

The COMBINED TEST

FIRST STAGE
Final Results Reported

Information for Patients

First Trimester
Risk Assessment
for
Down Syndrome



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MEDICAL SCREENING LABORATORY, INC.

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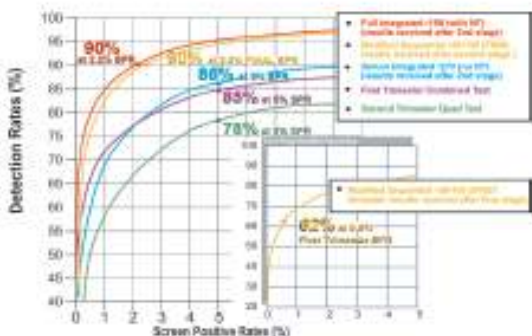
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The COMBINED Test

Early Risk Assessment

Various choices in Risk Assessment for Down syndrome can be found on the graph below. This brochure discusses the **Combined Test**.



Before undergoing risk assessment, please consider which options are best suited for you by discussing it with your healthcare provider.

Who is at risk?

Without screening, one baby out of every 700 would be born with Down syndrome. Although any woman may give birth to an affected baby, a woman's risk increases as she ages. The chart above compares the detection rates (the percentage of Down syndrome pregnancies that will be found) with the *screen positive rates* (the chance that a woman's test result will be called "positive" indicating an increased risk of having a baby with Down syndrome). For example, with the **2nd Trimester Quad Test** at a 5% *screen positive rate*, 78% of the cases of Down syndrome will be detected. With the **1st Trimester Combined Test**, at a 5% *screen positive rate*, 85% of cases of Down syndrome will be detected. The **Combined Test** can also detect approximately 85% of fetuses affected with Trisomy 18.

What are Down syndrome & Trisomy 18?

Down syndrome is the most common cause of severe mental handicaps and physical problems such as heart defects, visual and auditory difficulties in newborns. While it is not possible to assess how severely each Down syndrome baby will be affected, it is known that nine out of ten babies will survive their first year and nearly half of those will grow to maturity and reach 60 years of age.

Down syndrome occurs when either the whole or a segment of the long arm of chromosome 21 is present in three copies instead of two. Because Down syndrome is usually not inherited, a family with no previous history can still have a Down syndrome baby.

Trisomy 18, which is caused by an extra chromosome 18, results in serious mental retardation and physical deformities including major heart defects. Only 1 out of 10 babies affected with Trisomy 18 lives past the first year of life. As with Down syndrome, the risk of having an affected child gradually increases with age of the mother.

Why do you take age into account?

Any woman can have a baby with Down syndrome but the chance of this happening increases as a woman gets older. Your age is used in calculating your risk of having a pregnancy with Down syndrome. It means that an older woman is more likely to have a result in the higher risk groups (*screen positive*) and be offered a diagnostic test.

What is the Combined Test?

By utilizing information from an ultrasound of the baby and maternal serum analysis, the **Combined Test** is performed between 11 weeks and 0 days and 13 weeks and 6 days of pregnancy. It is suitable for women of all ages. The **Combined Test** is an assessment of risk identifying women who are at an increased risk of having a baby with Down syndrome, but it cannot determine definitely whether or not the baby is affected. Women with a greater risk can be offered diagnostic tests such as a chorionic villus sampling or an amniocentesis. These diagnostic tests will actually identify which fetuses are affected.

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What are the advantages of having the Combined Test?

The **Combined Test** is performed in the first trimester, thereby providing results at a point in pregnancy when early diagnostic testing such as chorionic villus sampling (CVS), is available as an option.

What does the Combined Test measure?

After a patient's serum is drawn, your healthcare provider and laboratory look for two substances in the serum that are markers of Down syndrome: Pregnancy Associated Plasma Protein-A (PAPP-A) and total beta-human chorionic gonadotropin (total β -hCG). In affected pregnancies, the PAPP-A tends to be lower than normal while the total β -hCG levels are usually elevated.

At the same time a specialized ultrasound called Nuchal Translucency (NT) measures the thickness of the fetal neck.

The values of these three markers are used together with the mother's age to estimate the risk of having a Down syndrome pregnancy. The results of the **Combined Test**, which will be sent to your healthcare provider, will usually be ready in two working days. Results will be classified as either *screen positive* or *screen negative*.

Does the Combined Test detect all pregnancies with Down syndrome?

No. Seventeen of twenty or 85% of pregnancies with Down syndrome will be detected (in the *screen positive* group). Therefore, three out of 20 (15 percent) of pregnancies with Down syndrome will have a *screen negative* result and so will be missed by the **Combined Test**. This is because risk assessment tests cannot completely distinguish affected from unaffected pregnancies.

