While most babies are born healthy, approximately 3-5% of babies born each year will have a birth difference or genetic condition. First trimester screening is one screening test which can alert a woman and her doctor that a pregnancy may have an increased risk for certain types of genetic conditions. Specifically, first trimester screening makes use of a blood test and ultrasound. The results of the blood screening and ultrasound can be used to estimate the chance that a pregnancy will have a chromosome condition, specifically, Down syndrome, Trisomy 18 or Trisomy 13 (trisomy 18/13). Down syndrome, trisomy 18 and Trisomy 13 occur when there is an extra chromosome in every cell and they involve birth defects and varying levels of intellectual disability. Babies with Down syndrome have distinctive physical features with mild to moderate intellectual disability and may also have other birth defects such as heart problems. Trisomy 18 and Trisomy 13 are less common than Down syndrome but they are serious conditions that include birth defects, severe disability, and shortened lifespan.

First trimester screening can have either one or two parts:

1. A blood sample from the patient is drawn between 9 and 13 weeks after the last menstrual period. Two proteins normally found in every pregnancy, hCG and PAPP-A, are measured from the patient’s blood samples. The levels of these pregnancy proteins are used to predict if the chances for these three chromosome conditions are increased or decreased.

2. An ultrasound, done by a certified ultrasonographer, measures nuchal translucency (NT) which is a fluid-filled space in the back of the baby’s neck between the 11th and 13th weeks. All pregnancies have some fluid collection behind the neck. In most pregnancies with chromosome conditions, the nuchal translucency measurement is larger than average. An increased nuchal translucency suggests a higher chance for a chromosome condition in the pregnancy. A nuchal translucency can be successfully measured 95% of the time.

If only the blood screen is performed, 60-70% of pregnancies with Down syndrome and Trisomy 18 will be detected. If both the blood sample and the nuchal translucency are measured, then approximately 90% of pregnancies with Down syndrome and 95% of pregnancies with Trisomy 18/13 will be detected. Nuchal translucency measurement with or without the blood sample may be useful in cases of twins or triplet pregnancies although the detection rates are somewhat lower.

What does it mean to be screen positive?
Each woman’s screen will give her a specific risk for Down syndrome and Trisomy 18/13 (ranging from less than 1% to greater than 10%) based on the pattern of her pregnancy proteins, her nuchal translucency measurement (see Table 1), and her age. If the screening test shows an increased chance for either Down syndrome or trisomy 18/13, the result is interpreted as "screen positive." A positive screen is not diagnostic, but suggests that there is an increased risk for birth defects and follow-up is recommended.

Table 1. Patterns used to determine increased risk for Down syndrome and Trisomy 18/13 in first trimester screening

<table>
<thead>
<tr>
<th></th>
<th>PAPP-A</th>
<th>Free-β hCG</th>
<th>Nuchal Translucency</th>
<th>Screen Positive when Risk of Condition is greater than:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Down syndrome</td>
<td>↓</td>
<td>↑</td>
<td>↑</td>
<td>~1 in 300</td>
</tr>
<tr>
<td>Trisomy 18/13</td>
<td>↓</td>
<td>↓</td>
<td>↑</td>
<td>1 in 150</td>
</tr>
</tbody>
</table>

When a pregnancy is identified as "screen positive" and ultrasound confirms the expected due date, follow up testing is offered to rule out Down syndrome, trisomy 18 and trisomy 13 or to provide a definite diagnosis. There are three options for follow up testing: chorionic villus sampling, amniocentesis and/or non-invasive prenatal testing. Genetic counseling is helpful to discuss the options for further testing/screening in the pregnancy including their benefits, limitations and risks.
What is CVS?
Chorionic Villus Sampling (CVS) is a procedure that samples a small piece of the developing placenta, or chorionic villi, in order to learn more about the chromosomes of the developing baby (fetus). Studying the cells from the placenta allows chromosome conditions to be detected. Sample tissue is usually obtained by passing a thin tube through the vagina and the cervix (opening to the womb). In some cases, CVS can be done using a needle that is inserted through the abdomen. CVS is performed in the first trimester of pregnancy between the 11th and the 13th week. CVS is a safe procedure, but does carry some risk for miscarriage (1/50-1/100). The procedure is performed by an experienced obstetrician using ultrasound guidance.

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 cells in the fluid are tested for chromosome conditions such as Down syndrome, trisomy 18 and trisomy 13. The level of AFP (a certain chemical) in this fluid is measured to determine if there is a neural tube defect (an opening alone the spine or brain of a developing fetus). Amniocentesis is a safe procedure, but does carry a small risk for miscarriage (less than 1 in 300). The procedure is performed by an experienced obstetrician using ultrasound guidance.

What is non-invasive prenatal testing?
Non-invasive prenatal testing (NIPT) is a blood test which analyzes the amount of cell-free fetal DNA in the mother’s blood. DNA is the genetic material that makes up chromosomes. This relatively new test can check for Down syndrome, trisomy 18 and trisomy 13 with near the same accuracy of CVS and amniocentesis without the risk of miscarriage. Positive results from NIPT should be confirmed by CVS or amniocentesis. A thorough review of the benefits and limitations of all the testing options can be discussed with a genetic counselor prior to making a decision for further testing following a positive first trimester screening result.

