New prenatal genetic test is much more powerful at detecting fetal abnormalities

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A nationwide, federally funded study has found that testing a developing fetus' DNA through chromosomal microarray (CMA) provides more information about potential disorders than does the standard method of prenatal testing, which is to visually examine the chromosomes (karyotyping). The results of the 4,000-plus-participant clinical study are being presented at the 32nd annual meeting of the Society for Maternal-Fetal Medicine in Dallas on Feb. 9, 2012. The study was recently published in the *American Journal of Obstetrics & Gynecology*.

In women having routine prenatal diagnosis, CMA detected additional genetic abnormalities in about 1 out of every 70 fetal samples that had a normal karyotype. When a birth defect was imaged by ultrasound, CMA found additional important genetic information in 6 percent of cases. These results suggest that CMA may soon replace karyotyping for prenatal testing, says Dr. Ronald Wapner, director of Reproductive Genetics at NewYork-Presbyterian Hospital/Columbia University Medical Center and vice chairman for research and professor of obstetrics and gynecology at Columbia University College of Physicians and Surgeons.

"Why would anyone want to continue to use the standard method, which gives only part of the answer?" says Dr. Wapner, who led the 34-center study funded by the Eunice Kennedy Shriver National Institute of Child Health and Human Development. "However, we will have to carefully transition this information into clinical practice - to educate physicians and patients, develop guidelines for its use, and learn how to best use it

to improve care."

CMA is not routinely used for prenatal testing but has become the primary genetic test to evaluate newborns with birth defects, as well as infants and young children with developmental delays.

Dr. Wapner describes the observed difference in accuracy between the two tests this way: "With karyotyping, we can see only when pieces of the genome of about 5 million base pairs are missing from a chromosome. With CMA, we can see missing pieces of fewer than 100,000 base pairs."

CMA is based on a method that determines whether the right amount of genetic material is present at numerous locations in the fetus' genome.

This study was the first to examine the two methods in a blinded head-to-head comparison. Fetal samples were collected from the amniotic fluid or placenta of 4,450 participants. "These were women who were seeking prenatal testing for the usual reasons, which could be age, increased risk of inheritable disease, or a structural abnormality in the fetus," Dr. Wapner says.

Each participant's sample was split and sent, in a blinded fashion, to one of four laboratories that perform CMA - NewYork-Presbyterian Hospital/Columbia University Medical Center, Emory University, Baylor College of Medicine or Signature Genetics. The other portion of the sample was sent to Genzyme Genetics for standard karyotyping.

Results show that CMA and karyotyping were equally effective at identifying chromosomal abnormalities such as the duplicate chromosomes that cause Down syndrome and Trisomy 18. But CMA provided significantly more clinically relevant information in two situations.

"In 6 percent of the cases where there's a structural abnormality of the fetus but karyotyping is normal, CMA will provide additional significant information," Dr. Wapner says. "And in about 1.7 percent of cases where the procedure was done because of the mother's age or similar concerns and the chromosomes were normal, CMA reveals additional information of concern."

Both tests offer information on conditions that can be life-threatening to a newborn baby or that can signal a possible health threat that might be treatable. "We are looking for the same thing in both tests," Dr. Wapner says. "But we find more abnormalities with CMA."

CMA can identify at least 150 known conditions and tell us exactly what the problem is and what it means for a child. Although karyotyping provides the same kind of information, CMA will likely provide more information on other potential disorders that might not otherwise be picked up such as intellectual disability or autism.

"It does not always mean that a child will necessarily develop these disorders, because many are due to multiple influences," Dr. Wapner says. "But it will help parents because they can be on the lookout for a particular disorder and have a treatment plan in place. I believe it is important to give parents as much information as they need about their child."

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