

Beth Israel Lahey Health



Beth Israel Deaconess Medical Center

# Testing for Chromosome Abnormalities

Department of Obstetrics  
and Gynecology

*Maternal-Fetal Medicine  
and Prenatal Genetics*

## *Congratulations on your pregnancy!*

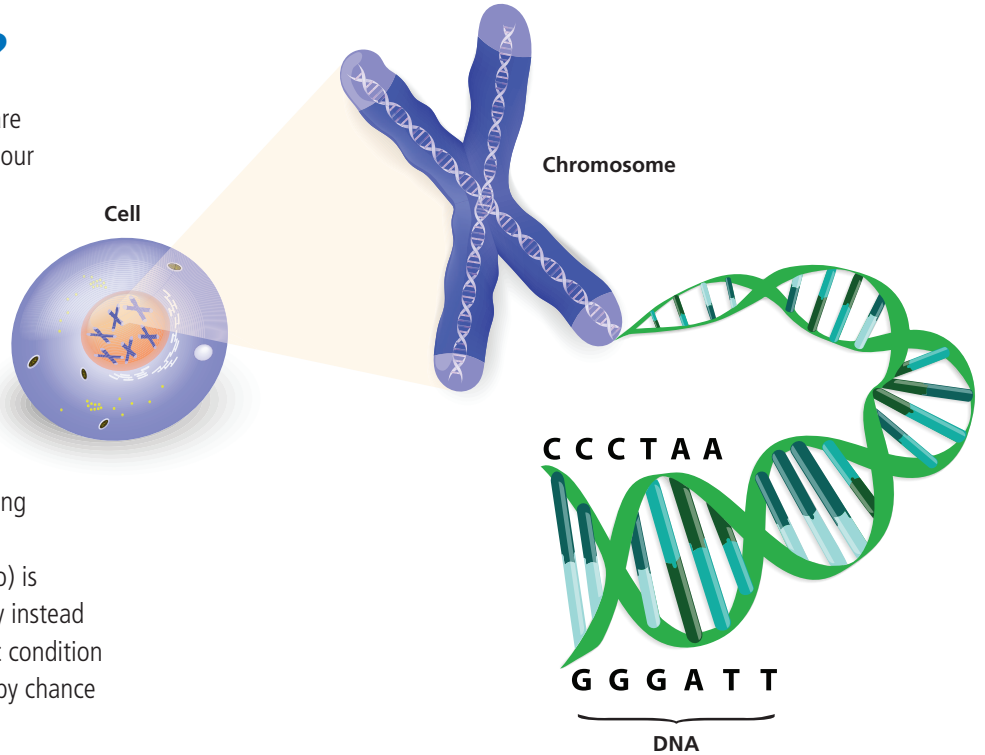
While most babies are born healthy, approximately 3-5% will be affected with certain birth defects or genetic conditions. In all pregnancies, tests are offered that can tell if the pregnancy may be at high risk for a condition called a chromosome abnormality. Decisions about testing in pregnancy are personal. Some choose not to have any testing done. Others find the information from testing to be helpful. We have made this booklet to give some information on the tests available. We hope that having this information and discussing it with your OB/GYN provider will help you to decide whether this testing makes sense for you and your family.

## What are chromosomes?

Our bodies are made of tiny cells. Chromosomes are the packages of genetic information (DNA) inside our cells. They contain the instructions for our growth and development.

Usually, each person has a total of 46 chromosomes in each cell. The chromosomes come in pairs (23 pairs). Each parent contributes one chromosome to each pair.

When a fetus (developing baby) has extra or missing chromosomes, it can lead to medical problems. An extra chromosome (three copies instead of two) is called a trisomy. A missing chromosome (one copy instead of two) is called a monosomy. This type of genetic condition doesn't usually run in families. It can happen just by chance in any pregnancy.



