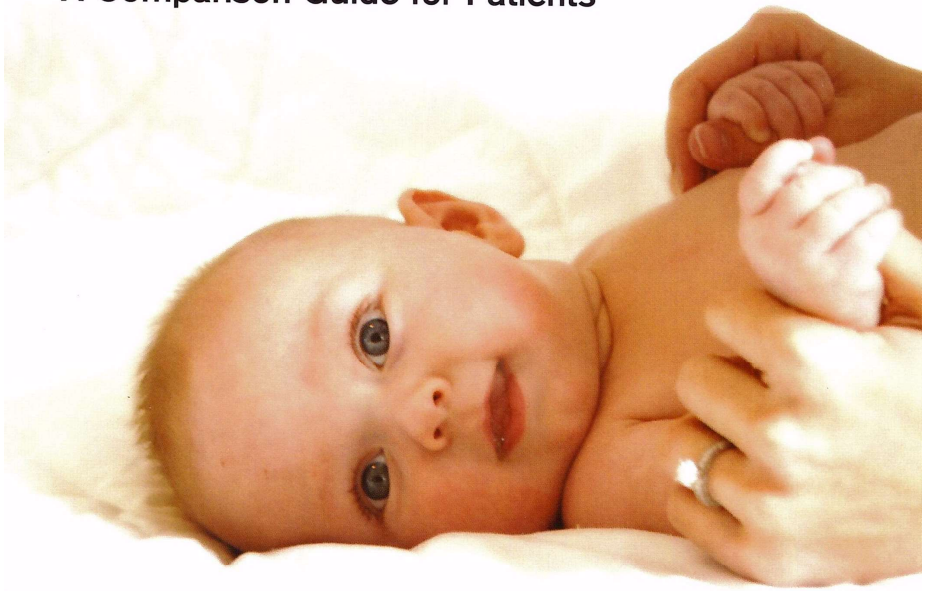
A Comparison Guide for Patients



Prenatal Screening for Down Syndrome and Open Neural Tube Defects

Beaumont

What is the difference between screening and diagnostic tests?

A screening test is a test that is used to identify women who may be at increased risk for having a baby with a problem. These results are usually reported as a ratio, for example the chance of the baby to have Down syndrome is one in 100. Diagnostic tests, like amniocentesis, are tests that give a definite result. For example, the amniocentesis result could indicate the baby has Down syndrome.

What are prenatal genetic screening tests?

Screening tests are available to help determine if your pregnancy is at increased risk for Down syndrome, spina bifida and other certain birth defects. You are encouraged to discuss the test with your health care provider before you decide whether you would like to be screened.

Why should I consider prenatal screening?

All pregnant women have a risk of having a baby with Down syndrome or an other birth defect. Screening tests help identify women at greater risk for having a baby with a particular birth defect so they can decide whether to have a diagnostic test to find out if their baby is affected. Those women who know that they do not want to have chorionic villus sampling (CVS) or amniocentesis under any circumstance may not wish to have a prenatal screening test during their pregnancy.

What is Down syndrome?

Down syndrome is caused by the presence of an extra chromosome, number 21, in the cells of the developing baby. About one in every 800 babies is born with Down syndrome. It is usually not inherited, so babies with Down syndrome are typically born to families with no history of the condition. Although Down syndrome occurs more frequently as mothers get older, about 70 percent of babies with Down syndrome are born to women younger than age 35. Down syndrome is always associated with mental disability and often with physical problems, such as heart defects. It is not possible to tell the degree of disability before the baby is born.

What are open neural tube defects?

Open neural tube defects, or ONTD, occur in about one to two in every 1,000 babies. Open spina bifida is an incomplete closure of the spine. It varies in severity depending on the location and size of the opening. Surgery to close the opening is usually performed shortly after birth but does not correct the possible problems with walking and bowel/bladder control. Closed spina bifida is where the spinal opening is covered with skin or thick tissue and is less severe and less common than open defects. Closed spina bifida will not be detected by the blood test.

What is Trisomy 18?

Trisomy 18, also known as Edwards syndrome, is a serious abnormality caused by the presence of an extra chromosome, number 18, in the cells of the developing baby. About one in every 5,000 babies is born with Trisomy 18. Like Down syndrome, these babies are typically born to families with no history of the condition. Babies with Trisomy 18 always have mental disability, often multiple birth defects and usually do not survive past the first year of life.

