

Screening for Chromosome Abnormalities/Genetic Conditions

Background

Our cells have 46 chromosomes, half of which we inherit from our mom and half from our dad. Sometimes, an error occurs resulting in an extra or missing chromosome in the baby. This leads to a particular syndrome depending on the chromosome involved. Down syndrome or Trisomy 21 is the most common chromosome abnormality affecting 1:830 live births. It is due to having 3 copies of chromosome 21 instead of 2. About 1 in 150 babies is born with a chromosomal condition. Down syndrome is an example of a chromosomal condition. However, not all conditions can be diagnosed prenatally.

What problems can chromosomal conditions cause?

Sometimes chromosomal conditions can cause miscarriage. This is when a pregnancy stops growing before 20 weeks. More than half of miscarriages are caused by chromosomal conditions. These conditions also can cause stillbirth, which is when a baby dies in the womb before birth but after 20 weeks of pregnancy. Each child born with a chromosomal condition is different. Some children with chromosomal conditions have intellectual disabilities or birth defects, or both. Some children with these conditions don't have any serious problems. The problems depend on which chromosomes are affected and how

How do you know if your baby has a chromosomal condition?

Screening versus Diagnostic Tests

The American Congress of Obstetricians and Gynecologists (ACOG) recommends that all pregnant women be offered prenatal tests for Down syndrome and other chromosomal conditions. A screening test tells you if your baby is more likely than others to have a certain chromosomal problem. Diagnostic tests give you a definite answer.

You can have screening tests or diagnostic tests in the first or second trimester of pregnancy. The advantage of first trimester screening is that you learn about your baby's risk for chromosomal problems relatively early in the pregnancy. If the risk is low, the results will offer you reassurance. If the risk is high, you may have the opportunity to consider a diagnostic test, which will allow you to find out whether your baby has a problem while you're still in your first trimester. You can also check your baby's blood for chromosomal conditions after he/she is born.

What screening tests are available?

1) Maternal Blood Screening-DNA based Screening (NIPT)

This screen provides a very accurate assessment of fetal risk for specific chromosome abnormalities using **maternal blood only**.

- **How the test works:** Fragments of placental DNA in the maternal blood are identified and analyzed. This screen can be done anytime in pregnancy after 10 weeks gestation. It is a single blood draw. On occasion, a repeat specimen is required if the first test does not give a result.
- **How good is the test:** This screen provides the highest detection rates with >99% detection for Down syndrome and the lowest false positive rate (0.1%) (a positive test when the condition is not present). It also evaluates chromosomes 13, 18, X and Y. NIPT is now able to screen for other specific chromosomal abnormalities if desired (Expanded screening).

Condition	Detection Rate	False Positive Rate
Down Syndrome	>99%	0.1%
Trisomy 18	>97%	0.1%
Trisomy 13	95-98%	0.25%
Gender	99.4% accuracy	0.6% error

2) Integrated or 2nd trimester screening



Integrated screening involves both 1st and 2nd trimester screening tests. This test is not as accurate as the NIPT and therefore has largely been replaced by it. For this test, 1st trimester screening is done at 11-13 weeks of pregnancy and includes a blood test and an ultrasound to look at the nuchal translucency (NT) and gives an initial early result. The NT measures the clear (translucent) space in the skin at the back of the baby's neck. Babies with chromosomal abnormalities tend to accumulate more fluid at the back of the neck during the 1st trimester causing the space to be larger. The NT screening can only be done between 11 and approximately 14 weeks of pregnancy.

Another blood test is done in the 2nd trimester and is added to the first-trimester information to give a final result. It gives you a single assessment of your risk after all these screening tests are completed. The 2nd trimester test, also known as a Quad screen, can also be done as a stand-alone screening test even without the 1st trimester component, but is not as accurate.

- **How good is the test:**

Condition	Detection Rate	False Positive Rate
Down Syndrome	90%	3%
Trisomy 18	90%	

Take-home messages

- All “non-invasive” tests are considered “screening” tests. Screening tests increase or decrease your risk. They cannot diagnose or exclude the possibility of a chromosomal abnormality. **Low Risk does not mean zero risk.**
- Diagnostic testing is available to all pregnant women regardless of age or family history.

What Diagnostic Tests are available?

- The two available diagnostic tests are Chorionic Villus Sampling (CVS) and Amniocentesis.

Chorionic Villus Sampling

- Placental cells are sampled through the abdomen or cervix depending on the location of your placenta.
- This can be done between 11 to 14 weeks providing the earliest diagnostic testing.
- Risk of miscarriage about 1/100 (1%) although has been reported as low as 1/300 (0.3%).

Amniocentesis

- Amniotic fluid containing fetal cells is sampled through the abdomen. This can be done after 15 weeks.
- Risk of miscarriage about 1/500 (0.3%) although has been reported as low as 1:1600 (0.06%).

Both these tests can detect many more and much smaller chromosomal abnormalities than the screening tests.

Take-home messages

- All pregnancies are at risk of having a baby with a chromosomal abnormality. Young age and negative family history do not exclude the possibility.
- “Screening” provides us a way to evaluate your individual risk of having a baby with a chromosomal abnormality.
- Screening is not diagnostic. It only increases or decreases your risk for the condition(s) being screened.
- Not all babies with a positive screen are affected. Confirmation of all positive results recommended to exclude the possibility of a false positive.
- False negatives may also occur with screening. Some babies with low risk screens may have a chromosomal abnormality.
- Diagnostic testing is available to everyone. However, it carries a small risk of miscarriage.
- All prenatal testing discussed is considered optional. You may decline any or all testing.