# What are the most common chromosomal abnormalities?

The most common differences related to the number of chromosomes are:

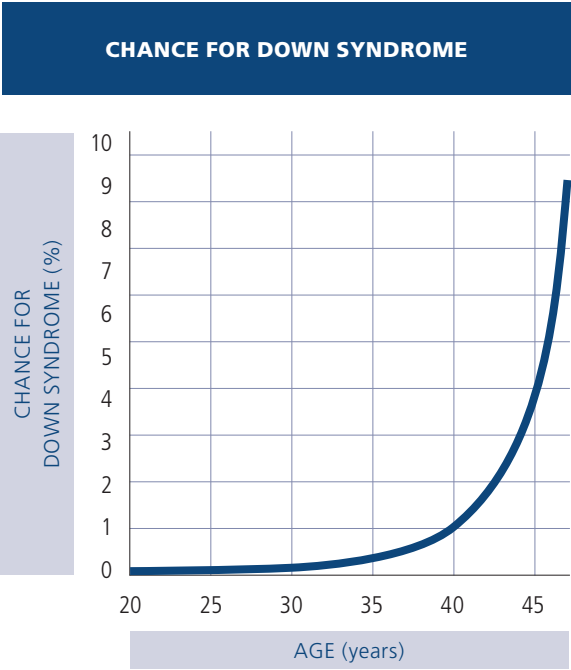
- **Down syndrome:** Down syndrome is also called trisomy 21. It happens when there is an extra copy of chromosome 21. This causes mild to moderate intellectual disability (what used to be called mental retardation), typical facial features, and, sometimes, birth defects. The range of intellectual disability in Down syndrome varies. Early treatment and education can help; however most adults who have Down syndrome are not able to live on their own.
- **Trisomy 13 and trisomy 18:** These happen when there is an extra copy of chromosome 13 or chromosome 18. If trisomy 13 or 18 is present, the pregnancy often ends in miscarriage. If the baby is born, he or she usually dies shortly after birth. Babies who survive have severe intellectual disability and health problems.
- **Sex chromosome differences:** The sex chromosomes, X and Y, determine whether a person is male or female. Girls/women usually have two X chromosomes. Boys/men usually have one X and one Y. Most people who have an extra or missing sex chromosome do not know it. Having a different number of sex chromosomes usually doesn't cause serious problems with development or thinking. Some affected children may have learning disabilities. If this happens, early treatment can help. Some affected people have infertility as adults.



*Down syndrome*

The chance for a chromosome abnormality to occur in a pregnancy increases with each year of age and can be estimated based on how old you will be when the baby is born. This is referred to as the age-related chance. For example, a 20-year-old has less than a 1/1000 chance of having a baby with Down syndrome; a 35-year-old has a 1/350 chance of having a baby with Down syndrome; a 40-year-old has about a 1/100 chance of having a baby with Down syndrome. So even though those who are older have a higher chance for these abnormalities, these abnormalities can occur in any pregnancy.

AGE (years)	CHANCE FOR DOWN SYNDROME
20	1 in 1,734
25	1 in 1,250
30	1 in 965
33	1 in 635
35	1 in 350
36	1 in 294
37	1 in 227
38	1 in 175
39	1 in 137
40	1 in 106
41	1 in 82
42	1 in 64
43	1 in 50
44	1 in 38
45	1 in 30





## What options are available to test for chromosome abnormalities?

If you are interested in receiving information about the chance for chromosome abnormalities in your pregnancy, there are screening tests and diagnostic tests.

## What is a screening test? What types are available?

A **screening test** estimates the chances of certain chromosome abnormalities in pregnancy. These tests are not invasive and pose no risk to the fetus. The results are based on your age and other factors. Screening tests are used to identify pregnancies that have an increased chance to have a chromosome abnormality, but they do not tell whether one is actually present. If you decide to have screening and your result suggests an increased chance of an abnormality, you will be given information about extra tests that may provide more information. If your results do not suggest an increased chance for an abnormality, extra testing may not be needed. Your doctor or genetic counselor will explain more about what your own results mean.

Screening tests have a risk of “false” results. That is, some people who have a pregnancy with a chromosome abnormality will be told their pregnancy is “low-risk.” Others who have a pregnancy with no chromosome abnormality will be told the pregnancy is “high-risk.” The chance for these “false” results depends on the test performed.