What is Smith-Lemli-Opitz syndrome?

Smith-Lemli-Opitz syndrome, or SLOS, is an uncommon genetic disorder caused by an error in the formation of cholesterol. About one in every 20,000 babies will be born with SLOS. It is associated with many problems in the developing baby, including mental disability and poor growth.

What are the screening test options available to me?

Option A: First trimester screen only

An ultrasound examination is done in the first trimester between the first day of the 11th week of pregnancy and the last day of the 13th week. The ultrasound must be done by either Fetal Imaging at Beaumont or by a Beaumont approved sonographer in your doctor's office. The approved sonographers need to have special certification because the ultrasound needs to be done in a specific manner to provide accurate measurements. This ultrasound will measure the thickness of the nuchal translucency, or NT, a space at the back of the baby's neck. In addition, a blood sample is taken at this time to measure the amount of two chemicals – pregnancy associated plasma protein-A, or PAPP-A, and human chorionic gonadotropin, or hCG. The screening result estimates your risk of Down syndrome and Trisomy 18.

Option B: Quad screen – second trimester screen only

A blood sample is taken in the second trimester, between 15 and 20 weeks of pregnancy, to measure the amount of four chemicals: Alpha-fetoprotein, or AFP; hCG; unconjugated estriol, or uE3; and inhibin-A, or inh-A. The screening result estimates your risk of Down syndrome, ONTD, Trisomy 18 and SLOS.

Option C: Serum integrated screen (first and second trimesters)

A blood sample is taken in the first trimester to measure PAPP-A. Another blood sample is taken in the second trimester to measure the concentration of the following four chemicals: AFP, hCG, uE3 and inh-A. The blood levels of all five chemicals will be integrated into a single screening result to estimate your baby's risk of Down syndrome, ONTD, Trisomy 18 and SLOS.

Option D: Full integrated screen (first and second trimesters)

This option combines the NT measurement and PAPP-A described in Option A and the levels of four chemical markers described under Option B. The NT thickness measurement and blood levels of all five chemicals are combined into a single screening result to estimate your baby's risk of Down syndrome, ONTD, Trisomy 18 and SLOS.

Option E: Sequential screen consists of two parts

Part 1: At 11 to 13 weeks of pregnancy, the NT measurement, PAPP-A and your age are combined to calculate a risk for Down syndrome and Trisomy 18. If the risk for either is increased, your physician will receive a report immediately. At this point, you will discuss options for diagnostic testing.

Part 2: If the first trimester risk for Down syndrome and Trisomy 18 is not increased, your physician will receive a preliminary report indicating that your screen is negative so far. You will be asked to return for a blood draw in the second trimester. The NT measurement and blood levels of all five chemicals (PAPP-A, AFP, hCG, uE3 and inh-A) are then combined into a single screening result to estimate your baby's risk of Down syndrome, Trisomy 18, ONTD or SLOS.

Comparison chart for the screening test options

	OPTION A: FIRST TRIMESTER SCREEN	OPTION B: SECOND TRIMESTER SCREEN	OPTION C: SERUM INTEGRATED SCREEN	OPTION D: FULL INTEGRATED SCREEN	OPTION E: SEQUENTIAL SCREEN
First trimester component (11-13 6/7 weeks)	Nuchal thickness/ ultrasound Blood sample	None	Blood sample	Nuchal thickness/ ultrasound Blood sample	Nuchal thickness/ ultrasound Blood sample
Second trimester component (15-20 weeks)	None	Blood sample	Blood sample	Blood sample	Blood sample (if 1st trimester negative)
When final report is available	1st trimester	2nd trimester	2nd trimester	2nd trimester	1st trimester if positive, otherwise 2nd trimester
Screens for:	Down syndrome Trisomy 18	Down syndrome Trisomy 18 ONTD SLOS	Down syndrome Trisomy 18 ONTD SLOS	Down syndrome Trisomy 18 ONTD SLOS	Down syndrome Trisomy 18 ONTD (2nd trimester only) SLOS (2nd trimester only)
Detection rate for Down syndrome	84 percent	86 percent	84 percent	88 percent	88 percent
Likelihood of screen positive for Down syndrome	7 percent	8-9 percent	2-3 percent	2 percent	2-3 percent
Available diagnostic tests after screen positive result	Chorionic villus sampling; Amniocentesis	Amniocentesis	Amniocentesis	Amniocentesis	Chorionic villus sampling 1st trimester only; Amniocentesis

ONTD = open neural tube defect
SLOS = Smith-Lemli-Opitz syndrome

What are the main differences among the testing options?

