## Prenatal Testing for Genetic Abnormalities

In the general population, greater than 95% of pregnancies result in babies born without birth defects, and 2% – 3% of pregnancies result in babies born with major and minor birth defects. Of babies born with defects, many of these conditions are treatable.

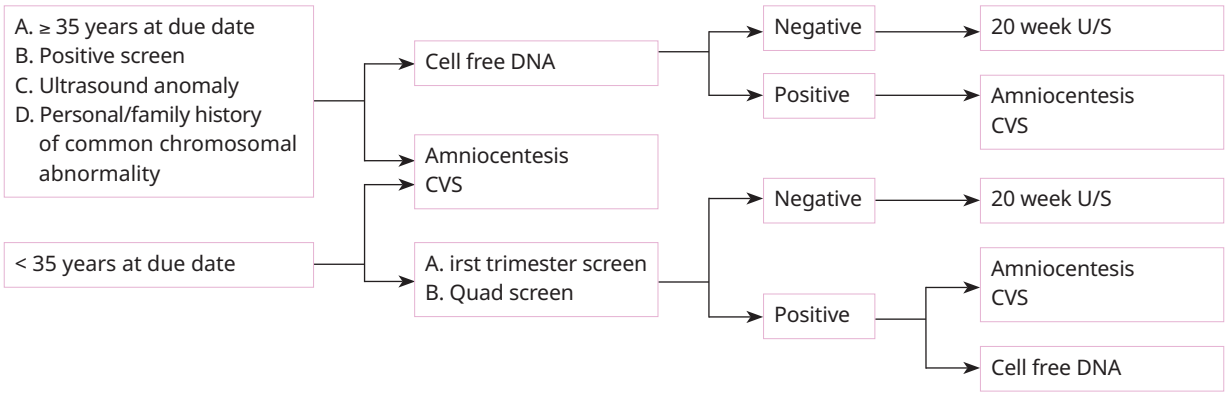
Some birth defects are caused by problems with chromosomes, structures that are located inside each cell of the body and contain the genes that determine a person's physical makeup. The most common chromosome disorder is called a trisomy, in which there is an extra chromosome. The most common trisomy is trisomy 21, Down syndrome. Other trisomies include trisomy 13 and trisomy 18. The risk of these trisomies and other chromosomal disorders can be associated with the age of the mother at delivery. The following table can identify the risk for your pregnancy.

| **Chromosomal Abnormalities in Liveborn Infants at Various Maternal Ages** | | |
|---|---|---|
| Maternal Age | Incidence: Down Syndrome | Incidence: All Chromosomal Abnormalities |
| 20 | 1/1667 | 1/526* |
| 21 | 1/1667 | 1/526* |
| 22 | 1/1429 | 1/500* |
| 23 | 1/1429 | 1/500* |
| 24 | 1/1250 | 1/476* |
| 25 | 1/1250 | 1/476* |
| 26 | 1/1176 | 1/476* |
| 27 | 1/1111 | 1/455 |
| 28 | 1/1053 | 1/435* |
| 29 | 1/1000 | 1/417* |
| 30 | 1/952 | 1/384* |
| 31 | 1/909 | 1/384* |
| 32 | 1/769 | 1/322* |
| 33 | 1/625 | 1/317 |
| 34 | 1/500 | 1/260 |
| 35 | 1/385 | 1/204 |
| 36 | 1/294 | 1/164 |
| 37 | 1/227 | 1/130 |
| 38 | 1/175 | 1/103 |
| 39 | 1/137 | 1/82 |
| 40 | 1/106 | 1/65 |
| 41 | 1/82 | 1/51 |
| 42 | 1/64 | 1/40 |
| 43 | 1/50 | 1/32 |
| 44 | 1/38 | 1/25 |
| 45 | 1/30 | 1/20 |
| 46 | 1/23 | 1/15 |
| 47 | 1/18 | 1/12 |
| 48 | 1/14 | 1/10 |
| 49 | 1/11 | 1/7 |

*47,XXX excluded for ages 20  32 (data not available) (Hook EB: Rates of chromosome abnormalities at different maternal ages. Obstet Gynecol 58:282, 1981)

These statistics can help you decide whether or not to pursue further genetic evaluation. If prenatal genetic testing is scheduled, the outcome of such testing can be useful in several ways. If test results reveal no abnormalities, this can be reassuring. If a genetic disorder is detected, further information can be gathered to assist you in the planning for a child with special needs or a consultation regarding pregnancy termination. No test is 100% accurate in detecting genetic abnormalities and no test can check for every genetic problem. A normal result can be reassuring, but does not guarantee the absence of a problem.

