

What is maternal serum screening?

Maternal serum screening tests help identify pregnancies at increased risk for Down syndrome, trisomy 18, or an open neural tube defect such as spina bifida. These tests have traditionally been performed in the second trimester and measure the levels of certain substances in maternal blood. Newer tests now combine first trimester fetal ultrasound measurements and maternal blood protein levels to predict risk. If you would like to learn more about maternal serum screening, please talk with your doctor, genetic counselor, or other healthcare provider.

Down syndrome (DS)

Down syndrome is also called trisomy 21. It is caused by the presence of an extra chromosome number 21 in every cell of the body. This results in birth defects such as mental retardation, specific facial features, heart defects, and decreased muscle tone. About half of individuals with DS live at least 50 years. Approximately one in 700 babies is born with DS. Although the risk of having a baby with DS increases as a woman ages, young women also have babies with DS.

Trisomy 18 (T18)

Trisomy 18 is caused by an extra copy of chromosome number 18 in every cell of the body, resulting in severe physical and mental birth defects. Almost all babies born with T18 die within the first year of life, many within the first week. The risk of having a baby with T18 increases as a woman ages.

Open neural tube defects (ONTDs)

Open neural tube defects are a group of disorders caused by a failure of the neural tube to close correctly very early in pregnancy. The neural tube is an embryonic structure that eventually becomes the baby's brain and spinal cord. ONTDs include anencephaly (failure of the skull and brain to form correctly), resulting in fetal death, and spina bifida (failure of the back bone and spinal cord to form correctly), usually causing some paralysis of the legs and poor bowel/bladder control. Approximately one in 1,700 babies is born with an ONTD. The risk of having an affected baby does not increase with the mother's age.

What testing choices do I have?

- First trimester screen
- Integrated screen
- Sequential screen
- Quadruple (quad) screen

How reliable is maternal screening at finding birth defects?

TEST	DETECTION RATE	SCREEN POSITIVE RATE
Down syndrome (DS)		
First trimester	85–90%	6%
Integrated	85–87%	1%*
Sequential	86%	1.6%
Quadruple	80%	4%
Trisomy 18 (T18)		
First trimester	80%	<1%
Integrated	90%	<1%
Sequential	90%	<1%
Quadruple	~80%	<1%
Open neural tube defects (ONTD)		
First trimester	n/a	n/a
Integrated	80%	1.5%
Sequential	80%	1.5%
Quadruple	80%	1–2%

*If nuchal translucency cannot be measured, the risk of a chromosome disorder is still calculated, but the screen positive rate is slightly higher.

MATERNAL SERUM SCREENING

Choices for Expectant Parents



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BD-PP-006, Rev 2, February 2018



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First trimester screen

The first trimester screen tests the levels of two substances present in a pregnant woman's blood: human chorionic gonadotropin (hCG) and pregnancy-associated plasma protein-A (PAPP-A). In addition, the results of an early ultrasound that measures the thickness of the skin at the back of the baby's neck (nuchal translucency or NT) is used to determine the risk for DS or T18. This test does not screen for ONTDs, so second-trimester screening for these birth defects still needs to be performed. Results of the DS and T18 screen are available in the first trimester.

Advantages:

- One blood draw (for DS and T18)
- Early result (first trimester)
- Excellent detection of DS and T18

Disadvantages:

- Does not detect ONTDs; another blood draw in the second trimester must be done for this purpose.
- Higher risk for positive result when the fetus does not have either disorder (false positive) compared to the integrated and sequential screens.

Integrated screen

The integrated screen requires two blood draws, one in the first trimester and one in the second trimester. An ultrasound in the first trimester to measure the baby's NT is recommended, but not required. The first sample is tested for PAPP-A. The second sample is tested for alpha fetoprotein (AFP), hCG, estriol (uE3), and inhibin-A (DIA). The integrated screen estimates risks for DS, T18, and ONTD, with results available in the second trimester after the second blood draw.

