



### What does a screen negative result mean?

If the risk of Down syndrome, based on the Integrated Test, is lower than 1 in 190 and the AFP level is less than two and one half times the normal level for your stage in pregnancy, then the result is called *screen negative* and a diagnostic test would not be offered.

Although a *screen negative* means that you are not at high risk of having a baby with Down syndrome or an open neural tube defect, a *screen negative* result does not completely rule out the possibility of a pregnancy with either of these abnormalities.

### Why do women with screen negative results occasionally have babies with Down syndrome or an open neural tube defect?

It is unusual for women to have a baby with either of these abnormalities, and it is even more unusual for a woman with a *screen negative* result, but it does sometimes happen.

This is because the screening test cannot completely distinguish affected from unaffected pregnancies. However small the risk is, we cannot rule out the possibility of the baby having Down syndrome or an open neural tube defect.

### What is Amniocentesis?

Amniocentesis is a procedure in which the doctor obtains a small sample of fluid that surrounds the developing fetus. The sample is then sent to the laboratory for testing. This fluid sample can be used to diagnose both chromosomal problems such as Down syndrome and Trisomy 18, as well as open neural tube defects such as spina bifida.

Amniocentesis is an invasive procedure, which means that there is a small risk of miscarriage (less than 1 in 200) associated with it. Results of the test for Down syndrome and Trisomy 18 will take about 7-14 days. Results of the test for spina bifida will take about 2-5 days.

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



### What are the advantages of risk assessment?

The test may give you and your healthcare provider important information about your pregnancy and your developing baby. If your baby is found to have a serious birth defect, you can receive professional counseling about how your child's physical and mental development may be effected. The individual capabilities and potential of children with birth defects are considerations which you may wish to discuss with your genetic counselor or other healthcare provider. Other options, such as adoption and termination of pregnancy may be discussed with you by your healthcare provider. Further information and support are available through groups such as your local Down Syndrome Society and Spina Bifida Association.

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

- March of Dimes [www.marchofdimes.com](http://www.marchofdimes.com)
- National Down Syndrome Society [www.ndss.org](http://www.ndss.org)
- National Association for Down Syndrome [www.nads.org](http://www.nads.org)
- Trisomy 18 [www.trisomy.org](http://www.trisomy.org)
- Smith-Lemli-Opitz Syndrome [www.smithlemliopitz.org](http://www.smithlemliopitz.org)
- Spina Bifida Association [www.sbaa.org](http://www.sbaa.org)



#### INTEGRATED TEST INFORMED CONSENT

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

- Yes, I want to have the Integrated Test.
- No, I do not want to have the Integrated 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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# The INTEGRATED Test

FIRST STAGE

## Information for Patients

First and Second Trimester Risk Assessment for Down Syndrome and Open Neural Tube Defects

SECOND STAGE  
Final Results Reported

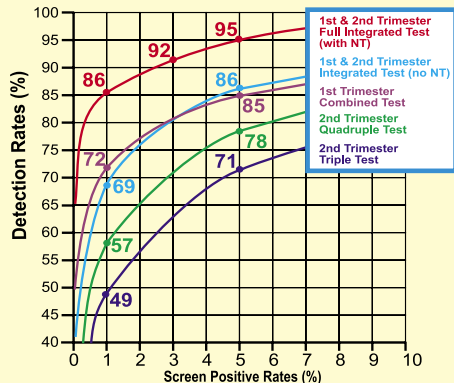


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# The INTEGRATED Test Risk Assessment

There are many choices for risk assessment for Down Syndrome as indicated on the graph below. This brochure discusses the Integrated test.



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

## What does the Integrated Test involve?

The Integrated test is performed in two stages. The first stage is ideally performed at 12 weeks of pregnancy, but any time between 11 and 13 weeks 6 days of pregnancy is acceptable. The second stage is ideally performed at 15 or 16 weeks of pregnancy but no later than 22 weeks.

### The first stage involves:

- An Ultrasound scan examination to precisely determine the gestational age of the pregnancy through the crown rump length.
- Taking a sample of your blood to measure the concentration of pregnancy associated plasma protein-A (PAPP-A).
- A Nuchal Translucency (NT) measurement between 11 weeks 0 days and 13 weeks 6 days.

### The second stage involves:

Taking a second sample of your blood to measure the concentration of the following four markers:

- alpha-fetoprotein (AFP)
- unconjugated estriol (uE3)
- inhibin-A
- human chorionic gonadotropin (total  $\beta$ -hCG)

By integrating the measurements from the first and second stages, a single risk assessment result is produced. The NT measurement and the levels of the five markers in your blood are used, together with your age, to estimate your risk of having a Down syndrome pregnancy.

In pregnancies with Down syndrome, PAPP-A, AFP and uE3 levels tend to be low and nuchal translucency measurement, inhibin, and total  $\beta$ -hCG levels tend to be raised. The level of AFP in the second blood sample is also used to determine if there is an increased risk of open spina bifida or anencephaly.

