Sequential screening (SS) is a test that can tell the chances that a pregnancy has Down syndrome (trisomy 21), trisomy 18, and open neural tube defects (ONTDs). The first part of the SS is generally performed in the first trimester and consists of a blood draw from mom and an ultrasound. Part two consists of a second blood draw from mom.

The first part of the sequential screen is similar to the first trimester screen (FTS), and the second part is similar to second trimester screening (STS). The first part of the sequential measures two proteins that are in mom’s blood that are coming from the pregnancy: pregnancy-associated plasma protein-A (PAPP-A), and human chorionic gonadotropin (hCG).

- Human chorionic gonadotropin (hCG): hCG is also produced by the placenta and crosses over into mom’s blood stream. hCG tends to be higher in pregnancies with Down syndrome and lower in pregnancies with trisomy 18.
- Pregnancy-associated plasma protein-A (PAPP-A): PAPP-A is produced by the placenta and crosses over into mom’s blood stream. Lower levels of PAPP-A increase the chances of Down syndrome or trisomy 18, and can also be associated with poor pregnancy outcomes, (miscarriage, low birth weight, and high blood pressure). However, keep in mind that most pregnancies that have low PAPP-A levels go on to produce healthy babies.

The results of the blood test is combined with the first trimester ultrasound, which measures the fetus to verify dating as well as pocket of fluid behind the baby’s neck called the nuchal translucency (NT). The lab uses a formula that includes the information from the blood work as well as the NT measurement to come up with a risk number. The second part of the sequential screen measures hCG again, as well as:

- Inhibin-A: Inhibin-A comes from the placenta. Levels of this protein in mom’s blood remain relatively constant through weeks 15-18 of the pregnancy. Pregnancies with Down syndrome tend to have higher than average levels of inhibin-A, while pregnancies with trisomy 18 tend to have lower levels of inhibin-A.
- Unconjugated estriol (uE3): uE3 is made by both the baby’s liver and the placenta. Levels of this protein rise throughout the pregnancy. Babies with Down syndrome or trisomy 18 tend to have lower levels of uE3.
- Alpha-fetoprotein (AFP): AFP is a protein produced in the baby’s liver during the second trimester of pregnancy. The levels of AFP generally increase the further into the pregnancy you are. AFP levels tend to be higher when the baby has an open neural tube defect (ONTD), such as spina bifida. With ONTDs, there is an opening in the skin and AFP has another ‘escape route’ out. AFP levels tend to be lower in pregnancies that have Down syndrome or trisomy 18.
The lab uses information from the blood draws and about the mom (age, weight, ethnicity, etc) to calculate a risk number. The results will be broken down by each condition that was screened for.

The first part of the sequential screen will usually give a risk for Down syndrome and trisomy 18. The results to not tell you ‘yes’ or ‘no’, but tell you the chance that the pregnancy has that condition. For example, the first part of the sequential screen may say that the risk for Down syndrome is 1 in 5,000, and the risk for trisomy 18 is 1 in 10,000. This means that if there were 5,000 women that had the exact same test result as you, only 1 would have a child with Down syndrome. Likewise, if there were 10,000 women with the exact same test result, only 1 would have a child with trisomy 18.

The second part of the sequential screen will give you a revised risk for Down syndrome and trisomy 18, as well as the risk for ONTDs.

A low-risk, or negative, SS means the chances are reduced for these conditions, but this test does not rule any medical conditions out. Similarly, a SS result that shows an increased risk does not mean that the pregnancy has that condition. If your results show an elevated risk, you may be offered further testing, such as a diagnostic prenatal test. It’s important to remember that most people who have a ‘positive’ or ‘high-risk’ SS will go on to have healthy babies.

People choose either to do or not to do prenatal genetic screening for many reasons. It is important to remember that this testing is voluntary and is not required.

**Your results are high-risk - now what?**

If you had a SS done with your primary OB-GYN, they may refer you to a high-risk pregnancy doctor called a perinatologist. You may also be referred to meet with a genetic counselor. These visits are designed to make sure to get more information and try to make sure you have all the necessary information to decide how to move forward. You may be offered further testing, including cell-free DNA, chorionic villus sampling (CVS), or amniocentesis. The choice to undergo further testing is yours, and is always voluntary.

**Your results are low-risk - now what?**

A low-risk test result means the chance that the pregnancy has those conditions is reduced but not eliminated. Only about 90% of pregnancies that have Down syndrome and trisomy 18 will have a positive SS, while 80% of pregnancies that have an ONTD will have a positive
SS. This means that 10-20% will have low-risk SS results. The chance that a pregnancy that does not have Down syndrome or trisomy 18 will have a high-risk test result, or a false positive, is about 5%.

**How do I decide whether to get STS or not?**

If you’re on the fence about whether or not to pursue STS, it may be helpful to consider the following:

- If the STS shows a high risk for a condition, would you pursue additional testing, such as CVS or amniocentesis?
- If not, would you be ok waiting until the baby is born to know for sure if they are affected?
- Would you want this kind of information to be better prepared?
- Would you consider doing anything differently if you knew a pregnancy was affected with one of these conditions, such as placing the baby up for adoption or not continuing the pregnancy?
- Does more information with the possibility of uncertainty make you nervous or anxious?

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