OPEN ARMS
MIDWIFERY, LLC

Prenatal Screening and Diagnostic Tests

The information below is in-depth and may take time to absorb. My hope is not to overwhelm, but to educate, allowing you to make an informed decision about prenatal testing. I believe it is important to understand the testing before you go into it. Many folks see early screening tests as a Pandora's Box because there can be so many personal, emotional and social impacts once the results of the test are tallied up.

Before beginning, it is VERY important to differentiate between a *screening* test and a *diagnostic* test.

- A screening can tell an individual woman whether she has a higher-than-average chance of carrying an affected baby. Screenings can be done in many ways. These tests either look for possible signs of a syndrome or calculate the risk for a syndrome. Screenings cannot determine if a baby has a syndrome – they can only indicate how likely it is for the baby to be affected with a given condition. Screening tests can have high false positive rates.
- A diagnostic test will actually inform if a condition or syndrome is present. Women can use the results of screening tests to decide whether or not to do a diagnostic test. Limiting diagnostic tests is desirable because they carry their own risks, especially the risk of causing miscarriage. It is desired to have a low false positive rate in a diagnostic test.

Screening Tests

Ultra-Screen® (Nuchal Translucency) – Ultra-Screen® combines ultrasound measurement of the fluid accumulation behind the neck of the fetus (nuchal translucency) with maternal serum markers (via maternal blood sample). Ultra-Screen® begins with an ultrasound examination between 11 weeks and 13 weeks, 6 days gestation. Crown-Rump Length and nuchal translucency are measured during the ultrasound.

- Crown Rump Length (CRL) is the length of the fetus from the crown of its head to its rump. It is measured for accurate pregnancy dating. At this point in pregnancy, the CRL is generally the same for all fetuses of the same gestational age. Later in pregnancy, however, CRL is not a reliable measure of gestational age because it varies greatly between individuals due to genetic effects on fetal growth.
- Nuchal translucency (NT) is fluid accumulation behind the neck of the fetus. NT is a specific marker for chromosomal aneuploidy. Aneuploidy is a genetic abnormality where the fetus has too many or too few chromosomes. Aneuploidy causes conditions such as Down syndrome.

At the time of the ultrasound exam, a dried blood sample is collected via finger stick. The lab analyzes the blood sample for free Beta human chorionic gonadatropin (hCG) and Pregnancy Associated Plasma Protein-A (PAPP-A). Patient specific risk for Down syndrome and Trisomy 18 is then calculated based on the patient's age, nuchal translucency measurement, free Beta hCG and PAPP-A.

Ultra-Screen® has been shown to detect 75-91% of Down syndrome pregnancies at a 5% false positive rate and 98% of Trisomy 18 pregnancies with a 1% false positive rate. These numbers come from a combination of the ultrasound, blood sample hormonal calculation. Non-branded versions of this test often also combine results from the QMS listed below to obtain risk calculations. It is important to complete all components in order to yield these high results. NT alone can only provide 60-70% detection of infants with DS, Trisomy 18, Trisomy 13 or heart defects.

Quad Marker Screen – One of the most common prenatal screening tests performed is a second trimester maternal serum screen known as the Quad Marker Screen (QMS). It a blood test completed between 15-19 weeks gestation. The test evaluates your risk for having a baby with a neural tube defect, Down syndrome (DS, Trisomy 21) and other genetic syndromes. Your calculated risk is then compared to other women your age.

A negative result does not mean you have an UNAFFECTED baby and a positive result does not mean you have and AFFECTED baby. Only 1 in 50 women who test positive will actually have an affected baby; the remaining 49 have had a "false positive". The detection rate for this test is between 60-70%. This means that the test will fail to detect 1 in 3 affected babies. Spina Bifida is the condition most commonly found with this test, and the detection rate is 70%.

The test looks at 4 hormones in the maternal blood:

- Alfa-fetal protein (AFP) - a protein produced by the baby's liver
- Unconjugated Estriol (UE) - a protein produced in the placenta and baby's liver
- Human Chorionic Gonadoptrophin (hCG) - a hormone produced by the placenta. Pregnancy tests also test for this hormone.
- Inhibin-A - a hormone produced by the placenta

The risk for having an affected child is calculated by comparing the level of these hormones in your blood to normal levels for pregnant women at the same point in pregnancy. The expected amounts of these hormones vary depending on how far along the pregnancy is. Therefore, knowing the exact gestation of a pregnancy is important for calculating the results. Dating of a pregnancy is done either by last menstrual period (LMP) or an early dating ultrasound. The most common reason for a positive test result is incorrect dating of the pregnancy.

