



CHOICES FOR EXPECTANT PARENTS

Maternal Serum Screening

ARUP[®] LABORATORIES

What is maternal serum screening?

Maternal serum screening (MSS) tests identify pregnancies at increased risk for Down syndrome, trisomy 18, or an open neural tube defect (ONTD) such as spina bifida. These tests measure the levels of biochemicals, chemicals, or analytes in maternal blood. The most accurate MSS tests 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

Down syndrome (DS) is also called trisomy 21. It is caused by an extra copy of chromosome 21 in every cell of the body. This results in birth defects such as intellectual disability, 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

Trisomy 18 (T18) is caused by an extra copy of chromosome 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 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 backbone 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.

What testing choices do I have?

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

First trimester screen

The first trimester screen tests the levels of biochemicals, chemicals, or analytes present in a pregnant woman's blood, specifically, human chorionic gonadotropin (hCG) and pregnancy-associated plasma protein A (PAPP-A). These levels, along with 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), are used to determine the risk for DS or T18. This test does not screen for ONTDs. Results 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
- Higher risk for positive result when the fetus does not have either disorder (false positive) compared with 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 dimeric inhibin A (DIA). The integrated screen estimates risk for DS, T18, and ONTDs. Results are available in the second trimester after the second blood draw.

Advantages

- Excellent detection of DS and T18
- Lowest chance of 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 described above, involves a blood draw in both the first and second trimesters, as well as an ultrasound in the first trimester to measure the baby's NT. Unlike the integrated screen, this 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 result will be “abnormal” in the first trimester, and no second sample will be required. 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 of a false-positive result
- Detects ONTDs
- Pregnancies at highest risk for DS and T18 identified in the first trimester

Disadvantages

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

Quadruple screen

The quadruple or 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 risk for DS, T18, and ONTDs, and results are available in the second trimester.

Advantages

- One blood draw
- Detects ONTDs

Disadvantages

- Higher chance of receiving a false-positive result than with the integrated and sequential screens
- Lower detection rate for DS and T18 than the other three tests

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

Most pregnancies that have abnormal test results are actually healthy pregnancies (the baby does not have DS, T18, or an ONTD). False-positive results occur because screening tests are designed to identify women who are at increased risk of having 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, but 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 options. A detailed ultrasound is recommended.

Prenatal cfDNA screening (previously referred to as noninvasive prenatal testing, or NIPT), chorionic villus sampling (CVS), or amniocentesis may be offered. cfDNA screening is also a screening test, but it is more accurate and requires 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 enable 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. Because CVS and amniocentesis are expensive and carry a small risk for miscarriage, the decision to have either of these tests is yours. cfDNA screening is not diagnostic like CVS and amniocentesis are, but it 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 during the pregnancy, arrangements for special care at delivery 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% 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.

How reliable is maternal screening for detecting birth defects?

TEST	DETECTION RATE	SCREEN POSITIVE RATE
Down syndrome (DS)		
First trimester	85%	6%
Integrated	87%	1%*
Sequential	86%	1.6%
Quadruple	81%	4–5%
Trisomy 18 (T18)		
First trimester	80%	<1%
Integrated	90%	<1%
Sequential	90%	<1%
Quadruple	~80%	<1%
Open neural tube defects (ONTDs)		
First trimester	n/a	n/a
Integrated	80%	1–2%
Sequential	80%	1–2%
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.



*A nonprofit enterprise of the University of Utah
and its Department of Pathology*

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BD-PP-006, Rev 5, July 2024