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Carrier Screening in Pregnancy for Common Genetic Diseases

Cystic Fibrosis, Spinal Muscular Atrophy, and Fragile X are a few common serious disorders that can occur even without a family history. These three tests are one time only simple blood tests that screen to determine if you are a carrier of the specific gene. A carrier is a person who has a gene that increases the risk to have children with a specific genetic disease. People do not know they are carriers until they have a blood test or an affected child. A negative test result significantly lowers, but does not completely eliminate the risk of being a carrier. Carrier testing is not able to detect all the genetic abnormalities that cause a particular disease.

These tests can be done either when you are planning a pregnancy or after you have become pregnant. The details of each genetic disease is listed below and are seen in all ethnicities and considered the most common. For individuals of Jewish Ashkenazi descent, it is recommended that carrier screening for Tay-Sachs disease, Canavan disease and Cystic Fibrosis are part of routine obstetric care. Details of the frequent genetic diseases among individuals of Jewish Ashkenazi ancestry are explained on the sheet attached.

Cystic Fibrosis (the most common inherited disease of children and young adults): CF is a disorder of mucus production and produces abnormally thick mucus leading to life threatening lung infections, digestion problems, poor growth and more. Symptoms range from mild to severe. The carrier frequency is 1 in 24 to 1 in 97 and both parents need to be carriers for a child to be affected (25% chance). One in 3500 children born are affected. *Recommended follow up to a positive result: test partner.*

Spinal Muscular Atrophy (SMA) (the most common inherited cause of early childhood death): SMA is a progressive degeneration of lower motor neurons. Muscle weakness is the most common type with respiratory failure by the age of 2 years old. Muscles responsible for crawling, walking, swallowing and head and neck control are most severely affected. The carrier frequency is 1 in 47 to 1 in 42 in the US and both parents need to be carriers for a child to be affected (25% chance). One in 11,000 children are affected. *Recommended follow up to a positive result: test partner.*

Fragile X Syndrome (the most common inherited cause of developmental delays): Unlike CF and SMA, this is an x-linked genetic disease and only carried in the mom. Unfortunately, 1 in 250 females are carriers and a child has a 50% chance of being affected if this is the case. 1 in 4000 boys are affected with Fragile X and 1 in 8000 girls are affected. Approximately 1/3 of all children born with Fragile X also have autism and hyperactivity. *Recommended follow up to a positive result: genetic counseling and prenatal diagnosis.*

Ashkenazi Jewish Descent: Studies have shown that there are certain diseases which are more common in the Ashkenazi Jewish population. The American College of Medical Genetics has recommended additional carrier screening for Tay-Sachs disease, Cystic Fibrosis, and Familial Dysautonomia. The advantages to screening programs are numerous, having aided in decreasing the incidence of Tay-Sachs disease to less than 10%. There are additional diseases which are less common, but also of concern within the Ashkenazi Jewish population. They include the following: Fanconi Anemia Group C, Niemann-Pick disease type A, Bloom Syndrome, Canavan disease, Gaucher disease, and Mucolipidosis IV. Please refer to the Table 1 below for a brief description of each of the diseases listed above.

Table 1. Autosomal Recessive diseases within the Ashkenazi Jewish population

Tay-Sachs disease:	Caused by a deficiency in an enzyme, this disease is characterized by loss of neurological function. The disease becomes progressively worse with each year of life. Though infants are usually without noticeable abnormalities at birth, they develop worsening weakness and loss of motor skills. They may also develop blindness, spastic muscle movements, and seizures. There is a 2-5 year life expectancy.	**Familial Dysautonomia:**	Also known as Riley-Day syndrome, this disease is characterized by progressive worsening of the neurological system. Neonates have increasing difficulty feeding, swallowing, and most develop gastroesophageal reflux disease. Some develop chronic lung disease. They are also oftentimes plagued with abnormal pain and temperature sensitivity in addition to abrupt, drastic changes in blood pressure.
Fanconi Anemia Group C:	A disease resulting from increased DNA damage. It is characterized by numerous clinical features, including decreased number of blood cells throughout the body, multiple congenital anomalies, mental retardation, increased risk of leukemia, and other cancers. The average age of survival is 8-12 years.	**Niemann-Pick disease type A:**	Resulting from an abnormality in enzyme storage, this disorder is characterized by feeding difficulty, enlarged abdominal organs such as the liver and spleen, abnormal motor movements, and progressively worsening neurological function. This, ultimately, leads to death between 3-5 years of age.
Bloom Syndrome:	A disease which results from the abnormal breakage and exchange of chromosomes. Those affected tend to be of small stature, have issues with infertility, immunodeficiency, possible late onset of non-insulin dependent diabetes mellitus, as well as mental retardation and delayed intellectual ability. The mean age of death is 28.	**Canavan disease:**	With most children dying within the first year of life, this disease affects the central nervous system heavily. It is caused by progressive degeneration of the brain. It is characterized by seizures, blindness, poor muscle tones, blindness, gastroesophageal reflux disease, and difficulty sleeping. Life expectancy is 2-3 years.
Gaucher disease:	A disease resulting from abnormalities with enzyme storage throughout the body. Clinical manifestations include anemia which causes fatigue, nosebleeds, easy bruising, and enlarged abdominal organs such as the liver or spleen. This is known to be one of the most prevalent among the Ashkenazi Jewish population.	**Mucolipidosis IV:**	This disease is also caused by the abnormal storage of enzymes throughout the body. It is characterized by progressive neurological degeneration, growth and motor skill stagnation. Though most experience a normal life expectancy, their quality of life is poor due to limited motor and neurologic function.