Four main types of screening tests for chromosome abnormalities are available: **Early risk assessment** (with or without “sequential screening”), **quadruple screen**, **cell-free DNA analysis (cfDNA)**, and **full fetal survey**.

- **Early risk assessment (ERA)/sequential screen:** ERA uses blood work and ultrasound. For this screen, the ultrasound looks at the “nuchal translucency.” This refers to fluid behind the neck of a fetus. It is normal for fluid to be there in the first trimester. The area of fluid is often larger in fetuses with chromosome abnormalities and certain other problems, including heart problems.

To do an ERA, blood is drawn between 9 weeks and 13 weeks of the pregnancy. The ultrasound can be performed between 11.5 weeks and 13 weeks. This test detects about 85-90% of fetuses with Down syndrome and about 90% of fetuses with trisomy 13 or trisomy 18.

After ERA screening, you may wish to have a second blood sample drawn at 15-21 weeks. This is termed sequential screening. This increases the chance of detecting Down syndrome and trisomy 18 to more than 92%. The results use information from the first and second blood tests and the first trimester ultrasound.

Sequential screening is thought to be most useful when the ERA results indicate an intermediate chance of an abnormality. If the ERA screen shows a very low chance for an abnormality, repeating the screen at 15-21 weeks is not likely to show different results. Those whose ERA results indicate a high chance for an abnormality might choose to have diagnostic testing or cfDNA (see next page).

- **Quadruple screen:** This is a blood test done between 15 and 21 weeks of pregnancy. It is offered to those who chose not to or were not able to have ERA performed. This test detects about 75-80% of fetuses with Down syndrome and about 65% of fetuses with trisomy 18.



- **Cell-free DNA analysis (cfDNA):** cfDNA is a blood test. It looks at small pieces of DNA from the pregnancy that can be found in the blood. These pieces can be tested to estimate the chance for Down syndrome, trisomy 18, trisomy 13, and sex chromosome abnormalities. This test is sometimes called noninvasive prenatal testing (NIPT). This test is currently offered to those who are at increased risk to have a pregnancy affected with a chromosome abnormality (due to age 35 or older or other factors). In high-risk individuals, this test can identify up to 99% of affected pregnancies. In some cases, insurance will not cover this test for those who are not at increased risk.

- **Full fetal survey:** This is an ultrasound performed during the second trimester of pregnancy. It is sometimes called a fetal anatomy survey. It uses sound waves to get pictures of the growing fetus. The purpose of this ultrasound is to see how the fetus is growing and to see if there are any noticeable physical problems. About half (50%) of fetuses with Down syndrome will have some sign on ultrasound. When certain abnormalities are seen, they increase the chance of a chromosome abnormality. If a physical problem is seen, many factors are considered to decide how high the increased chance is for you. They include your age, any previous blood screening results, and the type of abnormality that was seen.





## What if my screening test indicates an increased chance for a chromosome abnormality?

About 5% of those who have ERA, sequential screening, or quadruple screening will be told that their pregnancy has an increased chance to have a chromosome abnormality. This does **not** mean that a baby **has** a chromosome abnormality. In fact, for most pregnancies with this type of screening result, additional tests are normal and the baby is healthy. The **actual** chance of an abnormality depends on many factors and is specific for each pregnancy.

If your screening test indicates an increased chance, your doctor and/or genetic counselor will explain what the results mean for you. You will be told about any extra testing that could be done. This includes cfDNA or diagnostic testing (chorionic villus sampling and amniocentesis). Those who have cfDNA testing that indicates an increased chance for a chromosome abnormality are offered diagnostic testing.

