

Maternal Serum Screening

Introduction

Pregnancy can be an exciting time, but this excitement is often coupled with concern for the health of your baby. While the vast majority of newborns are healthy, some will have a physical problem called a birth defect.

Certain birth defects can be detected during pregnancy. One method of screening for birth defects is a blood test called maternal serum screening. Maternal serum screening allows you to learn more about your risk for having a baby with certain birth defects. This information explains maternal serum screening, defines the conditions for which it is done, and discusses what the screening results mean. If you have questions after reading this material, please discuss them with a member of your health care team.

What Can Maternal Serum Screening Tell Me About My Baby?

Maternal serum screening (MSS) is an optional test usually offered between weeks 15 and 22 of your pregnancy. This test is available from Mayo Clinic Laboratories as **Mayo ID: QUAD1 / Quad Screen (Second Trimester) Maternal Serum**. It provides information on your risk of having a child with Down syndrome or a neural tube defect. A risk for trisomy 18 (a rare and usually fatal condition) is also provided in cases where the risk is high. The screening does not provide a yes-or-no answer about the presence or absence of these conditions. Rather, the screening identifies pregnancies that may be in a higher risk group and, in turn, can serve as a guide to choosing further testing to confirm or rule out these conditions. The following are descriptions of the conditions.

Down syndrome

Down syndrome occurs in 1 in 800 live births. Every pregnant woman has a risk of having a child with Down syndrome. However, the risk increases as the age of the mother increases. For example, in mid-pregnancy, a 25-year-old woman has a risk of approximately 1 in 1,000 of carrying a fetus with Down syndrome. The risk for a 40-year-old woman is about 1 in 85. Down syndrome, also called trisomy 21, results when there are three copies of chromosome 21 in each cell rather than two. Children with Down syndrome have characteristic features that include a flat facial profile, upwardly slanted eyes, low set ears, a single deep crease across the center of the palm, and low muscle tone. People with Down syndrome have varying degrees of mental retardation and may also have other birth defects such as heart and intestinal abnormalities.

Neural tube defects

Neural tube defects (NTDs) occur in about 1 to 2 of every 1,000 live births. The neural tube in the fetus develops into the spinal cord and the brain. When the neural tube and the surrounding bony structures do not form properly, NTDs such as spina bifida and anencephaly may result. Spina bifida results when the backbone fails to form properly and the spinal cord may protrude from the back. This can damage the nerves controlling the lower part of the body. Individuals with spina bifida have varying degrees of leg weakness and paralysis and sometimes bladder and bowel problems. Some babies with spina bifida also have a collection of fluid on the brain called hydrocephalus. Hydrocephalus can be treated surgically, but may lead to learning problems. Anencephaly results when the upper end of the neural tube does not form properly, leading to severe malformations of the brain and skull. Babies with anencephaly are either stillborn or die shortly after birth.

Neural tube defects result from a combination of genetic and environmental factors, many of which are unknown. Neural tube defects may occur without other birth defects or can be a part of other conditions (such as trisomy 18). Neural tube defects form early, between the 17th and 30th day after conception. Some pregnancies affected by neural tube defects result in miscarriage or stillbirth.

Trisomy 18

Trisomy 18 occurs in about 1 in 8,000 births. The chance that a pregnancy is affected with trisomy 18 is higher in mid-pregnancy (about 1 in 2,400), however, a high percentage of these pregnancies result in miscarriage. The risk of a trisomy 18 pregnancy also increases with the age of the mother. Trisomy 18 results from having three copies of chromosome 18 in each cell instead of two. Trisomy 18 is more severe than Down syndrome. The clinical features of trisomy 18 include severe mental retardation, heart, lung and kidney abnormalities, and a significantly decreased life span. Only about 5 percent of children born with trisomy 18 survive beyond the first year of life.

How Is Maternal Serum Screening Done?

To receive maternal serum screening you must have your blood drawn between weeks 15 and 22 of your pregnancy. This blood sample then goes to a laboratory where technicians measure proteins in your blood that are produced by the unborn baby and/or the placenta. The proteins that are measured include: alpha-fetoprotein (AFP), unconjugated estriol (uE3), human chorionic gonadotropin (hCG) and inhibin. To determine the risk estimate for your pregnancy, these protein measurements are combined with other information about your pregnancy including how far along you are in your pregnancy, your age, weight, race and diabetic status, and whether you are carrying twins or a single baby. It is important that this clinical information be accurate. Absent or inaccurate information can result in incorrect results.

Elevations and/or decreases in the amounts of the proteins measured may be associated with an increased risk for Down syndrome, NTDs or trisomy 18. Table 1 shows the pattern of the proteins in the three conditions and whether the levels are typically higher or lower in affected pregnancies.

Table 1. Patterns of proteins in affected pregnancies

	AFP	Estriol	hCG	Inhibin
Neural tube defects	↑	–	–	–
Down syndrome	↓	↓	↑	↑
Trisomy 18	↓	↓	↓	–

Results of maternal serum screening are usually available within one week after the blood sample is collected. A member of your health care team will provide you with your screening results.