What is genetic counseling?
When a woman has a positive first trimester screening result, genetic counseling is recommended to review her results and discuss the available testing options. 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 first trimester screening result is positive can cause feelings of worry, fear, or helplessness in a patient. In most cases, the information provided by the genetic counselor, doctor, nurse or prenatal tests such as ultrasound, chorionic villus sampling, amniocentesis or NIPT can relieve many of the patient’s concerns and provide her reassurance about the health of the pregnancy. When a chromosome condition or birth defect is diagnosed, the doctor and genetic counselor inform the patient about the condition and discuss the patient’s choices for further testing, type of delivery and treatment options.

What other tests are suggested for women who have increased nuchal translucency?
If CVS, amniocentesis or NIPT studies are normal, sometimes the explanation for the increased measurement can be the presence of a heart defect. A detailed ultrasound of the heart, called a fetal echocardiogram, can be done later in pregnancy (usually between 20 and 24 weeks) to help determine if there is a heart defect. A second trimester ultrasound at 18-22 weeks is also suggested to screen for other birth defects that may be related to increased nuchal translucency. Many times the chromosomes are normal and an explanation is not found on ultrasound or after birth, and the child is born without a birth defect.

What follow-up is recommended after normal first trimester screening?
If first trimester screen result does not show an increased risk, second trimester screen (Maternal Serum Screen) for Down syndrome, trisomy 18 and trisomy 13 is not recommended. Separate screening for neural tube defects (NTD) in the second trimester is recommended (ideally between 15 and 18 weeks). Neither first trimester screening nor CVS screens for NTDs. Neural tube defects are birth defects that occur when the spinal cord does not close properly. A protein made by the pregnancy, but present in the maternal blood, maternal serum alpha-fetoprotein (MSAFP), is measured. Women with a high level of MSAFP are considered screen positive for neural tube defects. As a normal part of pregnancy, it is also recommended that an ultrasound be performed in the second trimester to assess the growth and development of the baby.

How does first trimester screening compare with second trimester screening?
When first trimester screening is done using both the blood test and the ultrasound for nuchal translucency, the detection rate for Down syndrome, trisomy 18 and trisomy 13 is higher than with traditional second trimester screening (see Table 2).
Table 2. Comparison of first trimester screening detection rates versus second trimester screening

<table>
<thead>
<tr>
<th></th>
<th>Down syndrome</th>
<th>Trisomy 18/13*</th>
<th>Neural Tube Defects</th>
<th>False Positive Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>First Trimester</strong></td>
<td>-90%</td>
<td>95%</td>
<td>---</td>
<td>&lt;5%</td>
</tr>
<tr>
<td>(PAPP-A/hCG and NT)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Second Trimester</strong></td>
<td>70-80%</td>
<td>70-80%</td>
<td>&gt;85%</td>
<td>4-5%</td>
</tr>
<tr>
<td>(Maternal Serum Screen AFP/hCG/uE3/DIA)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Second trimester screening does not include Trisomy 13

**Who should have the testing?**
First trimester screening is offered to all women who are in the first trimester of pregnancy without a family history of previous children with Down syndrome or Trisomy 18/13. Women who are over 35 or women have a family history of Down syndrome, trisomy 18, trisomy 13, or other chromosome conditions are usually offered genetic counseling and diagnostic tests such as CVS or amniocentesis as well as the option of first trimester screening.

The decision to have screening is best made by the patient. The patient and her husband/partner should decide if they would like to learn if the pregnancy is at an increased risk for having a chromosome condition. 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 chance of these conditions is not increased in their pregnancy.

If you have more questions about first trimester screening, talk to your doctor or contact a genetic counselor with USC Department of Obstetrics and Gynecology, 803-545-5775.

**Schedule for Prenatal Screening Tests:**

- 9weeks -- 13 weeks 6 days: 1st Trimester blood screen (hCG/PAPP-A)
- 11 weeks -- 13 weeks 6 days: Ultrasound Nuchal Translucency measurement
- 14 weeks -- 21 weeks 6 days: AFP only for spina bifida (blood test)
- **Or** Maternal Serum Screening (AFP/hCG/uE3/DIA) *(if first trimester screen is not performed)*
- 18 weeks -- 22 weeks: Ultrasound to screen for general development

**Schedule for Diagnostic Prenatal Tests:**

- 10 weeks -- 13 weeks: Chorionic Villus Sampling
- 16 weeks -- 20 weeks+: Amniocentesis
- 10 weeks -- 36 weeks: Non-invasive prenatal testing (NIPT)

*Patients interested in first trimester screening with both the blood screen and nuchal translucency should schedule their appointment between 11-13 weeks gestation. Those who might be interested in CVS if their screen came back positive would ideally be scheduled at 11 weeks gestation.*