What does a screen negative test mean?

If the risk of Down syndrome based on age and the level of the three markers is lower than one in 200, then the result is called *screen negative* and a diagnostic test would not usually be offered.

Although a *screen negative* test result means that the patient is not at high risk for having a baby with Down syndrome, a *screen negative* result does not completely rule out the possibility of a pregnancy with Down syndrome.

All patients undergoing first trimester screening and/or CVS should still consider a 16 week maternal serum AFP test to rule out open neural tube defects.

What does a screen positive result mean?

A *screen positive* result means that you are in a higher risk group for having a baby with Down syndrome. If your result is in this group, you will be offered genetic counseling to discuss your options, one of which is a diagnostic test. About one in 20 women who take the **Combined Test** are *screen positive* and have a risk greater than one in 200.

Most women with *screen positive* results do not have a pregnancy with Down syndrome. For example, of 50 women with *screen positive* results, only one would have a pregnancy with Down syndrome.

What further diagnostic tests will be offered if the results are screen positive?

Patients will be offered Chorionic Villus Sampling (CVS) or an amniocentesis. There is a small risk associated with these procedures. Patients who would consider CVS if they had a *screen positive* test should have the **Combined Test** as early as possible, preferably close to 11 weeks, 0 days. About one in 100 to 200 women has a miscarriage as a result of CVS and about one in 270 women has a miscarriage following an amniocentesis. The detection rate for Down syndrome after a CVS or amniocentesis is greater than 99 percent.

What is Chorionic Villus Sampling (CVS)?

CVS is a diagnostic procedure that extracts a small amount of placental material and tests these cells. The material may be obtained through the cervix of the uterus with a very fine straw or via a needle placed through the abdomen. The placenta is usually an excellent source for genetic material of the fetus. This test is performed transcervically or transabdominally between 10 to 12 weeks of gestation, but only transabdominally after 12 weeks gestation. Results are usually available in five to seven days, and the detection rate is greater than 99 percent for chromosomal abnormalities, such as Down syndrome. Follow-up evaluation for open neural tube defects is necessary.

What is Amniocentesis?

This diagnostic test, which can be performed after 15 weeks, collects a small amount of amniotic fluid from around the baby. The doctor inserts a very fine needle to extract the fluid which contains cells from the fetus. These cells are then cultured and examined for their genetic content. Test results are usually available in 7 to 14 days. If the chromosome results are negative, it will almost certainly rule out a Down syndrome pregnancy. In addition, AFP evaluation in amniotic fluid can rule out open neural tube defects.

Is there a test offered at a later date than the Combined Test?

Yes. The **Integrated 190 Test** is similar to the **Combined Test** in that it includes Nuchal Translucency testing and PAPP-A blood chemistries in the first trimester, but because the second stage of the test is performed after 15 weeks, CVS is no longer an option as a diagnostic test. However, it is a more accurate and comprehensive test because it includes the **Quad Test** as a second stage, which examines AFP, total β -hCG, uE3 and Inhibin A. This second stage is recommended to be drawn at 15 to 16 weeks, but can be performed up to 22 weeks.

The possible detection rate for Down syndrome is 90 percent (five percent more accurate than the **Combined Test**) with only a 2.15% screen positive rate. Patients receive their results within 72 hours after the second trimester blood chemistries are taken, usually around 16 to 17 weeks. Additionally, in contrast to the **Combined Test**, the **Integrated 190 Test** helps identify pregnancies at increased risk for open neural tube defects.



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What happens if a birth defect is discovered through the Combined Test ?

If your baby is found to have a serious birth defect, you can receive professional counseling from your healthcare provider and/or genetic counselor about how your child's physical and mental development may be affected. The individual capabilities and potential of children with birth defects are considerations which you may wish to consider in your decision-making process.

One option would be to continue the pregnancy and make arrangements for appropriate medical services at and after delivery. Other options such as adoption and termination of pregnancy will be discussed with you by your healthcare provider.

Further information and support are available through groups and local organizations as listed below:

National Down Syndrome Society

<http://www.ndss.org>

National Association for Down Syndrome

<http://www.nads.org>

March of Dimes <http://www.marchofdimes.com>

Trisomy 18 <http://www.trisomy.org>

Smith-Lemli-Opitz Syndrome

<http://www.smithlemliopitz.org>



COMBINED TEST INFORMED CONSENT

I have read and understand the information in this pamphlet regarding screening for The Combined Test.

- Yes, I want to have The Combined Test
 No, I do not want to have The Combined Test

Patient Name: _____

Patient Signature: _____

Date: _____

IMPORTANT: Retain Copy in Patient File



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The information included in this pamphlet is not intended as a substitute for personal medical advice. Specific situations always require a personal consultation with your healthcare provider.

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