While most babies are born healthy, approximately 3-5% of babies born each year will have birth defects. Prenatal testing can provide women with information about the health of their unborn baby. Maternal Serum Screening (MSS) is one such screening test which can alert a woman and her obstetrician that a pregnancy may have an increased chance for certain types of birth defects. Approximately 95% of women tested will have a negative (normal) screening result. Of those women with an a positive (increased risk) screening result, only a small number of these pregnancies will be found to have a birth defect after further testing. In some cases, a pregnancy with a birth defect will not be identified by MSS.

MSS is a blood test which measures the amounts of three or four chemicals that are normally present in the mother’s blood during pregnancy: alpha-fetoprotein (AFP), human chorionic gonadotropin (hCG), unconjugated estriol (uE3), and dimeric inhibin (DIA). In some pregnancies, low and/or high levels of these pregnancy proteins suggest that the chance for a birth defect is increased. MSS should be drawn before the 21st week (5th month) of pregnancy, usually between 15 and 18 weeks from the first day of the last menstrual period. A result is considered screen positive when the chemicals indicate a significant risk for Neural Tube Defect, Down syndrome, or Trisomy 18. Since some unaffected pregnancies may be screen positive, further counseling and testing is suggested.

WHAT DOES IT MEAN TO BE SCREEN POSITIVE FOR NEURAL TUBE DEFECT?
A neural tube defect (NTD) is an opening of the spine (spina bifida) or skull (anencephaly) which could result in serious problems for a baby, including paralysis, intellectual disabilities, or even death. The specific cause for these types of birth defects is not yet known. Approximately 1 in every 750 babies in South Carolina has a neural tube defect. In most of these cases, there is no family history of NTD.

When a fetus (unborn baby) has an open neural tube defect, there is usually an elevated (high) level of AFP in the fluid around the fetus (amniotic fluid) and in the mother’s blood. Approximately 85% of open NTD in a fetus can be identified by the AFP screening test. A result is considered “screen positive for NTD” when the level of AFP in the mother’s blood is higher than usual. There are several reasons the level of AFP may be higher in the mother’s blood than an open NTD. A pregnancy which is further along than expected (for example, 18 weeks rather than 15 weeks) will often have a higher level of AFP. A twin or triplet pregnancy may also have a higher level of AFP in the mother’s blood. Less frequently, birth defects other than open NTD or pregnancy complications such as poor fetal growth or preterm labor may be found when the AFP level is high.

Several tests are recommended when MSS is positive for neural tube defects. In some cases, a repeat AFP screening may be considered. Ultrasound may be suggested to check the growth of the fetus and to rule out a twin or triplet pregnancy. Ultrasound can be useful in detecting some birth defects such as NTD. When ultrasound confirms the due date and does not detect twins or triplets, amniocentesis is suggested to measure the amount of AFP in the amniotic fluid, since this is a more reliable test for open NTD than the blood test.

WHAT DOES IT MEAN TO BE SCREEN POSITIVE FOR DOWN SYNDROME?
Down syndrome is one of the most common causes of intellectual disability, affecting one in every 700 babies born. Babies with Down syndrome have distinctive physical features with mild to moderate intellectual disabilities and may also have other birth defects such as heart problems. Down syndrome, also called Trisomy 21, is a chromosome condition. In most cases, when a baby is born with Down syndrome, there is no previous family history of this condition. Although the chance of having a baby with Down syndrome increases with maternal age, babies with Down syndrome are born to women of all ages. Women who will be 35 years or older at the time of delivery may consider other prenatal tests instead of MSS due to the increased chance of any chromosome condition. Both chorionic villus sampling in the third month and amniocentesis in the fourth or fifth month can test for Down syndrome as well as other serious chromosome conditions. A relatively new blood test called non-invasive prenatal testing (NIPT) can also screen high risk pregnancies for Down syndrome with near the same reliability as CVS or amniocentesis, but without the risk of miscarriage. Women who are over 35 and choose to proceed with MSS should be aware that there is an increased chance for the screen to be “positive” based on their age alone.
Approximately 65% of pregnancies affected with Down syndrome will have values of AFP, hCG, and uE3 that cause the pregnancy to be “screen positive for Down syndrome”. Adding DIA to AFP, hCG, and uE3 increases the detection rate to approximately 70% while decreasing the screen positive rate. MSS is considered “screen positive for Down syndrome” when the levels of the chemicals indicate a significant risk for Down syndrome of greater than 1 in 270 (greater than the risk for the average 35 year old).

