Prenatal Genetic Testing

down syndrome, trisomy 18, cystic fibrosis

Pregnancy is a time of great joy and excitement. But for many, it is also a time of anxiety and unanswered questions. Will my baby be normal? What if he has Down syndrome? Will she get the cystic fibrosis disease that runs in our family?

In this article, we will explore three of the more common genetic conditions that are detectable during pregnancy and the ways we can test for them.

Down Syndrome

With its typical facial features and mental deficiency, Down syndrome is familiar to most of us. It occurs when the baby has three copies of the 21st chromosome (hence its other name, trisomy 21), instead of the usual two copies. Affecting about 1 out of every 700 live births, it is the most common chromosomal abnormality. Its risk goes up with increasing maternal age, especially over age 35.

How do we screen for this condition? First, some historical background. In the 1970s, amniocentesis was routinely offered to all women age 35 and older, so that the number of chromosomes could be counted under a microscope. However, because only about 25% of Down syndrome babies are born to mothers over 35, that meant 75% of cases went undetected before birth.

Then, in the 1980s, second-trimester blood tests evaluating various biochemical markers were developed. Accuracy increased as more markers were added over the years: The "double screen" picked up about 70% of babies with the condition. Detection rates improved to 75% for the "triple screen" and 80% for the "quad screen." The addition of ultrasound during the second trimester did not significantly enhance these results.

A breakthrough came about in the early 1990s, when researchers noticed that first-trimester babies with Down syndrome had thickening of the tissue at the back of their neck. Measurement of this nuchal translucency (NT) with ultrasound resulted in detection rates around 75%. Therefore, a single ultrasound exam in the first trimester produced results equivalent to the second-trimester triple screen, but with the advantage of having an answer several weeks earlier.

The state-of-the-art is now NT plus a first-trimester blood test (80% detection, which is equivalent to a quad screen with earlier results) or, even better, NT plus first- and second-trimester blood tests (90% detection with only a 5% false-positive rate).

Trisomy 18

Trisomy 18, as its name implies, occurs when there are three copies of the 18th chromosome. Although less common than Down syndrome (1 in every 3000 pregnancies), it has much more serious consequences. Many of these babies are stillborn or die in infancy. When they do survive past infancy, they have multiple physical abnormalities and a shortened lifespan. As with Down syndrome, its prevalence goes up as maternal age increases.

As it turns out, trisomy 18 is another of the many chromosomal abnormalities that result in thickening of the NT. The same first- and second-trimester blood tests that screen for Down syndrome do an equally good job screening for trisomy 18. NT plus a first-trimester blood test detects about 80% while NT plus first- and second-trimester blood tests detect about 90% of cases.

Using NT and blood tests to provide a risk assessment for Down syndrome and trisomy 18 permits the doctor to identify not only those pregnancies that would most benefit from chorionic villous sampling (CVS) or amniocentesis, but also those pregnancies for which these procedures may not be necessary.

Cystic Fibrosis

Cystic fibrosis is an inherited disease caused by a mutation in a gene associated with the production of sweat and other bodily fluids. Affected babies get one abnormal gene from each carrier parent. It is most common among Caucasians and Ashkenazi Jews. Approximately 1 out of every 25 people of European descent are carriers of the mutant gene. This translates to about 10 million American carriers. Unlike trisomies 21 and 18, the number of chromosomes is normal.

The major problem with cystic fibrosis is susceptibility to frequent lung infections. This leads to lung damage and often to lung failure, requiring lung transplantation. Other complications include diabetes, infertility, and sinus infections.

In the past, these individuals did not survive past young adulthood. Although there is no cure for the disease, improvements in treatment have prolonged their life expectancy and decreased the number of complications.

Testing for cystic fibrosis is two-tiered. One is to test the parents to determine if either or both are carriers. Since there are more than 1,000 potential mutations of the gene that causes cystic fibrosis, it is not feasible to test for all mutations. Therefore, all labs screen for the most common mutations, which can range anywhere from about 20 to almost 100 mutations. If the mother tests negative for these mutations (this can be tested on the blood that is drawn for trisomy 21 and 18 screening), the chances are very low that her baby will be affected.

After birth, neonates can be screened for the gene as well. In Pennsylvania, this neonatal testing became mandatory on July 1, 2009. If the screening test is positive, the definitive test to diagnose cystic fibrosis is the sweat test, which examines how concentrated the salt is in the sweat. Persons with cystic fibrosis have very salty sweat.

What is the best way to screen for genetic problems during pregnancy?

The American Congress of Obstetricians and Gynecologists recommends that obstetricians discuss first-trimester screening with all pregnant women. This consists of a nuchal translucency measurement, performed by a Certified ultrasound technologist, and a blood test. You can get even more accurate results by adding a second blood test during the second trimester. Finally, if cystic fibrosis runs in the family or if you and your spouse are of European heritage, you should consider getting the genetic test to determine if you are carriers of the defective gene. What great news it would be to find out that your baby's risk of Down syndrome, trisomy 18, and cystic fibrosis is low!

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