**Screening Progression and Available Tests**

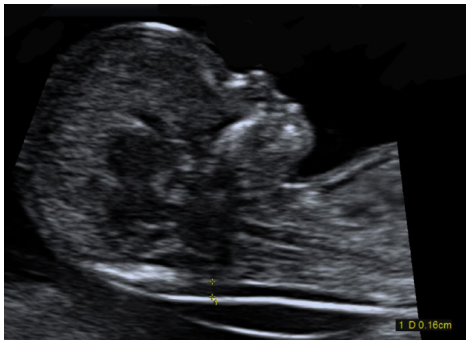



**Nuchal Translucency Ultrasound (NT)**

The Nuchal Translucency Ultrasound is a valuable screening tool that can help identify babies who have an increased risk for chromosomal abnormalities such as Down Syndrome (trisomy 21), Edwards Syndrome (trisomy 18), Patau Syndrome (trisomy 13), and Turner Syndrome. It can also identify babies with an increased risk for defects of the heart, abdominal wall, and skeleton. Using sound waves, the ultrasound is a safe and painless screen, with no associated risks.

The NT is performed between 11 and 13 weeks 6 days, when the baby's nuchal translucency, the clear tissue located at the back of a baby's neck, can be measured. Babies with genetic abnormalities or structural conditions have more fluid in the NT than babies without abnormalities. If your baby's NT measurement is thicker than normal, it does not mean your baby has a genetic abnormality. The NT is not a diagnostic test, it can only indicate a higher risk for an abnormality. To confirm or rule out a diagnosis of an abnormality, additional screening is needed, such as a Non-invasive Prenatal Testing (NIPT)/cell free DNA blood screen, or an amniocentesis. In addition, an NT can measure basic anatomy. Babies can have physical abnormalities even with normal chromosomes.

Physical abnormalities indicate an increased risk for genetic or structural conditions. If your NT indicates increased risk for an abnormality, your provider will discuss additional testing.



**Chorionic villi sampling (CVS)**
During this test, done between 10 and 12 weeks of pregnancy, a tiny piece of the placenta is obtained. Results are usually available within a few days. CVS is done to check for a specific genetic problem – such as the trisomies discussed above – or other genetic diseases such as cystic fibrosis or Tay Sachs, if there is a family history of these diseases. The risk of miscarriage from the procedure may be slightly higher than that of amniocentesis, so patients considering this test must balance the benefit of detecting a chromosomal abnormality with the risk of the procedure. If you choose this option, we will refer you to a Maternal Fetal Medicine (MFM) specialist who will perform the procedure.

**Amniocentesis**
An "amnio" is usually performed around 16 weeks of pregnancy, and is used to diagnose whether or not a fetus has certain genetic disorders or defects. A small amount of fluid (less than one ounce) is taken from around the fetus. This fluid is sent to the laboratory for testing, and results are available within one to two weeks. The risk of miscarriage after this procedure is estimated to be 1 in 300 to 500. Therefore, the risk of the procedure should be balanced against the benefit of detecting a disorder. Although a normal amniocentesis can rule out many genetic disorders, including trisomy 21, 13, and 18, it does not guarantee a normal newborn. If you choose this option, we will refer you to a Maternal Fetal Medicine (MFM) specialist who performs this procedure.

**Firsttrimester screening**
This involves a blood test performed at 10 weeks which measures the levels of the proteins PAPPA and hCG, and an ultrasound performed at 12 to 13 weeks to measure a fluid filled space behind the baby's neck (nuchal translucency or NT). These results are combined to estimate the chance of having a baby that has Down syndrome, trisomy 13, or trisomy 18. An increased risk does not mean a chromosomal condition has been diagnosed; you will be offered further genetic counseling and a diagnostic test (CVS/amniocentesis) for a definitive diagnosis. The test will detect up to 87% of Down syndrome and 90% of trisomy 13/18.

**Quad screen**
This blood test is offered between 15 to 20 weeks, though is optimally performed between 15 and 18 weeks. This test is most commonly used by patients who did not have the opportunity to undergo first trimester screening and do not desire invasive or cell free DNA testing. The test measures levels of alpha-fetoprotein (AFP), unconjugated estriol (uE3), human chorionic gonadotropin (hCG), and inhibin A. A certain combination of values may indicate increased risk for trisomy 13/18/21 and neural tube defects. The detection rate of this test is 75% - 85%, which means that up to 25% of abnormalities are missed. An abnormal result does not necessarily mean that the fetus is affected; the false positive rate is five percent. If an abnormal result is obtained, genetic counseling and an amniocentesis are offered to confirm the diagnosis.

**Cell free DNA (cfDNA) testing**
With this screening test performed after 10 weeks of pregnancy, a sample of the patient's blood is obtained to examine the amount of fetal DNA to determine whether the fetus may have an increased risk of trisomy 13/18/21. Approximately 98% of cases with Down syndrome are identified. There is a false positive rate of

less than 0.5%. These are considered laboratory developed tests, they are not subject to FDA approval. The American College of Obstetrics and Gynecology recommends this test only for women at increased risk for an abnormal number of chromosomes (women 35 or older at delivery, ultrasound findings suggestive of increased risk of trisomy, history of a prior pregnancy with a trisomy, positive test for trisomy – including first trimester combined or quad screen, parental balanced Robertsonian transolocation with increased risk of fetal trisomy 13 or 21. A patient with an abnormal result will be offered genetic counseling and CVS/ amniocentesis to confirm a diagnosis.