Optional Genetic Testing

The optional genetic tests that are available include screening tests and diagnostic tests.

Screening tests are risk free but do not provide a definite diagnosis. They only estimate the likelihood of a problem. As with all medical tests, there are sometimes false negative (normal) or false positive (abnormal) results.

Prenatal screening is now available specifically for Down syndrome (Trisomy 21), Edwards syndrome (Trisomy 18) and Patau syndrome (Trisomy 13). Trisomy means having three copies of a chromosome instead of the usual two copies.

Down syndrome is the most common trisomy. The likelihood of having a baby with Down's increases in a gradual linear fashion until age 30 and then increases exponentially. For a woman giving birth at the age of 25, the risk is 1 in 1300. At age 35, the risk is 1 in 365, at which time the chance of having a baby with Down syndrome becomes greater than the chance that having an amniocentesis will cause a miscarriage. At age 45, the risk is about 1 in 30. People with Down syndrome can have significant physical problems in addition to intellectual disabilities. They may be born with structural heart problems, hearing problems, and problems with the intestines, eyes, bones and thyroid gland.

Edwards syndrome is the second most common trisomy. It occurs in about 1 in 2500 pregnancies and in about 1 in 6000 live births. Fifty percent of Edwards syndrome babies are stillborn, and less than 10% survive to their first birthdays. A small number are living into their 30s, though with significant developmental delays that do not allow them to live independently.

Patau syndrome (Trisomy 13) is the third most common trisomy. It occurs in about 1 in 16,000 live births. It is associated with severe intellectual and physical disabilities, several of which are life-threatening. Only 5-10% of children with this condition live more than a year.

Sex chromosome testing is also available for detection of gender. The most common sex chromosome abnormality is Turner syndrome (Monosomy X), which occurs in about 1 in 2000-2500 births. Monosomy means having one copy of a chromosome instead of the usual two copies (or there may be two X chromosomes but one is missing important genetic material). Females with Turner syndrome are usually infertile. They have growth and sexual development issues, and may have heart and/or kidney problems. Growth hormone and hormone replacement therapy are being used to help with some of the problems.

Some tests also check for an increased risk of open **neural tube defects** such as spina bifida. Neural tube defects involve incomplete formation of the spinal cord, brain, or the tissues that enclose them. They occur in about 1 per 1000 births. The severity of the resulting problem depends on the location of the defect. Children with spina bifida often have problems with bowel and bladder control, and some may have attention deficit disorder or other learning difficulties. The likelihood of having a baby with a neural tube defect is significantly decreased by taking an adequate amount of folic acid (at least 800mcg daily), preferably before pregnancy occurs.

At present, the most commonly used screening test is the **Sequential Screen** (SS). The SS involves two sets of blood work. The blood tests are done at 11-13+ wks and again at (ideally) 16-18 wks. The detection rate is about 90% for Trisomy 21 with a 4% false positive rate. There is about a 90% detection rate for Trisomy 18 and 80-85% for Trisomy 13 with false positive rates of less than 0.5%. Results are called to the patient 5-7 days after the second blood test is drawn. A test for open neural tube defects is included in the SS. The SS is currently considered "standard of care" and is offered to all patients and covered by most if not all insurance companies.

An ultrasound exam at one of the perinatal testing centers between 11 and 13 wks gestation may also be ordered to measure the thickness of the embryonic neck fold or nuchal translucency (NT). A thickened NT has been found to be a marker for Down syndrome.

The newest test available is called the **Non-Invasive Prenatal Test** (NIPT). The NIPT involves a blood test that isolates and analyzes cell free fetal DNA that is circulating in the maternal blood. About 5% of the time, an insufficient amount of fetal DNA is obtained to run the test. When that happens, there is no charge and repeat testing is offered. In about 65% of those cases, the second test will yield a result. The results are generally available in 10-12 days, and a call will be made to you by the lab personnel if the test is abnormal or cannot be done. The test is not accurate in multiple gestation pregnancies or those achieved with a donor egg. The detection rate for trisomy 13, 18, and 21 is up to 99% with a 0.1% false positive rate. **Insurance companies that cover this test are now requiring pre-authorization and this process is taking up to 3 weeks**. The test is most likely to be covered for high risk patients - women who will be 35 or older at the time of delivery, women with an abnormal ultrasound finding or other genetic screening test like the Sequential Screen, and women who have had a prior pregnancy complicated by a genetic or structural abnormality. There is no longer a low out of pocket cost option for low risk patients. The NIPT does not test for open neural tube defects. A separate test called the maternal serum alpha-feto-protein (MSAFP), can be done to screen for that at 15-18 wks.