## What is Down syndrome?

Down syndrome is caused by the presence of an extra chromosome number 21 in the cells of the developing baby. In an unscreened population about 1 in every 700 (1.4 per 1000) babies is born with Down syndrome. Usually it is not inherited and so a baby can be affected even if there is no history of Down syndrome in the family.

Down syndrome is the most common cause of severe mental disability and is often associated with physical problems such as heart defects or difficulty with sight and hearing. It is not possible to assess the degree of handicap before the baby is born. About 9 out of 10 babies with Down syndrome will survive their first year and nearly half of these will reach 60 years of age.

## What are open neural tube defects?

The two main kinds of open neural tube defects (ONTDs) are spina bifida and anencephaly.

Babies with spina bifida have an opening in the spine that can result in damage to the nerves controlling the lower part of the body. This causes weakness and paralysis of the legs, and sometimes bowel and bladder problems. Babies with problems are also more likely to have a collection of fluid on the brain, called hydrocephalus, which can be treated surgically but may lead to mental disability.

Babies with anencephaly have a large part of the skull missing and the brain is not properly formed. They always die before or very soon after they are born. In about 1 in every 5 babies with spina bifida the spinal opening is covered with skin or thick tissue. This is called closed spina bifida and will not be detected by the blood test. This condition is usually less severe than open spina bifida.

## Can other abnormalities be identified?

Yes. The risk of two other disorders can be estimated. One is Trisomy 18, a rare and usually fatal disorder caused by the presence of an extra number 18 chromosome in the cells of the developing baby. The risk of Trisomy 18 can be estimated using PAPP-A, AFP, uE3 and total  $\beta$ -hCG, and is reported only when the risk is high. The second is called Smith-Lemli-Opitz syndrome, a genetic disorder caused by an error in the synthesis of cholesterol. Smith-Lemli-Opitz syndrome is associated with many problems in the developing baby, most important are mental retardation and poor growth. The risk of Smith-Lemli-Opitz syndrome can also be estimated using AFP, uE3 and total  $\beta$ hCG and is reported only when risk is high.

## What is a risk?

A risk is the chance of an event occurring. For example, a risk of Down syndrome of 1 in 100 means that if 100 women have this test result, we would expect that 1 of these women would have a baby with Down syndrome and that 99 would not. This is the same as a 1% chance that the baby has Down syndrome and a 99% chance that the baby does not.

## 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. We use age as one of the factors when working out your risk of pregnancy with Down syndrome. It means that an older woman is more likely to have a result in the higher risk group (*screen positive*) and be offered a diagnostic test.

## Why wait until the second stage to have a risk estimate?

By using information from both stages the test is safer and more effective than a test using information from the first stage alone. It will distinguish affected from unaffected pregnancies more effectively, reducing the chance that a Down syndrome pregnancy is missed. It also reduces the chance that you will need an invasive diagnostic test, such as amniocentesis.

## What happens if the ultrasound scan shows that I am too late for the first stage of the test?

We cannot report a screening result for the Integrated Test. You could have a screening test based on the second stage alone (the AFP+QUAD test).



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## What happens if I cannot attend for the second blood test?

If you do not attend for the second stage of the Integrated test, a screening result cannot be reported. We will try to contact your healthcare provider on two occasions after the recommended date for your second blood sample. If we do not receive your second blood sample a Down syndrome risk is given based on information from the first stage only.

If you know you will not be able to attend for the second blood test, please discuss this with your doctor. You could have the screening based on the first blood test and the ultrasound examination alone (the Combined test) but this is less effective than the Integrated Test.

## When will the results of the second stage be available?

The results of the test are usually ready within three working days of the second blood sample being taken. Results are sent to your doctor, midwife or healthcare professional.

The result will be either **screen negative** or **screen positive**.

*Screen positive* results are telephoned and faxed to your doctor, healthcare professional, or midwife. If you do not receive your results or have further questions please telephone LENETIX® at (516) 248-0036 to speak to a genetic counselor.

## What does a screen positive result for Down syndrome 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 a diagnostic amniocentesis.

The result is called *screen positive* if the risk of Down syndrome in your pregnancy is 1 in 190 or greater. About 1 in every 50 women screened will be in this risk group. Most women with *screen positive* results do not have a pregnancy with Down syndrome.

## What does a screen positive result for open neural tube defects mean?

A *screen positive* result means that you are in a group with an increased risk of having a baby with an open neural tube defect. If your result is in this group, you will be offered an ultrasound scan examination at 18 to 20 weeks of pregnancy, and possibly an amniocentesis. This is organized by your doctor or hospital. The result is *screen positive* if the AFP level is equal to or higher than two and one half times the normal (median) level for your stage in pregnancy.