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Citations:

a. ACOG Committee Opinion Number 442. Preconception and Prenatal Carrier Screening for Genetic Diseases in Individuals of Eastern European Jewish Descent. October 2009.
b. Gross SJ, Pletcher BA, Monaghan KG, Professional Practice and Guidelines Committee. Carrier screening in individuals of Ashkenazi Jewish descent. Genet Med 2008; 10:54.
c. Eng CM, Schechter C, Robinowitz J, et al. Prenatal genetic carrier testing using triple disease screening. JAMA 1997; 278:1268.
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f. Auerbach, AD, Buchwald M, Joenje H. Fanconi anemia. In: The Genetic Basis of Human Cancer. In: Vogelstein, B, Kinzler, KW (Eds), McGraw Hill, New York 1998. p. 317.

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CONTENT FOR AVAILABLE GENETIC TESTING

My signature below indicates that I have read, or had read to me, the above information on **Greenbrier Obstetrics and Gynecology, P.C.: Carrier Screening in Pregnancy for Common Genetic Diseases** form and I understand it. Before signing this form, I have had the opportunity to discuss carrier testing further with my doctor, someone my doctor has designated, or with a genetics professional. I have all the information I want, and all of my questions have been answered.

*****INSURANCE COVERAGE: Coverage of these tests is subject to copays, coinsurance, and deductibles. Certain insurances may require pre-authorization and criteria to be met.**

I have decided that:

☐ I want CF carrier testing.

☐ I do not want CF carrier testing.

☐ I want SMA carrier testing.

☐ I do not want SMA carrier testing.

☐ I want Fragile X carrier testing.

☐ I do not want Fragile X carrier testing.

For patients of Ashkenazi Jewish descent:

☐ I want Tay-Sachs, Canavan carrier testing.

☐ I do not want Tay-Sachs, Canavan carrier testing.

_____ _____

Patient's Name Printed Date

_____ _____

Patient's Signature Witness

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Available Genetic Testing

First Trimester Screening: This is an optional noninvasive evaluation that combines a maternal blood screening test with an ultrasound evaluation of the fetus to identify risk for specific chromosomal abnormalities, including Down Syndrome Trisomy-21 and Trisomy-18. In addition to screening for these abnormalities, a portion of the test (known as the nuchal translucency) can assist in identifying other significant fetal abnormalities, such as cardiac disorders. The First Trimester screening is performed between the 11th and 13th week of pregnancy at Maternal Fetal Medicine (MFM). The blood screen measures two pregnancy related hormones: hCG and PAPP-A. The ultrasound evaluation measures nuchal translucency (fluid beneath the skin behind baby's neck). The screening test does not detect neural tube defects. An additional blood test is drawn at 16-21 weeks for open spina bifida. It is important to realize that a positive result does not equate to having an abnormality, but rather serves as a prompt to discuss further testing such as the Non Invasive Prenatal Testing (NIPT), chorionic villus sampling (CVS) or amniocentesis.

Sequential Screening: This test is done at Maternal Fetal Medicine (MFM) for pregnant women at increased risk for fetal chromosomal abnormalities due to advanced maternal age (patients currently age 35 and up or age 35 at the time of delivery) or personal/family history of chromosomal abnormalities. This includes the First Trimester Screening (First trimester blood test and ultrasound) and a second trimester blood work sample at 16-21 weeks of pregnancy.

Serum Integrated Screening I and II: This test provides information about the risks for having baby with Down syndrome, trisomy 18, or an open neural tube defect. The test requires two blood samples from you, one taken between 10-13 weeks, and the second one between 15-21 weeks of pregnancy. These two blood tests are calculated, and your risk assessment will be available after the second blood work is completed. This has an estimated Down syndrome detection rate of 88.1% with a false positive rate of 6.0%. A negative result means that the chance of you having a baby with Down syndrome, trisomy 18, or an open neural tube defect is low. It is important to realize that an abnormal or positive result does not equate to having an abnormality, but rather serves as a prompt to discuss further testing such the Non Invasive Prenatal Testing (NIPT), chorionic villus sampling (CVS) or amniocentesis.