The differences among the testing options are the timing of the testing, the available diagnostic tests after a screen positive result, the detection rate for Down syndrome and the chance of having a screen positive result. All five tests have a similar detection rate for Down syndrome, but your chances of having a screen positive result are greater with the first trimester only or second trimester only screens. This means you will be more likely to have to consider having a CVS or amniocentesis. The chance of having a screen positive result for Down syndrome with the integrated screening or sequential tests is lower, especially for the full integrated screen. This means that you are less likely to have to consider having diagnostic testing. A chart comparing the screening test options can be found on the opposite page.

How are the test results reported?

The result is reported as either "screen positive" or "screen negative" for Down syndrome or ONTD. Information about Trisomy 18 or SLOS will only be reported if your risk is increased. The results will be available at your physician's office about seven days from the last blood draw.

What does a screen positive result mean?

A screen positive result means that you are in a high-risk group for having a baby with the particular birth defect and will be offered a diagnostic test.

First trimester screen

The result is screen positive if the risk for Down syndrome is one in 230 or higher. A screen positive result for Trisomy 18 is at a risk of one in 100 or higher. This test does not screen for ONTD.

Second trimester screen

The results could be screen positive for Down syndrome, Trisomy 18, ONTD or SLOS. The result is screen positive for Down syndrome if at mid-pregnancy the risk is one in 270 or higher, the Trisomy 18 risk is one in 100 or higher or the SLOS risk is one in 50 or higher. The result is screen positive for an ONTD if the serum AFP is approximately two times higher than expected for the gestational age at which you have the test.

Serum integrated screen

The results could be screen positive for Down syndrome, Trisomy 18, ONTD or SLOS. The result is screen positive for Down syndrome if at mid-pregnancy the risk is one in 110 or higher, the Trisomy 18 risk is one in 100 or higher or the SLOS risk is one in 50 or higher. The result is screen positive for an ONTD if the serum AFP is approximately two times higher than expected for the gestational age at which you have the test.

Full integrated screen

The results could be screen positive for Down syndrome, Trisomy 18, ONTD or SLOS. The result is screen positive for Down syndrome if at mid-pregnancy the risk is one in 110 or higher, the Trisomy 18 risk is one in 100 or higher or the SLOS risk is one in 50 or higher. The result is screen positive for an ONTD if the serum AFP is approximately two times higher than expected for the gestational age at which you have the test.

Sequential screen

If your risk of having a baby with Down syndrome or Trisomy 18 is increased after the first trimester blood draw, you will be notified immediately. If diagnostic testing (CVS or amniocentesis) is negative, you will probably return for a blood draw for AFP testing at 16 to 18 weeks; this allows for ONTD risk assessment. If the first part of the sequential screen is negative, you will continue on as though you are having a full integrated screen performed (see above and Option D in table).

Not all women with screen positive results have an affected pregnancy. In fact, most women who are screen positive will have a normal baby.

What does a screen negative result mean?

Your screening test result will be read out as screen negative if the calculated risk is lower than the risks described in the previous section. A diagnostic test is usually not offered for screen negative results. **Although a screen negative result means that your risk of having a baby with one of these birth defects is low, a screen negative result cannot rule out the possibility of a baby with any of these abnormalities.**

Do the screening tests detect all pregnancies with Down syndrome, Trisomy 18, ONTD or SLOS?

No. About 85 percent of the cases of Down syndrome are detected (classified as "screen positive"). This means that about 15 percent of pregnancies with Down syndrome are missed (classified as screen negative). About 80 percent cases of ONTD are detected by the second trimester screen, serum and full integrated screens, while about 20 percent are missed. The first trimester screen does not detect ONTD. About 60 percent of cases of Trisomy 18 are detected by the screening tests. The detection rate of SLOS from the serum and full integrated screening tests is not known.

Why do you take my age into account?

Any pregnant woman may have a baby with Down syndrome or Trisomy 18, but the chance of this happening increases as a woman gets older. Therefore, we use age as one of the factors when calculating your risk of having a pregnancy with Down syndrome or Trisomy 18. It means that an older woman is more likely to have a result in the higher risk group (screen positive) and will be offered a diagnostic test.