When a pregnancy is identified as “screen positive for Down syndrome,” ultrasound, amniocentesis and/or NIPT are suggested as follow-up. A pregnancy that is not as far along as expected (for example, 15 weeks instead of 18 weeks) will often have low AFP and uE3 values. When ultrasound confirms the expected due date, amniocentesis is the most accurate test to confirm or rule out the diagnosis of Down syndrome. Some patients may opt to have NIPT or ultrasound only with the understanding that these screenings may be less reliable than amniocentesis.

### SUMMARY OF RISK ANALYSIS

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<tr>
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<th>uE3</th>
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<td>------</td>
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<td>-----</td>
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<td>Low</td>
<td>------</td>
<td>------</td>
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**WHAT DOES IT MEAN TO BE SCREEN POSITIVE FOR TRISOMY 18?**

Trisomy 18 is a chromosome condition that is less common than Down syndrome. It is a very serious condition which includes birth defects, severe intellectual disabilities, and early death. Trisomy 18 does not usually run in families.

A MSS is considered “screen positive for Trisomy 18” when levels of the AFP, hCG, and uE3 are low in the mother’s blood. Most pregnancies with low levels do not have Trisomy 18. Approximately 70% of pregnancies with Trisomy 18 will have a “positive” screen. MSS is considered “screen positive for Trisomy 18” when there is greater than a 1 in 100 chance for the pregnancy to be affected with Trisomy 18. Ultrasound, amniocentesis and/or NIPT are suggested tests when a pregnancy is identified as screen positive for Trisomy 18.

**WHAT IS AMNIOCENTESIS?**

Amniocentesis is a procedure used to remove a small amount (2-3 tablespoons) of the fluid from the water bag surrounding the fetus. The level of AFP in this fluid is measured to determine if there is a neural tube defect. The cells in the fluid are tested for chromosome conditions such as Down syndrome and Trisomy 18. Amniocentesis is a safe procedure, but does carry a small risk for miscarriage. The procedure is performed by an experienced obstetrician using ultrasound guidance.

**WHAT IS GENETIC COUNSELING?**

When a woman has a positive MSS result, genetic counseling is recommended to review her results and to discuss the choices of testing available. The goal of genetic counseling is to provide the patient with as much information as necessary to make the choices that are best for her. Learning that a MSS result is positive can cause feelings of worry, fear and helplessness in a patient. In most cases, the information provided by the genetic counselor, doctor, nurse or prenatal tests such as ultrasound and amniocentesis can relieve many of the patient’s concerns and provide her reassurance about the health of the pregnancy. When a birth defect or chromosome condition is diagnosed, the genetic counselor and doctor inform the patient about the condition and discuss the patient’s choices for further testing, type of delivery and treatment options.
HOW ACCURATE IS MATERNAL SERUM SCREENING?
As a screening test, MSS identifies if a pregnancy is at a higher risk for NTD, Down syndrome, or Trisomy 18. Of all pregnancies that are affected by one of these conditions, 85% of those with NTD, 70% of those with Down syndrome, and 70% of those with Trisomy 18 will be identified as high risk by MSS. Amniocentesis, which is often recommended as the diagnostic follow up, is highly accurate at determining if any of these conditions are present.

Approximately 5% of women tested by MSS will have a positive screening result. Of those women with a positive screening result, only a small number of these pregnancies will actually be found to have a NTD or chromosome condition after further testing. In some cases, a pregnancy with a birth defect will not be identified by the screening test.

WHO SHOULD HAVE THE TESTING?
Maternal serum screening is usually offered to all women during their pregnancy who are under the age of 35 years at the expected due date and do not have a family history of a previous child with NTD, Down syndrome or Trisomy 18. Women who are 35 years or older and those with a family history of any of these conditions are often offered the choice of genetic counseling and amniocentesis rather than MSS.

The decision to have MSS is best made by the patient. You and your husband/partner should decide if you would like to learn whether your pregnancy is at risk to be affected by an open NTD, Down syndrome or Trisomy 18 before delivery. For some, this information is important in making decisions about the best course of treatment or management of the pregnancy. For most, a screen negative result offers some level of reassurance that the chances of these conditions are not increased in their pregnancy.