fetal birth defect. Late in the pregnancy, amniocentesis is performed to determine if the fetal lungs have matured. Both tests are relatively safe. While amniocentesis and CVS are more invasive than a screening test, they are very safe and accurate procedures.

How is amniocentesis performed?

Amniocentesis is performed by inserting a long thin needle through the abdomen and into the uterus to remove a small amount of the amniotic fluid surrounding the fetus. A variety of tests can be performed on the cells in the fluid and the fluid itself. The fetal chromosomes can be evaluated to determine if the fetus has Down syndrome or Trisomy 18. Specific genetic tests may be requested by your doctor depending on your history and the results of the carrier screening tests.

How is CVS performed?

CVS is done by inserting a long thin needle through the abdomen and into the placenta to remove a sample of placental tissue fragments. Alternatively, a small catheter is inserted through the vagina and the cervix into the placenta to remove a sample.

What if amniocentesis or CVS shows that my baby will have a birth defect?

If your baby is found to have a serious birth defect, you will receive counseling about what this will mean for the infant, you and your family. The genetic counselor and your doctor will provide you with information about what options are available during and after pregnancy.



CYSTIC FIBROSIS CARRIER SCREENING

What is cystic fibrosis?

Cystic fibrosis is a genetic disease that causes respiratory and digestive problems and affects one in every 3,300 people in the United States. Treatments are available but in general, people with cystic fibrosis have a shortened life span.

What is the purpose of cystic fibrosis carrier screening?

Cystic fibrosis carrier screening determines whether or not individuals carry a mutation in one of their cystic fibrosis genes and if they are at increased risk of having a child affected with cystic fibrosis. The test requires a simple blood sample and results are usually ready within seven to 14 days.

What if both my partner and I are carriers?

If both partners are cystic fibrosis carriers, there is a 25 percent chance with any pregnancy of having a child with cystic fibrosis. Prenatal testing by chorionic villus sampling or amniocentesis can be performed to determine if the unborn baby has inherited the abnormal cystic fibrosis genes from both parents. Testing the baby after birth is also an option if a couple does not want prenatal diagnosis.

Will the cystic fibrosis carrier screen detect all cystic fibrosis carriers?

No. There are rare abnormalities (mutations) in the cystic fibrosis gene that the current screening cannot detect. Negative results from cystic fibrosis carrier screening significantly lowers, but does not completely eliminate the risk of being a carrier.



GENETIC DISEASES IN ASHKENAZI JEWISH (EASTERN/CENTRAL EUROPEAN) HERITAGE

What is the purpose of genetic screening based on race/ethnicity?

A number of genetic disorders occur more frequently in certain ethnic populations. It is estimated that in the Ashkenazi Jewish population, one in six individuals is a carrier for one of the following genetic conditions:

- Bloom Syndrome
- Canavan Disease
- Cystic Fibrosis
- Familial Dysautonomia
- Fanconi Anemia
- Gaucher Disease
- Mucopolysaccharidosis Type IV
- Niemann-Pick Disease
- Tay-Sachs Disease

Some of these diseases are severe and could result in the early death of a child. Carrier screening is available for all of these diseases with a simple blood test.

What if we are both carriers?

If you are both carriers of a gene for the same disease there is a 25 percent chance with any pregnancy of having a child affected by it.



SICKLE CELL AND OTHER HEMOGLOBINOPATHIES

What are hemoglobinopathies?

Hemoglobin is a protein found in red blood cells that carries oxygen throughout the body. Hemoglobinopathies are a group of disorders that affect red blood cells. Common types of hemoglobinopathies include, sickle cell anemia, hemoglobin SC disease, sickle beta thalassemia, and alpha thalassemia.

What is sickle cell anemia?

Sickle cell anemia occurs when an abnormal form of hemoglobin is produced. Instead of easily moving through the bloodstream, sickle cells can clog blood vessels and deprive the body's tissues and organs of the oxygen they need to stay healthy.

