



About Maternal Serum Screening

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Introduction

As part of your prenatal care, your doctor will offer you a blood test during the second trimester of pregnancy which measures alpha-fetoprotein (AFP), human chorionic gonadotropin (hCG), unconjugated estriol (uE3), and sometimes dimeric inhibin A (DIA). The purpose of this test is to identify pregnant women who may be at increased risk for having a baby with either Down syndrome, trisomy 18, or an open neural tube defect (ONTD).

Down syndrome, trisomy 18, and neural tube defects are not in my family. Why do I need to have this test?

These birth defects are usually **not** inherited and are usually not present in a person's family. However, every pregnant woman has a chance to have a baby with one of these health problems. This is true regardless of how many healthy children they may already have.

The second trimester maternal serum screening (MSS) blood test is a **screening** test, to determine who in the pregnant population should be offered additional studies to make sure their baby is healthy. About 1 in every 740 babies born has Down syndrome, about 1 out of every 1000 babies born will have an open neural tube defect (either anencephaly or spina bifida), and between 1 in 5000 and 1 in 6000 babies will be born with trisomy 18. Signs suggestive of Down syndrome, trisomy 18, and open neural tube defects cannot always be seen on ultrasound.

The chance for a baby to be born with Down syndrome or trisomy 18 increases as a woman becomes older. (Even so, the majority of babies with Down syndrome are born to women under 35 years of age). Women 35 years of age or over should not rely solely on the second trimester MSS blood test to detect Down syndrome and trisomy 18. Due to the higher risk of Down syndrome and trisomy 18 in this group based on age alone, women 35 years or older at delivery should consider amniocentesis or chorionic villus sampling (CVS) to determine whether their unborn baby has normal chromosomes.

Nine out of ten babies born with ONTDs are born to families who do **not** have a previous family history for ONTDs. For families who already have relatives with some type of neural tube defect, the chance for their unborn baby to have an ONTD **may be higher** than the general population risk. Genetic counseling is recommended for these families to best assess their risk and options for testing, as well as informing patients of specific vitamins (folic acid) found to reduce the recurrence risk for this group of birth defects.

How is maternal serum screening done?

A small sample of blood is obtained from the mother's arm between 15 and 20 weeks of pregnancy and the amounts of AFP, hCG, uE3, and sometimes DIA are measured in the lab. The results are then sent to your doctor once the testing is complete.

What does the maternal serum screening testing measure?

The test measures either three or four proteins that are made by the baby and the placenta: AFP, hCG, uE3, and sometimes DIA. The number of proteins tested for depends on the laboratory performing the testing. When three proteins are tested the test is sometimes called the "triple screen". When four proteins are tested the test is sometimes called the "quad screen".

AFP, or alpha-fetoprotein, is made by the baby's liver during the second trimester of pregnancy and is normally filtered into the fluid surrounding the baby (amniotic fluid), and finally crosses the placenta

into the mother's blood. Adults usually do not produce AFP in measurable quantities (unless they have a certain medical problem), so that AFP comes strictly from the baby (or babies).

HCG, or human chorionic gonadotropin, is produced only by the placenta, or afterbirth. Like AFP, it is also found in the mother's blood during pregnancy.

UE3, or unconjugated estriol, comes from both the baby's liver and the placenta. It, too, is a substance strictly related to pregnancy.

DIA, or dimeric inhibin A, comes from the placenta. Levels in maternal serum remain relatively constant through the 15th-18th week of gestation in normal pregnancies.

The normal values of each of these substances changes with each week of pregnancy. This is why the results are expressed in multiples of the median, or MOMs. The MOM tells how close your value is to the median (average) value for that week of pregnancy. For example, "0.5 MOMs AFP" means there is **half** as much AFP as is usually found during that week of pregnancy, while "2.5 MOMs AFP" means there is **two and one half times** the usual amount of AFP for that particular week of pregnancy.

About Down syndrome

Down syndrome is a disorder resulting from the presence of an extra #21 chromosome. A chromosome is a structure in your cells that contains your inherited material, or genes. Humans usually have 46 total chromosomes in every cell of their body. Having too many or too few chromosomes results in birth defects, health problems, and frequently mental retardation or learning problems. There have been several hundred different types of chromosome abnormalities seen in humans, with clinical outcomes ranging from near normal to life threatening. Children with Down syndrome, for example, have specific facial features and some level of mental retardation. They may also be born with a heart problem, gastrointestinal tract (stomach) problem, or other birth defects.