What Do Maternal Serum Screening Test Results Mean?

Results of maternal serum screening are referred to as either screen positive or screen negative, along with a numerical estimation of risk (1 in X). Laboratory determined cutoff values are used to classify a risk as either screen positive or negative. For example, the cutoff value for Down syndrome is 1 in 270, and for neural tube defects the cutoff is an AFP value that is more than 2.5 times higher than the expected value at a given gestational age. Any value higher than the cutoff is classified as screen positive. Trisomy 18 risks are reported when they are greater than or equal to a risk of 1 in 100.

Screen positive results

A screen positive result indicates that the value(s) obtained from the screening process exceeds the specified cutoff. A screen positive result does not mean that your child has the condition. Rather, it indicates your risk level for having a baby with one of the above birth defects may warrant further testing. If your result is screen positive, you will have the option to pursue further diagnostic testing. Approximately 1 out of every 15 women screened will have a screen positive result. Most of these women will not have an affected child. The chance of having a screen positive result for Down syndrome increases with the age of the mother.

Screen negative results

A screen negative result indicates that your risk for having a child with Down syndrome, or a neural tube defect is below the specified cutoff. For example, for Down syndrome it is less than 1 in 270. A screen negative result does not provide a guarantee that your child will not have Down syndrome or a neural tube defect. Because this is a screening process, not all affected pregnancies can be identified. Screening will detect about 3 out of 4 pregnancies affected with Down syndrome or an open neural tube defect, and almost all pregnancies with anencephaly. Maternal serum screening will miss about 1 in 4 affected pregnancies.

What Happens if My Maternal Serum Screen Is Positive?

Maternal serum screening is not a diagnostic test that gives you a yes-or-no answer about the presence of a birth defect. There are a variety of reasons (unrelated to the health of your baby) why your screen may be positive. The most common reasons are: incorrect pregnancy dating, multiple pregnancies (twins or triplets) and normal marker variation. If you have not already had an ultrasound to date your pregnancy, this will typically be offered at this time.

A dating ultrasound can be used to detect a fetal heartbeat, determine the gestational age of your pregnancy and determine how many fetuses are present. If your dating differs significantly or if you are carrying multiple fetuses your screening results will need to be reinterpreted using the new information.

If the dating ultrasound confirms your pregnancy dating, you may be offered a more detailed high-resolution ultrasound. High-resolution ultrasound can identify many cases of open neural tube defects. In addition, it can be used to screen for other physical features associated with Down syndrome or trisomy 18 (such as heart, intestinal and kidney abnormalities). It is not possible to make a diagnosis of Down syndrome or trisomy 18 from an ultrasound scan. If other findings associated with the conditions are seen, this provides further indications for diagnostic testing; however, the absence of other findings does not rule out the conditions.

If your screening result remains positive after the dating ultrasound and the high-resolution ultrasound, you will be offered more accurate diagnostic testing such as amniocentesis.

Amniocentesis

In amniocentesis, a needle is used to withdraw a few teaspoons of fluid from the amniotic sac surrounding the developing fetus. Ultrasound is used to help your doctor guide the needle safely. Amniotic fluid contains cells from the fetus. These cells are grown and analyzed to determine if Down syndrome or trisomy 18 is present. It can take up to 2 to 3 weeks to receive results, although preliminary results are often available earlier. Biochemical testing of the amniotic fluid can also be used to diagnose neural tube defects. Amniocentesis is 99 percent accurate at determining if Down syndrome or trisomy 18 is present. Amniocentesis does not provide information about other types of birth defects. Thus, even with a normal amniocentesis result, some babies may still have a birth defect.

It is important to know that the amniocentesis procedure has a miscarriage rate of approximately 0.2 percent (1 in 500) to 0.3 percent (1 in 300). This means that for every 300–500 women having an amniocentesis, one will have a miscarriage as a result of the procedure. Your health care provider will discuss the risks, limitations and benefits of the amniocentesis procedure with you.

If invasive testing is declined, another option is the cfDNA screening test. Ask your health care provider for more information.

What if a Birth Defect Is Shown to Be Present?

If a birth defect is detected, your health care provider will give you as much information as possible about the condition and discuss the options available to you. Counseling, support groups, and other community resources are available to help you in your decision-making process.

Is Maternal Serum Screening Right for Me?

Maternal serum screening is optional. It is your decision whether you would like to have the screening. Some women decide the screening information would not be useful to them and choose not to pursue it. Others feel they may gain reassurance from the results. For the few pregnancies in which a birth defect is present, early detection allows a person to discuss all options and plan for a special delivery when necessary. Each person's decision is a personal one based on individual values and beliefs and on how they might use the information.

If you have questions regarding this information, discuss them with a member of your health care team.

This material is for your education and information only. This content does not replace medical advice, diagnosis or treatment. New medical research may change this information. If you have questions about a medical condition, always talk with your health care provider.

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