High AFP levels may indicate that the baby has an open neural tube defect. High AFP levels may also indicate that the fetus is older than was thought or that the woman is expecting twins. Lower than normal AFP levels could indicate that a woman is at higher risk for having a baby with Down syndrome.

Levels of hCG and Inhibin-A are higher than normal when a woman has an increased risk of having a baby with Down syndrome. Lower than normal levels of Estriol may also indicate that a woman is at high risk for having a baby with Down syndrome.

Fetal Anomaly Scan (FAS, also known as a 20 week ultrasound) – Most women are offered a detailed ultrasound scan at about 20 weeks to see if your baby is developing normally. This is known as the Fetal Anomaly Scan (FAS).

The vast majority of babies are normal. However all women, whatever their age, have a small chance of delivering a baby with a physical or a mental problem. Many such abnormalities can be diagnosed and ruled out with the FAS. Reasons to have this scan include:

• To reassure you that your baby is likely to be normal
• To confirm the gestational age of your pregnancy
• To confirm the number of babies and, if twins, whether they are identical or not
• To detect birth defects, such as a spina bifida or heart problems
• If you are concerned about the chances of chromosome problems like Down syndrome this scan can search for subtle markers that may suggest a higher risk that your baby may have one of these problems
• If you want to know your baby's gender this can usually be seen at this scan

When you attend for this scan you will likely be told about everything seen during the scan. If you wish to have certain information remain unknown you must advise the ultrasonographer of the things that you do not want to know about, such as your baby's gender or markers for chromosome problems.

This ultrasound scan is very accurate but unfortunately it cannot diagnose 100% of congenital abnormalities. If the scan is complete, it is expected to pick up at least 95% of cases of spina bifida, 80% of cases of cleft lip or palate, and 60% to 70% of cases of congenital heart disease. This scan can also identify 50% to 70% of cases of Down syndrome, however other first trimester screenings are better for this as already noted.

Sometimes babies with chromosomal abnormalities have signs called ultrasound markers. These include, but not limited to, thick skin in the neck, excess fluid in the kidneys, short arms or legs, or white spots in the baby's heart or abdomen. While some babies with chromosomal abnormalities have these markers, it is important to remember that many normal babies also have these signs. The only way to diagnose or exclude a chromosomal problem for certain is to have an amniocentesis.

Diagnostic Tests

Chorionic Villi Sampling (CVS) – CVS is a diagnostic test for genetic abnormalities and is performed between 11-12 weeks gestation. Chorionic villi are tiny fingerlike growths in the placenta. An initial ultrasound is done to determine the position of the uterus, the size of the gestational sac, and the position of the placenta within the uterus. Depending on where the placenta is located, CVS can be performed through the cervix (transcervical) or through the abdomen (transabdominal). The techniques are thought to be equally safe and effective for obtaining samples. Both the transcervical and the transabdominal CVS are performed with ultrasound guidance. In this invasive test, a sample of the developing placenta is taken via a thin tube.

The sample is then used to study the DNA of the baby. The test can reveal genetic abnormalities such as, Down Syndrome, Trisomy 18, Tay-Sachs disease, hemoglobinopathies, etc… The difference with this test is that it provides a definitive diagnosis of one of these conditions or syndromes, whereas the previous screening test mentioned, determine risks. CVS does not detect neural tube defects as this is not a genetic abnormality. If neural tube defects or Rh incompatibility (difference in Rh blood types between mom and baby) are a concern, other tests will be employed to determine this.

CVS is a newer test and carries high risk of miscarriage. Studies show miscarriage rates between 1 in 25 and 1 in 100. CVS has also been associated with limb abnormalities in the baby (1 in 3,000). This test, while diagnostic, can still yield results that do not give an accurate picture of your baby. It is possible that cells removed by CVS are reported normal when actually the baby is affected with an unusual mosaic form of Down syndrome, where not all fetal cells contain the chromosomal abnormality. Alternatively, the baby may have mosaic cells, resulting in an abnormal CVS result, but be unaffected by the syndrome.