In a pregnancy where the baby has Down syndrome, the AFP and uE3 tends to be somewhat lower than average, while the hCG and DIA tends to be elevated.

About Neural Tube Defects

Neural tube defects result when the neural tube, or developing spine, fails to close properly. During pregnancy, the human brain and spine begins as a flat plate of cells which "rolls" into a tube, called the neural tube. If all or part of the neural tube fails to close, leaving an opening, this is known as a "neural tube defect" or NTD. This opening may be left exposed, or can be covered with bone or skin. There are two main types of NTDs: anencephaly and spina bifida. Anencephaly occurs when the neural tube fails to close at the base of the skull, causing a serious defect of brain development. Babies with anencephaly are stillborn or usually live for only a few days.

Spina bifida occurs when the neural tube fails to close along the spine, often damaging the spinal cord or tissue which surrounds the spinal cord. Babies born with spina bifida may have minimal or transient (temporary) problems, or, may have permanent, often serious, physical problems. These may include paralysis, lack of bowel and bladder control, hydrocephaly (water on the brain), and mental retardation. In most cases one or more surgeries may be necessary.

In a pregnancy where a baby has an ONTD, the AFP "leaks" out of the opening in the back or skull, causing extra AFP to cross the placenta into the mother's blood during pregnancy. Therefore, the value of AFP is higher than average.

About trisomy 18

Trisomy 18 (Edward's syndrome) is caused by the presence of three #18 chromosomes. Unfortunately, the presence of the extra #18 chromosome prevents proper development of the baby's brain, heart, and other organs, but in some cases these are too subtle to be seen on ultrasound. Many

pregnancies with trisomy 18 are miscarried. Those babies which go full term are born with many health problems, which are usually incompatible with long term survival.

In a pregnancy where the baby has trisomy 18, the AFP, hCG, and uE3 tend to be somewhat lower than average.

What other factors can affect this test?

- **The dates of your pregnancy.** The levels of AFP, hCG, uE3, and DIA that are considered “normal” are different for each week of pregnancy. Estimating the week of pregnancy from the first day of your last menstrual period (called LMP) sometimes results in inaccurate dating of a pregnancy. Ultrasound examination can correct this discrepancy, and the AFP, hCG, uE3, and DIA levels can then be recalculated.
- **The number of babies.** Two (or more) babies generally produce higher levels of AFP, hCG, uE3, and DIA.
- A woman’s weight at the time of the test, her age, her race, her family history, and whether or not she has insulin dependent diabetes, will also be factored into calculating her maternal serum screening test results.

If my maternal serum screening test is abnormal, does this mean my baby has one of these health problems?

No, because the maternal serum screening test is a **screening** test, which means it is **NOT** diagnostic. On average, the maternal serum screening test will detect 69% - 81% of babies with Down syndrome and 80% of babies with an open neural tube defect. Exact detection rates for each condition depends on the number of proteins tested for and the particular laboratory performing the testing. **A normal pregnancy is still the most likely outcome, even after an abnormal maternal serum screening test.**

If the maternal serum screening test results are abnormal, what happens next?

Your doctor may recommend one or more of the following:

- **Repeat the MSS blood test.** This is usually only done if the AFP is elevated, or if the test was performed too early in your pregnancy.
- **Detailed ultrasound examination.** This ultrasound can help to properly date the pregnancy and/or carefully examine the physical features of the baby.
- **Genetic counseling.** A genetic counselor can thoroughly explain your MSS test results and discuss further testing options.
- **Amniocentesis.** If the ultrasound does not provide an explanation for the MSS test results, amniocentesis can be performed to examine the baby’s chromosomes.

It is important to remember that the MSS blood test is a screening test, and that most of the time pregnancies with an abnormal MSS blood test will result in the delivery of a normal baby. In addition, MSS testing will not detect all babies with these defects.

What if my baby does have a problem?

If a health problem is found in your unborn baby by additional testing, your doctor will discuss what this information means for your pregnancy and your options. Your doctor may also refer you to speak with a genetic counselor or other specialists for further information regarding your baby’s findings. If you have any questions about this information, or if you would like to make an appointment for genetic counseling, call Emory Genetics at 1-800-366-1502.