Who is a carrier of sickle cell disease?

Sickle cell disease affects 1 in 375 African Americans. It is estimated that 1 in 12 African Americans carry sickle cell trait. The disease can also affect those of Mediterranean, Caribbean, South and Central American, Arabian, or East Indian ancestry. A blood test called hemoglobin electrophoresis is done to determine if you are a carrier of sickle cell trait.

People who have sickle cell trait do not have sickle cell anemia or symptoms of the disease, but they can pass the sickle cell gene to their own children. When both parents have sickle cell trait, there is a 25 percent chance with each pregnancy that their child will have sickle cell disease.

How is thalassemia diagnosed?

Thalassemia is a common genetic disease that causes serious anemia. To diagnose thalassemia and other hemoglobinopathies, doctors use a blood test called a complete blood count (CBC) and a hemoglobin electrophoresis. The primary purpose of hemoglobinopathy screening is to identify couples at risk for having children with this severe form of anemia and to offer couples who are at 25 percent risk the option of prenatal diagnosis.



DOWN SYNDROME SCREENING

Why should I consider having a screening test for Down syndrome?

Down syndrome occurs in approximately 1 in 800 births. The older a woman is at the time of her delivery, the greater the chance that she will have a baby with Down syndrome. However, a woman at any age can have a baby with Down syndrome. There are several types of screening tests available that are used to assess your risk for having a baby with Down syndrome.

Should I have this test if there has never been anyone in our families with Down syndrome?

In over 95 percent of the families in which a child is born with Down syndrome, there has never been anyone else in the family with the condition. A very small percentage of Down syndrome is inherited in families. If you or your partner have a relative with Down syndrome, please let your doctor or genetic counselor know prior to having this test.

If I am over 35 years of age, should I consider having a screening test first to identify my risk of having a child with Down syndrome before deciding about an amniocentesis or CVS?

Some pregnant women over 35 years of age plan to have a diagnostic test such as CVS or amniocentesis. However, other patients find that the screening result helps them to make a decision regarding whether CVS or amniocentesis is the right choice for them. These options require more extensive counseling by our genetic counselors before you make this important decision. If you will be over 35 years of age when you deliver, please contact one of our genetic counselors for more information.

First Trimester Screening for Down Syndrome

First trimester screening for Down syndrome is available to all pregnant women between gestational weeks 10 and 13. This screening method is not a diagnostic test — it was developed to inform physicians and their patients earlier in the pregnancy whether their baby is at increased risk for having Down syndrome or Trisomy 18.



How is the first trimester screening test performed?

The first trimester screening process involves the following:

- **Ultrasound**

The ultrasound is performed to measure nuchal translucency (NT), or the area of fluid at the back of the baby's neck. The accumulation of fluid is normal; however, if an increased amount is found, this may indicate an increased risk for chromosome abnormalities, congenital heart defects and other genetic disorders. A fetal echocardiogram may be recommended if the NT measurement is increased.

- **Blood test**

The blood test measures two levels of proteins, hCG and PAPP-A, which are normally found in pregnant women.

The levels of hCG, PAPP-A, and the NT measurement are combined with the age of the mother to assess her risk for having an infant with Down syndrome and Trisomy 18.

What are the advantages of first trimester screening?

If the results of the first trimester screening show a low risk, this will help reduce the mother's anxiety earlier in the pregnancy. A low risk result only indicates that the risk of having a child with Down syndrome or Trisomy 18 is reduced.

If results of screening show an increased risk for Down syndrome, prenatal diagnosis by chorionic villus sampling (CVS) at 11 to 13 weeks, or by an amniocentesis in the second trimester (after 15 weeks) can be offered to determine if the fetus is affected.

Determining problems earlier in the pregnancy allows women to prepare for a child with health problems. If the mother decides to terminate the pregnancy, she can do so earlier with the utmost privacy and confidentiality since her pregnancy may not yet be visible to other people.

How accurate is first trimester screening?