Advantages:

- Excellent detection of DS and T18
- Lowest chance for false-positive result
- Detects ONTDs

Disadvantages:

- Later result (second trimester)
- Two blood draws
- No result if the second blood draw is not collected
- Possible anxiety while waiting to have the second blood draw
- Loss of opportunity for an early diagnostic test (i.e., chorionic villus sampling or CVS)

Sequential screen

The sequential screen, like the integrated screen (above), involves a blood draw in both the first and second trimester, as well as an ultrasound in the first trimester to measure the baby's NT. Unlike the integrated screen, the sequential screen

requires the NT measurement and will be interpreted in both the first and second trimesters for DS and T18 risk. If the risk for either condition is considered to be very high after the first blood draw, the test will be resulted out as "abnormal" in the first trimester and no second sample will be required. However, since only a small percentage of screens will be called "abnormal" in the first trimester, most women will need to provide a sample in the second trimester, after which they will receive their final results.

Advantages:

- Excellent detection of DS and T18
- Low chance for a false-positive result
- Detects ONTDs
- Pregnancies at highest risk for DS and T18 identified in the first trimester

Disadvantages:

- Most women will get their result in the second trimester.
- Most women will have two blood draws.

Quadruple screen

The quad screen requires a single blood draw in the second trimester. This sample is tested for AFP, hCG, uE3, and DIA. The quad screen estimates risks for DS, T18, and ONTD, with results available in the second trimester.

Advantages:

- One blood draw
- Detects ONTDs

Disadvantages:

- Higher chance for the test to be a false positive compared to the integrated and sequential screens
- Not quite as reliable at detecting DS and T18 as the other three tests

My screen came back as "abnormal." What does this mean?

Most pregnancies that have abnormal test results are actually normal pregnancies (the baby does not have DS, T18, or an ONTD). False positives occur because screening tests are designed to identify women who are at increased risk to have a baby with certain birth defects. These screening tests are not diagnostic tests. A positive screening test result does NOT mean that your baby has a birth defect, only that he/she is at increased risk of having one.

What is recommended when a test result is abnormal?

Your doctor or genetic counselor will discuss additional testing that can be done to determine if your baby does or does not have a birth defect. Most often, a detailed ultrasound is

recommended. Non-invasive prenatal testing (NIPT), chorionic villus sampling (CVS) or amniocentesis may be offered. NIPT is also a screening test, but one that is more sensitive and which has a very low false positive rate. It involves only a blood draw. In CVS, a small piece of the placenta is tested. Amniocentesis involves testing a small amount of the fluid surrounding the baby. Both CVS and amniocentesis allow the laboratory to directly examine the baby's chromosomes to accurately identify DS and T18. Amniocentesis, especially when paired with an ultrasound, can also test for ONTDs. Since CVS and amniocentesis are expensive and have a small risk for miscarriage, the decision to have either of these tests is yours. NIPT is also expensive, and is not diagnostic like CVS and amniocentesis are, but does not put the pregnancy at risk.

What happens if additional testing shows that my baby has a birth defect?

If a birth defect is detected, you will be given as much information as possible about the condition.

Several options may be available, including increased surveillance of the pregnancy, arrangements for special care at delivery and/or after the baby is born, or discontinuation of the pregnancy. Your doctor or genetic counselor can discuss your test results and options with you.

Does a negative test result guarantee that my baby does not have a birth defect?

Maternal serum screening detects most, but not all, pregnancies affected with DS, T18, or ONTDs. A small number of babies with DS, T18, or ONTDs will not be identified by these tests. Other kinds of birth defects are unlikely to be detected. All pregnancies have a 2–3 percent background risk of having a birth defect. This test screens for the three most common birth defects, but not for all birth defects.

A note about the positive screen rate

A certain percentage of tests are interpreted as "positive." These positives include affected babies (true positives) and unaffected babies (false positives). Most screen positive results are actually false positives.

If you would like to learn more about maternal serum screening, please talk with your doctor, genetic counselor, or other healthcare provider.