A diagnostic test does not produce results that are falsely positive or negative. However, as demonstrated with the example above, what our DNA is coded for is not always revealed in an obvious manner. It is also possible that maternal cells have been collected as well as noted in the following possible complications with this test.

Possible complications include the following:

- Rupture of membranes (rupture of the amniotic membrane)
- Spontaneous miscarriage
- Infection
- Bleeding
- Rh incompatibility in the mother
- Contamination of the sample with maternal cells

Amniocentesis - This test is usually performed between 15-19 weeks. Amniocentesis is done either to study genetics, look for structural defects or determine lung maturity (usually done late in pregnancy). During the procedure, one to two tablespoons of the baby's amniotic fluid are removed via a needle through the mother's abdomen under guided ultrasound. Some of the baby's cells are contained within the fluid; these are then extracted and grown in a lab. The chromosomes, proteins and chemicals produced by the baby in these cells are then tested for abnormalities.

Amniocentesis can reveal genetic conditions such as Down Syndrome and also test for structural defects such as spina bifida (open spine, where the vertebrae fail to close), anencephaly (a condition in which the brain is incomplete

or missing). Many other conditions, including cystic fibrosis, hemophilia and sickle cell disease, can be diagnosed using amniocentesis as well, but only if there is a specific reason to test for these conditions.

Results can take up to two weeks (long enough for cells to grow and be tested). Amniocentesis causes miscarriage in between 1 in 50 and 1 in 200 pregnant woman overall. Miscarriage rates tend to be lower in women who have the procedure done in the second trimester versus the first trimester. A miscarriage can take place up to three weeks after the procedure. Cramping and Rh sensitization or also known risks with amniocentesis.

Genetic amniocentesis accurately identifies certain genetic disorders, such as Down syndrome. But amniocentesis can't identify all birth defects, including heart defects, clubfoot or cleft lip and palate. When maturity amniocentesis indicates lung maturity, the risk of a false reading is less than 1 percent.

Additional Considerations

Because they do not carry a risk of miscarriage, prenatal screening tests have been promoted as "no-risk" tests to women (especially younger women) who may not consider themselves likely to have a baby with Down syndrome or another genetic syndrome and may not consider invasive testing. However, waiting for the results of prenatal tests causes stress and anxiety for many pregnant women, even when the results are normal. Pregnancy can be very emotional and likely vulnerable time in one's life. When mothers experience a large degree of stress over the wellbeing of their baby, emotional bonding can be delayed. Ordinarily, such anxiety would mobilize a mother's protective instincts, and she would draw closer to her baby. However, this protective instinct is difficult to express during this time and a mother might protect herself by emotionally distancing herself from her baby and the pregnancy.

Screening and diagnostic testing has been created to allow women who choose to terminate a pregnancy to do so in the earlier stages of pregnancy, when the risk to the women is lower. For a woman who does not intend to terminate her pregnancy if an abnormality is discovered, prenatal testing may provide information that will help her prepare for birthing and raising an affected child. On the other hand, testing may create stress around the pregnancy and increase the risk of miscarriage without changing the course of action the mother will take. Research indicates that maternal grief may be the same regardless of the chosen path.

The reality is many women choose to have one or a combination of these test to provide reassurance. Often testing can provide that reassurance and yet, a lot of the anxiety relieved by testing may be created by the testing in the first place. Tests do have limited detections rates. I have tried to note some of these above, however it is impossible to note them all. There are plenty of disabilities and disorders that prenatal testing does not detect.

The assumption that a finding always indicates something undesirable, rather than another aspect of human diversity is a message that runs deep in our culture. All this testing does pose some ethical questions about the type of society we are trying to create; one that celebrates differences or one that attempts to eradicate uniqueness? This line of thinking may not be appropriate for all families.

Prior to having any of these tests, I feel you must understand what information the tests can provide. I encourage you to then ask yourself what that information will mean for you and your family and what will you do with that information.

This summary may have stirred up many questions for you and your partner. I would be happy to discuss these and any other concerns with you and your partner. If we cannot find answers together, genetic counselors are available for more in-depth look at each test and genetic possibility.