ADVANCED OBSTETRICS & GYNECOLOGY

"Comprehensive Healthcare for Women"

PRENATAL TESTING FOR FETAL STRUCTURAL AND GENETIC ABNORMALITIES

Most infants develop normally, both in terms of the growth/development of their organs, and their chromosomal makeup. Unfortunately, approximately 3% of newborn infants have a structural abnormality (aka "birth defect") or a chromosomal abnormality.

Testing is available to evaluate the structural development of the infant, and to evaluate for chromosomal/genetic abnormalities. The problems associated with a structural abnormality depend on which organs are involved and how severely they are affected. Chromosomal abnormalities usually result in infants with multiple problems, including intellectual impairment and multiple health concerns.

While testing can help identify many problems with the development of an infant, even when all testing is normal, there is still a chance that the baby may have a health problem. In addition, sometimes there are "false positive" results, which prompt anxiety and extra testing, even though there is actually no problem.

There are two main reasons to consider testing for structural and/or genetic abnormalities of the infant:

- Testing can help determine if the infant has a medical condition that will require special care either during the pregnancy or more commonly, after birth.
- Some patients would consider terminating the pregnancy if a significant structural or genetic abnormality is detected.

Testing for Structural Abnormalities:

1. **12 week ultrasound:** Some structural abnormalities can be detected during this early ultrasound study, but because the infant is small, detection of birth defects is limited.
2. **The alpha fetoprotein blood test (AFP):** Done at 16 weeks gestation, this test helps to identify infants who may have problems with brain or spinal cord development. It can also aid identification of pregnancies at greater risk of prematurity, small babies and other complications. When the AFP result is abnormal, extra fetal monitoring is often performed during the pregnancy.
3. **19-20 week ultrasound:** We recommend a comprehensive ultrasound to assess the infant's anatomy at 19-20 weeks gestation.
4. **Fetal echocardiogram:** When the risk of a fetal heart defect is increased, a specialized ultrasound of the fetal heart can be performed at approximately 22 weeks gestation.

Testing for Genetic Disorders:

The risk of having an infant with chromosomal disorders increases with maternal age. The most common numeric chromosomal abnormality that may lead to a liveborn infant is Down syndrome. This occurs when the baby has an extra 21st chromosome. An affected child has mental retardation, birth defects and an abnormal appearance. Your risk of having a baby with Down syndrome increases with maternal age. For instance, a 20 year old has a 1 in 1400 chance, a 30 year old has a 1 in 900 chance, a 35 year old has a 1 in 270 chance and a 40 year old has a 1 in 100 chance.

Other genetic abnormalities of concern include Trisomy 13 or 18 (three copies of those chromosomes rather than two). Those abnormalities often cause fetal malformations that can be seen on ultrasound. Trisomy 13 and 18 are severe abnormalities, and the infants usually pass away before their first birthdays. All of the tests described below **assess risk** for these three abnormalities.

Non-invasive SCREENING tests:
(These tests assess a risk, but do not make a diagnosis.)

1. **Sequential Screen:** This testing provides an estimate of the risk of having a baby with Down syndrome (Trisomy 21) or Trisomy 18, but does not indicate whether the baby definitely does or does not have the genetic condition. This test consists of an ultrasound and blood test at 12 weeks, and another blood test at 16 weeks. Those results, plus the mother's age, are used together to create a risk assessment. If the risk for Down syndrome is high, Chorionic Villus Sampling or Amniocentesis is offered for diagnosis. Using this protocol, 90% of infants with Down syndrome are detected, but some are missed. In addition, there is a 5% false-positive rate – this means that 5% of patients are told the risk is increased and are offered additional testing, even though the infant is truly healthy. The accuracy of this test may be lower in twin pregnancy.

2. **Cell-free DNA:** This test involves drawing a sample of the mother's blood after 10 weeks gestation, and DNA from the pregnancy that is in the mother's bloodstream is analyzed. This test will identify most cases of Down syndrome, but a small number of cases will be missed. The test can also report fetal gender. If the Cell-free DNA testing suggests a genetic abnormality, Chorionic Villus Sampling or Amniocentesis is advised.

   Given the high accuracy of the cell-free DNA test, if you choose to have the cell-free DNA test, it is not necessary to do the full sequential screen. If the cell-free DNA test is done and results are normal, additional testing will include the *12 and 20 week ultrasounds*, and the *AFP test*.

   - ✧ **For women who are 35 and older, or who are at increased risk for having a baby with an extra chromosome, testing is available for common fetal chromosome abnormalities, including trisomy 21(Down syndrome), trisomy 18 (Edwards syndrome), and trisomy 13 (Patau syndrome). The test can also report fetal gender and sex-chromosome abnormalities.**

   - ✧ **For women who are younger than 35, carrying a singleton pregnancy, and whose pregnancies are considered to be at average risk - testing is available for common fetal trisomies (Down syndrome and Edwards syndrome). The test can also report fetal gender. For average risk women, this test is generally not covered by insurance plans, and must be paid directly by the patient.**

Invasive DIAGNOSTIC tests:
(These tests are used to make a more definitive diagnosis of a genetic abnormality during pregnancy)

- **Chorionic Villus Sampling (CVS):** Chorionic villus sampling is a test done at approximately 11 weeks gestation under ultrasound guidance. A small piece of placental tissue is obtained either through the cervix or through the mother's abdomen. Because the infant and the placenta share the same chromosome makeup, in most cases the infant's chromosomes can be assessed by testing the placental tissue. The chromosomes are evaluated for numeric chromosomal abnormalities (extra or missing chromosomes or large rearrangements). The test is more than 99% accurate for identifying infants with numeric chromosome abnormalities, such as Down Syndrome. However, there is an associated 1:200 risk of pregnancy loss with the procedure.