Women who miss the correct time frame to have the nuchal fold measurement for the SS have the option of having one of two other screening tests that only involve blood work. The **Quad Screen** (MSS4) checks for Tri 13, 18 and 21 and for open neural tube defects. It is best done at 16-18 wks but can be done from 15-20 wks. The MSS4 detects 80% of Tri 18 and 21 with a 5% false positive rate, and 80% of babies with open neural tube defects with a 1-3% false positive rate. The **Penta Screen** (MSS5) is similar to the MSS4 but can be done up to 22+ wks. The MSS5 detects 83% of Tri 21, and 60% of Tri 18 with a 5% false positive rate. Only 2% of the pregnancies found to be at increased risk for Tri 21 actually have an affected fetus. For Trisomy 18, 11% of the pregnancies found to be at increased risk are actually affected fetuses. Quad and Penta Screen test results are reported as a risk ratio such as 1 in 10,000 or 1 in 50 for each potential problem. If an elevated risk is found with any of the screening test options, a targeted ultrasound will be offered to check for structural abnormalities and your insurance company may then cover the NIPT. However**, none of the non-invasive tests identify all of the babies that have these problems, and some babies with no problems will incorrectly be identified as having a problem**. Consequently, patients who would consider terminating a pregnancy identified as having an increased risk of one of the chromosome abnormalities mentioned above should follow up with a definitive invasive diagnostic test.

Diagnostic tests include chorionic villous sampling (**CVS**) and **amniocentesis**. These tests are not recommended for everyone because the procedures themselves may cause a miscarriage. The risk is approximately 1 in 200 for CVS and 1 in 300 for amniocentesis. They are offered to patients with positive screening test results. They are also offered to patients who have an increased risk because of maternal age, personal history or family history (if desired, without first having a screening test done). Chorionic Villous Sampling (CVS) involves sampling of placental tissue and is done at 10-12 wks gestation. The results can be incorrect 1% of the time because of placental mosaicism (sometimes the placenta has a slightly different chromosomal make-up than the fetus). CVS does not include a check for open neural tube defects. A separate test for that can be done later in the pregnancy. Amniocentesis involves sampling of amniotic fluid. For genetic testing purposes it is usually done at 16 wks gestation but can be done any time after 15 wks. Amniocentesis allows a check of the amount of alpha-feto-protein (AFP) in the amniotic fluid itself to check for open neural tube defects. Therefore, amniocentesis is the follow-up diagnostic test after an abnormal screening test result for neural tube defects. Patients desiring an invasive test are asked to schedule an appointment with the genetic counselor before having the test.

Based on the results of CVS or amniocentesis, some patients decide to terminate their pregnancies. Others continue their pregnancies but have the testing because they feel that finding out about potential problems in advance is helpful. It gives them time to research the resources that are available and to be as prepared as possible.

Knowing what to expect can make the delivery experience and early post-partum time easier. If there *is* something best handled immediately after delivery, arrangements can be made for moms to have their babies at the best possible place.

Summary of Screening Tests

Test	NIPT	Sequential Screen	Quad	Penta
Timing Blood work	As early as 9-10 wks	2 blood draws: 11-13+ wks and 16-18 wks	15-18 wks ideally but up to 20+ wks	15-18 wks ideally but up to 22+ wks
Ultrasound	11-13+ wks	11-13+ wks	N/A	N/A
Sensitivity*				
Down (Tri 21)	99%	90%	80%	83%
Edwards (Tri 18)	99%	90%	80%	60%
Patau (Tri 13)	99%	80-85%		
False Positive Rate				
Down (Tri 21)	0.1%	4%	5%	2%
Edwards (Tri 18)	0.1%	Less than 0.5%	5%	11%
Patau (Tri 13)	0.1%	Less than 0.5%	**	**
% Positive	**	3.7	5%	**
Incl. Neural Tube Test	no	yes	yes	yes
Incl. Ultrasound	yes	yes	no	no
Advantages	Highest detection rate	Next highest detection rate	Available if ultrasound window is missed for other tests	Available if ultrasound window is missed for other tests
Disadvantages	Costly and requires insurance pre-authorization, does not test for open neural tube defects at the same time but a separate test for that can be done later in pregnancy		No 1st trimester info, Lower sensitivity	No 1st trimester info, Lower sensitivity

*Sensitivity is the percentage of babies that actually have the problem that are identified with the test (true positives)

** Information not available