Tetra Screening/AFP: This is a blood test which can identify a patient who may be at an increased risk of having a baby with Down syndrome, trisomy 18, or an open neural tube defect. It is done between 15-21 weeks of your pregnancy, though the optimal time is between 16-18 weeks. Detection rate is 81% with a false positive rate of 5%.

MaterniT21/QNatal (Sentara and Quest): This test is intended for pregnant women at increased risk for fetal chromosomal abnormalities due to advanced maternal age (patients currently age 35 and up or age 35 at the time of delivery), fetal ultrasound abnormality suggestive of aneuploidy, personal or family history of chromosomal abnormalities, abnormal serum screening test or twin pregnancy at age 32. MaterniT21 is a simple safe and accurate non-invasive prenatal blood test for fetal chromosomal abnormalities for Trisomy 18, 21, 18 and several sex chromosome abnormalities. The test also offers an optional analysis for fetal sex. This test can be performed as early as 10 weeks gestational age. An additional blood test is done 16-21 weeks for open spina bifida.

Informaseq (Labcorp): This is a simple, safe, and accurate non-invasive prenatal blood test for fetal chromosomal abnormalities, Trisomy 13, Trisomy 18, Trisomy 21, and several sex chromosome abnormalities. It is intended for pregnant women at increased risk for fetal chromosomal abnormalities due to advanced maternal age (patients currently age 35 and up or age 35 at the time of delivery), fetal ultrasound abnormality suggestive of aneuploidy, personal or family history of chromosomal abnormalities, abnormal serum screening test or twin pregnancy at age 32. The test also offers an optional analysis for fetal sex. This test can be performed as early as 10 weeks of pregnancy. Detection rate for Trisomy 21 is greater than 99.9%. An additional blood test is done at 16-21 weeks for open spina bifida.

Chorionic villus sampling: Often referred to as CVS, is a diagnostic test for identifying chromosome abnormalities and other inherited disorders. This test can be done between 11-14 weeks of pregnancy at Maternal Fetal Medicine (MFM). It involves removing some chorionic villi cells from the placenta at the point where it attaches to the uterine wall. The CVS procedure collects larger samples and provides faster results than amniocentesis. It detects chromosome abnormalities (i.e. Down syndrome) and genetic disorders (i.e. cystic fibrosis). This test is different from amniocentesis in that it does not allow for testing for neural tube defects. Although CVS is considered to be a safe procedure, it is recognized as an invasive diagnostic test that does pose potential risks. Miscarriage is the primary risk related to CVS occurring 1 out of every 100 procedures. There is also an increased risk of fetal limb malformation with this procedure.

Amniocentesis: Amniocentesis is a diagnostic test that may be recommended by your health care provider following an abnormal serum screening result. It detects chromosome abnormalities, neural tube defects and genetic disorders such as Down syndrome, cystic fibrosis, and spina bifida. It is done between 16-22 weeks of your pregnancy at Maternal Fetal Medicine (MFM). An ultrasound is used as a guide to determine a safe location for the needle to enter the amniotic sac so the fluid may be safely removed. A sample of amniotic fluid is collected through the needle. The procedure takes about 45 minutes, although the collection of fluid takes less than five minutes. The amniotic fluid, which contains cells shed by the fetus, is sent to the laboratory for analysis. There is a risk of miscarriage and infection with this procedure.

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CONSENT FOR AVAILABLE GENETIC TESTING

My signature below indicates that I have read, or had read to me, the information on **Greenbrier Obstetrics and Gynecology, P.C.: Available Genetic Testing** form and I understand it. I have also read or had explained to me the specific disease(s) or condition(s) tested for, and the specific test(s) I am having, including the test descriptions, principles and limitations. I have had the opportunity to discuss the purposes and possible risks of this testing with my doctor or someone my doctor has designated. I know that genetic counseling is available to me before and after the testing. I have all the information I want and all of my questions have been answered.

*****INSURANCE COVERAGE: Coverage of these tests is subject to copays, coinsurance, and deductibles. Certain insurances may require pre-authorization and criteria to be met.**

I choose to be tested for:

- ☐ First Trimester Screening
- ☐ Sequential Screening
- ☐ Serum Integrated Screening I and II
- ☐ Tetra screening/AFP
- ☐ MaterniT21/QNatal
- ☐ Informaseq
- ☐ Chorionic villus sampling (CVS)
- ☐ Amniocentesis
- ☐ I decline all genetic testing.

_____ _____

Patient's Name Printed Date

_____ _____

Patient's Signature Witness