The first trimester detection rates for Down syndrome are 80 to 85 percent accurate. A negative screening test is usually reassuring. It is important to understand that screening tests will not detect all cases of Down syndrome. Therefore, it is possible that a woman with a screen result that shows a low risk can still give birth to a child with Down syndrome.

Screening tests can also give false positive results. A false positive result (showing an increased risk) does not mean that your baby definitely has Down syndrome, but indicates that you may wish to have further testing.

**Second Trimester Screening for Down Syndrome
(15 to 20 weeks gestation)**

An **integrated screening test** is a combination of first and second trimester screening. This offers the highest detection rate (90 to 95 percent) for Down syndrome. Women who are found by the test to have a higher risk of having a child with Down syndrome have the option of amniocentesis to determine if the fetus is affected.

Ultrasound in the second trimester is a less reliable screening test for Down syndrome. However, if an abnormality is seen, your physician may offer a diagnostic test such as amniocentesis.

Screening for Down syndrome in the second trimester (15 to 20 weeks) is also available by a blood test. The blood test, called the **Multiple Marker Screen (MMS)**, measures four proteins and uses the levels to determine your risk for having a child with Down syndrome, Trisomy 18 and neural tube defects (spina bifida and anencephaly).



The four specific substances measured in the mother's blood originate from the fetus, the placental tissue, or a combination of both. These substances are called alpha fetoprotein (AFP), human chorionic gonadotropin (hCG), unconjugated estriol (uE3), and inhibin A. The test detects approximately 80 percent of Down syndrome pregnancies

What if the MMS screening test shows that my risk for Down syndrome is increased?

If your test results show an increased risk, then you will be counseled by your doctor and/or one of our genetic counselors about the results.

The first step is to have an ultrasound examination. Sometimes the blood test results are higher or lower than we expect simply because your pregnancy is not quite as far along or is more advanced than we calculated by your last menstrual period. In this case, the expected date of your delivery and the interpretation of your test may be changed after the ultrasound scan. If your risk for Down syndrome is still increased, you may decide to have an amniocentesis to test for Down syndrome in the fetus.



NEURAL TUBE DEFECT SCREENING

Why should I consider having this test?

Measuring AFP level by a blood test as part of the MMS test also checks for birth defects known as **spina bifida** (open spine deformity) and anencephaly (absent skull). One out of every 1,000 babies in the U.S. are born with these defects. About 80 percent of the time when a woman is carrying a child with spina bifida or anencephaly, her blood test will show a higher than normal AFP level.

Should I have this test if there has never been anyone in our families with spina bifida or anencephaly?

In 90 to 95 percent of the cases in which a child is born with spina bifida or anencephaly, there has never been anyone else in the family with this problem.

What if my partner or I have a relative with spina bifida or anencephaly?

A family history of spina bifida, anencephaly or other spinal cord problems may indicate a higher than expected risk. Our genetic counselors can help determine what your risk is and what type of test would be best for your situation.

If my blood test shows a high level of AFP, does that mean that my child will have spina bifida or anencephaly?

No, not necessarily. There are many other reasons why the AFP level may be higher than normal in a woman's blood. In fact, most women with a higher than expected level of AFP will have normal babies. Sometimes the AFP blood test may be repeated and this result may show a normal level. An ultrasound often explains why the AFP level is high. For example, pregnancy may be further along than realized, or the woman may be carrying twins. Ultrasound can detect about 90 percent of neural tube defects.



What if my blood test shows a high level of AFP and the ultrasound does not show a reason for this: does this mean spina bifida?

No, not necessarily. Once again, most women in this situation have normal pregnancies. However, amniocentesis may be suggested to measure AFP in the amniotic fluid since this is a very accurate way to determine if the fetus has spina bifida. Patients with elevated blood AFP levels that are unexplained have an increased risk for complications later in pregnancy and are watched more carefully by their doctors in the third trimester.

What if you find that my baby has spina bifida or some other birth defect?