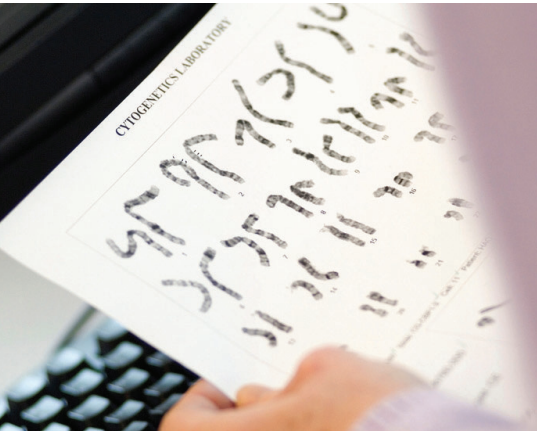
## What if my screening test is reassuring?

This means that the chance for the most common chromosome abnormalities is low. In this case, more tests for these conditions are not usually recommended.

*It is important to remember that screening tests cannot say for sure that your fetus does or does not have Down syndrome, trisomy 13, trisomy 18, or other chromosome changes. If your screening shows "low" chance, or if you don't have screening, you may still choose to have a diagnostic test (CVS or amniocentesis, explained on next page).*

# What is a diagnostic test? What types are available?

A diagnostic test can tell whether a chromosome abnormality is actually present. Anyone who is pregnant can choose to have a diagnostic test, regardless of the risk of chromosomal abnormalities. These tests can count the chromosomes and look for any differences, including those that are less common. The two types of diagnostic tests are **chorionic villus sampling (CVS)** and **amniocentesis**. Both types involve taking some tissue or fluid from the uterus (womb). Because of this, there is a small chance that these tests could cause a miscarriage.



- **Chorionic villus sampling (CVS):** CVS involves taking small pieces of the placenta at 10-13 weeks of pregnancy. In some cases, the sample is taken through the vagina, using a small tube. In other cases, it is taken through the abdomen (belly), using a needle. The doctor decides which is best, based on where the placenta is located in the uterus. The doctor uses ultrasound to locate a place to take the sample. The chance of having a miscarriage caused by CVS is estimated to be about 1 in 400 (0.25%).
- **Amniocentesis:** Amniocentesis can be done after 15 weeks of pregnancy and involves taking a sample of the fluid surrounding the fetus. To obtain the fluid, a needle is inserted into the pregnant abdomen. The doctor uses ultrasound to locate a place to take the sample. The chance of having a miscarriage caused by amniocentesis is estimated to be about 1 in 900 (0.1%).

*Remember, there are no tests that can find all birth defects or genetic differences. Even when all results are normal, there is still a small chance for abnormalities that cannot be detected before birth.*

# Prenatal Testing – Gestational Timeline for Routine Options

Provided by the Center for Maternal Fetal Medicine and Prenatal Genetics

DS: Down syndrome T18: trisomy 18 T13: trisomy 13

WEEKS GESTATION	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	
<b>Genetic Counseling</b>	Any time – Earlier is always better.																			
<b>Early risk assessment (ERA)</b> DS: 85-90% detection rate, 5% screen positive rate T18, T13: 90% detection rate, 0.3% screen positive rate	Part 1 blood: 9w0d–13w6d NT ultrasound: 11w0d–13w6d																			
<b>Sequential screen</b> DS: 92% detection rate, 5.5% screen positive rate T18, T13: 95% detection rate, 0.3% screen positive rate	Part 1 blood: 9w0d–13w6d NT ultrasound: 11w0d–13w6d Part 2 blood: 15w0d–21w6d																			
<b>Cell-free DNA analysis (cfDNA)</b> DS, T18, T13: up to 99% detection rate, <1% screen positive rate	Any time after 9w0d																			
<b>Nuchal translucency (NT) ultrasound</b> DS: 75% detection rate, 5% screen positive rate	11w0d–13w6d																			
<b>Chorionic villus sampling (CVS)</b> Diagnostic for DS, T13, T18 and other chromosome abnormalities 1 in 400 risk of miscarriage	10w0d–13w6d																			
<b>Amniocentesis</b> Diagnostic for DS, T13, T18 and other chromosome abnormalities 1 in 900 risk of miscarriage	Any time after 15w0d																			
<b>Full fetal survey (fetal anatomy survey)</b> DS: >50% detection rate, 10-15% screen positive rate	18w0d–22w0d																			

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