A woman's age is not taken into account when calculating risks for ONTD or SLOS as these conditions have the same chance of happening in all pregnancies, regardless of the woman's age.

What are the tests that will be offered if my screening test is screen positive?

It depends on your particular screening test and its result.

If the first trimester test result is screen positive for Down syndrome or Trisomy 18, chorionic villus sampling, or CVS, or amniocentesis will be offered.

If the second trimester test result is screen positive for Down syndrome, Trisomy 18 or SLOS, an amniocentesis will be offered, sometimes accompanied by a detailed ultrasound examination. If the test is screen positive for an ONTD, a targeted ultrasound examination is offered and an amniocentesis can be considered as well.

If the serum integrated test result is screen positive for Down syndrome, Trisomy 18 or SLOS, an amniocentesis will be offered, sometimes accompanied by a detailed ultrasound examination. If the test is screen positive for an ONTD, a targeted ultrasound examination is offered and an amniocentesis can be considered as well.

If the full integrated screening test result is screen positive for Down syndrome, Trisomy 18 or SLOS, an amniocentesis will be offered, sometimes accompanied by a detailed ultrasound examination. If the test is screen positive for an ONTD, a targeted ultrasound examination is offered and an amniocentesis can be considered as well.

If the first part of the sequential screen is positive for Down syndrome or Trisomy 18, CVS or amniocentesis will be offered. If the second part of the sequential screen is positive your physician will follow the approach described under full integrated screening (see paragraph above).

What is chorionic villus sampling, or CVS?

A CVS is offered between the 10th and 14th week of pregnancy. CVS is an outpatient procedure performed under ultrasound guidance. CVS involves taking a sample of placental tissue by passing a plastic tube through the vagina and cervix or by inserting a needle through the abdominal wall (using local anesthetic). The CVS sample contains cells that can be used to tell whether the baby has Down syndrome, Trisomy 18 or other chromosome problems. The results typically take two to three weeks. Between one in 100 and one in 200 women undergoing CVS may have a miscarriage as a result of the procedure.

What is an amniocentesis?

Amniocentesis is typically performed between 16 and 20 weeks gestation. Amniocentesis is a procedure in which a small sample of fluid that surrounds the baby is removed by passing a thin needle through the abdominal wall and into the uterus under ultrasound guidance. Cells in the fluid from the baby will be isolated and analyzed to tell whether or not the baby has chromosome problems like Down syndrome or Trisomy 18. From the remaining fluid, AFP can be isolated to detect ONTD. If the pregnancy is at risk for SLOS, part of the fluid sample can be sent to test for that condition. The results usually take two to three weeks. Between one in 200 and one in 400 women undergoing amniocentesis may have a miscarriage as a result of the procedure.

What is an ultrasound examination and what will it show?

Ultrasound machines use sound waves to look at the developing baby. This procedure called sonography is often used in the first trimester to check fetal age or the number of babies present. In the second trimester, sonography provides a more detailed examination of portions of the baby's body. Sonography cannot be used to diagnose Down syndrome or Trisomy 18, but it can often identify spina bifida and other fetal abnormalities sometimes associated with Down syndrome, Trisomy 18 or SLOS.

Does a CVS or amniocentesis guarantee that my baby will be free of all birth defects?

No test can guarantee that your baby is free of all birth defects, but if the result of the CVS or amniocentesis is negative, it will rule out Down syndrome and many other chromosome abnormalities.

Is prenatal genetic screening mandatory?

No. Screening is absolutely optional. The purpose of the information provided in this pamphlet is to help you understand your options should you wish to undergo screening.

Which is the best screening test?

This depends upon when during pregnancy you begin testing, how much you would like to avoid the diagnostic tests and when you would like the results. Experts believe that for most patients, the full integrated screen is best because it offers a high detection rate with a low rate of diagnostic (invasive) testing by amniocentesis. But your situation may be different. This should be discussed with your physician.

For more information:

If you have further questions, please speak with your physician.

If you would like to make an appointment to meet with a genetic counselor to discuss your screen positive results, you may contact the Beaumont Reproductive Genetics Program by calling 248-551-0395.

To make an appointment for fetal ultrasound in the division of Fetal Imaging at Beaumont, please call 248-898-2070.

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