In cases such as this, our genetics staff will help explain the results of the test as well as discuss all possible options with you, including delivery and raising a child with special needs.



GLOSSARY

Genetic Conditions

Bloom Syndrome - Is characterized by short stature, sun-sensitive facial skin lesions, and an increased susceptibility to infections. Individuals have a higher incidence of leukemia and certain cancers. Approximately 1 in 100 Ashkenazi Jews is a carrier of this condition.

Canavan Disease - Children with this condition develop normally until age two to four months, followed by progressive loss of previously attained skills. Most children with this disease die by the age of five. An estimated 1 in 40 Ashkenazi Jews is a carrier for this disease.

Cystic Fibrosis - Is a serious, life-threatening disease in children. It affects various body systems by producing abnormally thick secretions that can obstruct the pancreas, intestines, bile ducts, and air passages in the lungs. The carrier rate among all Caucasian individuals is approximately 1 in 25.

Down Syndrome - Also called "trisomy 21," occurs when there is an extra chromosome 21 present in cells of the fetus. A child with an extra chromosome 21 will have mental retardation and the characteristic appearance of Down syndrome. About 40 percent of children with Down syndrome are also born with serious heart problems. Down syndrome occurs in approximately 1 in 800 births. The older a woman is at the time of her delivery, the greater the chance that she will have a baby with Down syndrome.

Familial Dysautonomia - A disease that causes the autonomic and sensory nervous systems to malfunction affecting the regulation of body temperature, blood pressure, stress response, normal swallowing and digestion. An estimated 1 in 30 Ashkenazi Jews is a carrier of this condition.

Fanconi Anemia - A disease associated with short stature, bone marrow failure and a predisposition to leukemia and other cancers. Some children may have learning difficulties or mental retardation. Approximately 1 in 89 Ashkenazi Jews is a carrier for this condition.

Gaucher Disease - A condition that varies in age of onset and in the progression of symptoms. The initial symptoms include a painful, enlarged and overactive spleen, anemia and low white blood cell count. Bone deterioration is a major cause of pain and disability. Approximately 1 in 14 Ashkenazi Jews is a carrier of this condition. Treatment is available.

Mucopolipidosis IV - Is caused by the accumulation of specific harmful substances throughout the body. Individuals with this condition experience varying levels of motor and mental retardation, with developmental delays often manifesting themselves as early as the first year of life. Other symptoms can affect the eyes, such as corneal clouding, and retinal degeneration. Approximately 1 in 100 Ashkenazi Jews is a carrier of this condition.

Niemann-Pick Disease - A condition in which a harmful amount of a fatty substance accumulates in different parts of the body. A progressive neurodegenerative disorder that leads to death by three years of age. The carrier rate in the Ashkenazi Jewish population is approximately 1 in 90.

Neural Tube Defects: Spina Bifida - Is a neural tube defect in which the bones of the spine do not completely form, and the spinal canal is incomplete. Anencephaly is a severe and usually fatal defect that occurs when the skull and brain fail to develop.

Sickle Cell Anemia - Occurs when an abnormal form of hemoglobin is produced. Instead of easily moving through the bloodstream, sickle cells can clog blood vessels and deprive the body's tissues and organs of the oxygen they need to stay healthy. Sickle cell disease affects 1 in 375 African-Americans and more than 1 in 50,000 Americans.

Tay-Sachs Disease - Children with Tay-Sachs develop normally until about four to six months of age when the central nervous system begins to degenerate. Individuals with this condition lack an enzyme called hexosaminidase. The child loses all motor skills and becomes blind, deaf and unresponsive. Death usually occurs by the age of four. The carrier rate in the Ashkenazi Jewish population is approximately 1 in 25.

Trisomy 18 Syndrome - Caused by the presence of an extra number 18 chromosome, which leads to multiple abnormalities. Many of these abnormalities make it hard for infants to live longer than a few months. Trisomy 18 syndrome occurs in approximately 1 in 6,000 live born infants.