- **Amniocentesis:** Amniocentesis is performed using ultrasound guidance. A needle is guided into the sac around the infant and a sample of amniotic fluid is obtained. Within this fluid, fetal cells can be isolated, and those cells can be tested for numeric chromosomal abnormalities (extra or missing chromosomes or large rearrangements). An amniocentesis is more than 99% accurate for these types of disorders; however, it has an associated 1:300 risk of pregnancy loss.

- **Microarray Analysis:** New technology allows expanded testing of specimens from amniocentesis or CVS procedures. Chromosome material can be tested for hundreds of genetic syndromes. 2% of procedures in low-risk patients will find that the infant has a potentially harmful genetic abnormality. The possibility of finding an abnormality is higher in high-risk patients (older mothers, family history of genetic abnormalities, or abnormal non-invasive testing). These genetic abnormalities can only be detected with amniocentesis or CVS.

Due to the complexity of the decision process for invasive testing (CVS or amniocentesis), our doctors recommend that you speak with a genetic counselor should you want to consider invasive testing, to make certain that you are fully aware of the pros, cons and limitations of all available testing options.

Additional Genetic Screening Considerations:

1. **Sex chromosome abnormalities:** Normal women have two X chromosomes. Men have an X and a Y. When there is either an extra or a missing sex chromosome, it can lead to health conditions and intellectual impairment. At the current time, the only tests that can detect these abnormalities are the full Cell-Free DNA (done only for high-risk patients), CVS and amniocentesis.

2. **Testing for specific genetic diseases:** If your infant is at risk for a specific familial genetic disorder (such as cystic fibrosis), then a CVS or amniocentesis is required to identify if the infant will be affected. Specific genetic disorders generally are only sought in the chromosome analysis if there is a known increased risk.

3. **Standard carrier testing for genetic disorders:** Carriers for genetic diseases are typically healthy, but if two parents are carriers for some disorders, they have a chance of having an infant with a serious illness. Blood from either/both parents can be tested to see if you are a carrier for certain genetic disorders, and to know if your infant may be at risk. For most patients, we offer carrier testing for *cystic fibrosis, spinal muscular atrophy* (the most common type of muscular dystrophy), *fragile X* (the most common inheritable form of mental retardation, *thalassemia* (a dangerous blood disorder), *tay-sachs disease* and other disorders. If both parents are a carrier for one of these disorders, it is typically only possible to see if the baby will have a serious illness by doing a CVS or amniocentesis.

4. **Expanded carrier testing for genetic disorders:** A blood test is available that can check mothers and fathers for the carrier state of more than 200 genetic disorders. If one or both parents are carriers of a genetic disorder, and the infant may be at risk, then an amniocentesis or CVS will be needed to determine if the infant may be affected. If your infant is deemed to be at risk of a significant genetic disorder, an amniocentesis or CVS will be needed to determine if the infant will be affected. The decision for expanded carrier screening is complicated by this potential need for additional invasive diagnostic testing, and because the actual extent of disability in the baby is sometimes not certain until after birth, even when the infant is confirmed to have inherited a genetic disorder. Even when the test is negative, there is still a chance that you carry a genetic disorder that the test cannot detect. Expanded carrier screening is typically not covered by insurance plans, and is not available for some insurance plans. Inform the staff if you would like to consider EXPANDED CARRIER SCREENING.

5. **Genetic counseling:** A consultation with a Genetic Counselor can be arranged to help you better understand the genetic risks to your infant, and help you to choose the best genetic tests for you during the pregnancy. As part of the counseling session, the counselor performs a detailed family history for genetic issues, and may help identify potential genetic risks for your infant. There are multiple testing options available during your pregnancy, and a genetics counselor can help you choose the best options for you, given your personal preferences, and based on a full genetic history of your family. **Inform the staff if you would like a consultation with a genetic counselor.**

Insurance coverage for the testing noted above is variable depending on insurance carrier and/or policy type. It is important that you understand your insurance coverage, as there may be a significant out-of-pocket expense for some of these tests.

Each patient must decide for herself which testing (if any) is most appropriate, based on her risks of having an infant with a genetic or structural disorder, and her personal feelings about testing. The only testing that our practice recommends as mandatory is the 19-20 week ultrasound to assess the infant's growth and development.

Please bring this document to your first prenatal visit so that your doctor can review this information and answer any questions that you may have.

By signing below, I am acknowledging receipt of this handout, and I have had an opportunity to discuss my questions with a doctor.

- ☐ I would like a consultation with a Genetic Counselor.
- ☐ I want Sequential Screening for genetic abnormalities. (Not done if Cell-Free DNA test done.)
- ☐ I will be 35 or older on my due date, or have other risk factors that increase my risk of having a baby with a genetic abnormality, and I want Cell-Free DNA screening for genetic abnormalities.
- ☐ I will be younger than 35 on my due date, and I want Cell-Free DNA screening for genetic abnormalities.
- ☐ I would like to have the STANDARD CARRIER SCREENING for myself and/or the infant's Father to check for the carrier state of genetic disorders.
- ☐ I would like to have the EXPANDED CARRIER SCREENING for myself and/or the infant's Father to check for the carrier state of more than 200 genetic disorders.
- ☐ I want Chorionic Villus Sampling for more definitive genetic diagnosis, rather than non-invasive screening. A counseling session with a Genetic Counselor is mandatory before this test is performed.
- ☐ I want Amniocentesis for more definitive genetic diagnosis, rather than non-invasive screening. Under most circumstances, a counseling session with a Genetic Counselor will be mandated before this test is performed.
- ☐ I decline screening for chromosomal abnormalities.

_____	_____	_____
Name (Printed)	Signature	Date