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Noninvasive Prenatal Testing

Every couple wants the guarantee of a "normal" child. Historically, parents would have to wait until birth to determine whether their offspring were chromosomally abnormal (affected by an aneuploidy). There was no opportunity for these parents to prepare themselves for children with special needs. The need for a screening test was identified. The challenge lay in the balance of how to develop testing methods which were not harmful to developing fetus or mother but also provided, with a reasonable reliability, either reassurance to the parents or indications for further diagnostic testing. Enter the era of the non-invasive prenatal test. Of note, this article does not address pre-implantation genetic diagnosis which is offered through artificial reproductive technology nor does it address testing in multiple gestations.

In the early 2000s, each pregnant woman was offered basic genetic screening, referred to as the QUAD screen. This included blood sample generally taken between 15-19 weeks of estimated gestational age. Four specific hormones were typically measured. Standardized curves were published which allowed for the interpretation of hormone levels (e.g. high, normal, or low). Patterns emerged as data was collected from both normal and aneuploidy fetuses. Once each hormone level was determined, the risk of a pregnancy affected by one of the three most common genetic trisomies was calculated (Trisomy 13, 18, and 21). The results would be reported into three general categories—low, normal, or high risk. The risk analysis would be presented to the parents, and recommendations were either for routine prenatal care or referred to a Maternal Fetal Medicine Specialist.

By the mid-2000s, new data was emerging on the utility of early ultrasound in identifying patients at risk of a Trisomy 13 fetus. This was typically offered to the high risk population at 11-13 weeks of gestational age and focused on the presence of absence of the fetal nasal bone as well as the thickness of the nuchal fold (i.e. back of the neck). Given the widespread availability of ultrasound, this was quickly adapted as the best screening test for this group.

In 2011, cell-free fetal DNA became a commercially available screening test and was recommended by both the American College of Obstetricians and Gynecologists as well as the Society for Maternal-Fetal Medicine for those women in the high risk population. This group includes women at or above 35 years, fetuses with ultrasonographic findings increasing the risk of a chromosomal abnormality, those with a history of previously affected offspring, and women with positive first or second trimester conventional screening tests (see above).

Cell-free fetal DNA is primarily placental in origin and will screen only for most common trisomies and sex chromosomes. Testing is typically done at the end of the first trimester. There are multiple technologies at work; however specificity remains over 99%. False positive rates are approximately 1% in the high risk population. The caveat with these laboratories is that there is no standardization of how much fetal fraction (amount of the cell-free DNA in the maternal blood that is of fetal not placental origin) is required to provide the most accurate result as the majority of cell-free DNA is placental in origin. The chromosome of the placenta does not always match those of the fetus. This gets even more convoluted in patients who do have a chromosomally abnormal fetus with a normal placenta and for those who are obese as testing often comes back positive or unreportable due to a lower than average free fetal fraction.

Cell-free DNA was marketed initially to the high risk obstetric population; however, data has recently become available on the performance of this test in general obstetrics. The specificity is similar to the high risk faction; however, the positive predictive value is lower. This means that the false-positive rate is much greater in the low risk populace. Thus, the American College of Obstetricians and Gynecologists continue to affirm that standardized screening is the first choice for these individuals.

In summary, speak with your physician. Provide them with a detailed medical and family history so that they can assess the appropriateness of various screening tests to determine which is best suited for you and your baby. Remember, you can elect for cell-free DNA as your screening test even if you do not meet high risk criteria; however, the performance of this test is more poor with a higher false positive rate. This technology is rapidly evolving and recommendations regarding testing reflect developments and new research. Therefore, your obstetrician-gynecologist will help you in determining the most effective, accurate, and appropriate method for non-invasive prenatal screening for your individual pregnancy.

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