# Fetal Genetic Disorders Test Being Developed

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GRAPEVINE, TEX. — Researchers are attempting to develop a first-trimester cervical swab test to detect fetal genetic disorders.

While the test still is under development, if proven effective, it could provide noninvasive, earlier prenatal screening and possibly eliminate the need for amniocentesis and chorionic villi sampling (CVS).

**In a pilot study, the researchers took cervical swab specimens from 17 women in the first trimester, and trophoblasts were detected in all.**

"Early prenatal diagnosis to detect fetal genetic disorders is desired by both expectant mothers and physicians to make informed decisions," Farideh Z. Bischoff, Ph.D., of Baylor College of Medicine, Houston, said at a meeting sponsored by the American College of Medical Genetics.

"Current methods of prenatal testing carry a small but finite risk of miscarriage, and the results rarely are available before 12 to 16 weeks of pregnancy, due to the time required for cell culture," Dr. Bischoff said.

Recovery and analysis of fetal trophoblast cells would provide a safe alternative approach for rapid noninvasive prenatal diagnosis, she said.

The researchers are using micro electro mechanism system (MEMS) channels to isolate, purify, and characterize fetal trophoblasts from maternal transcervical mucous specimens. The trophoblast cells migrate from the placenta to the endocervical canal.

In a pilot study, the researchers were able to take cervical swab specimens from 17 women during the first trimester, and trophoblasts were detected in all.

The swab specimens were taken during the first trimester of pregnancy, between 8 and 12 weeks. Samples were washed and processed using a novel MEMS device coated with a proprietary reagent and trophoblast specific antibody.

Although only 0.02% to 1.94% of the initial total cell populations were trophoblasts, the recovered cell population was determined to be predominately of trophoblast origin. Trophoblast isolation was optimal in samples not contaminated by blood.

Now investigations are underway to detect fetal chromosomal aneuploidy and diagnostic potential using fluorescent in situ hybridization and polymerase chain reaction–based methods, Dr. Bischoff said. ■

# *Patients Who Have Had Invasive Procedures More Open to Carrier Testing*

GRAPEVINE, TEX. — Patients referred for genetic testing are more likely to agree to carrier status testing if they already have accepted an invasive procedure.

A study of 3,131 patients referred for genetic testing found that individuals were more likely to accept cystic fibrosis carrier testing and were more likely to accept both CF and fragile X syndrome (FXS) carrier testing if they underwent an invasive procedure such as amniocentesis.

"Patients who underwent such a procedure were more than twice as likely to accept both screening tests, compared with patients who had declined invasive testing, said Amy Cronister, the study's lead author and regional manager of genetic services, Genzyme Genetics, Phoenix, Ariz.

This finding suggests that there may be specific populations of patients who generally tend to avoid genetic testing, and other populations for whom the concept of genetic testing is much more acceptable, she said at a meeting sponsored by the American College of Medical Genetics.

Overall, 33% of referrals agreed to carrier status testing for CF and 28% for FXS; 25% accepted CF and FXS testing; and 64% declined both. Significantly fewer (11%) accepted one test but declined the other.

There was no difference in carrier testing acceptance in patients referred because of maternal age and those with a positive maternal serum screening, Ms. Cronister said.

The study included patients referred for prenatal genetic counseling during a 22-month period because of maternal age, positive maternal serum screening, chemical exposure, or parental anxiety. The patients were offered both CF and FXS carrier testing on the basis of population screening only.

Because they would be more likely than the general population to accept CF and FSX screening, patients with a known or suggestive family history of either disease were excluded from the study.

Additionally, because CF risk is linked to ethnicity, only patients of white and Ashkenazi Jewish backgrounds, for whom the risk of being a CF carrier is 1 in 25 people, were included in the study. ■

# Couples Accept Prenatal Genetic Testing With CMA

## *There was a 71% acceptance rate of chromosome microarray analysis in those undergoing amnio or CVS.*

GRAPEVINE, TEX. — Chromosome microarray analysis may play a vital role in the diagnosis of genetic disorders prenatally, Christine Eng, M.D., commented during a meeting that was sponsored by the American College of Medical Genetics.

Although chromosome microarray analysis (CMA) already has an established role in the genetic evaluation of both children and adults, its use still is being evaluated in the prenatal setting.

**Only 13% of the initial tests showed inconclusive results. All abnormalities detected by karyotype also were detected by CMA.**

"This study represents the initial use of CMA in pregnancies being monitored due to increased risk of chromosomal abnormalities," said Dr. Eng of Baylor College of Medicine, Houston.

"It demonstrates a high level of acceptance and accuracy."

Dr. Eng and her associates discovered that there was a 71% acceptance rate of CMA among couples in which the woman was undergoing amniocentesis or chorionic villi sampling (CVS).

Reasons for acceptance of the CMA test included having a previous child with anomalies, an abnormal ultrasound finding, maternal age, and a desire to learn as much as possible about the current pregnancy.

Reasons for declining testing included the perception that the disorders being tested were rare and concern that the test results would raise anxiety.

The study also demonstrated that the CMA test is highly accurate: Only 13% of the initial tests showed inconclusive results.

The study was undertaken to determine the reliability of CMA to detect cytogenetic abnormalities in fetal samples, design a program of parental counseling, and assess acceptance of CMA among couples who were undergoing prenatal diagnosis.

A total of 38 couples, who were recruited among patients undergoing amniocentesis or CVS, agreed to participate in the study.

Of the 38 samples assessed in the study, 60% were amniotic fluid and 37% were CVS. One was a fetal blood sample.

Indications for prenatal testing included advanced maternal age (58%), anomalies detected on fetal ultrasound (26%), and having a previously affected child (13%), Dr. Eng reported.

All genetic abnormalities that were detected by karyotype also were detected by CMA and consisted of three cases of trisomy 21, according to Dr. Eng.

In addition, in five of the cases (13%) initial CMA analysis yielded inconclusive results that required study of parental samples for further clarification.

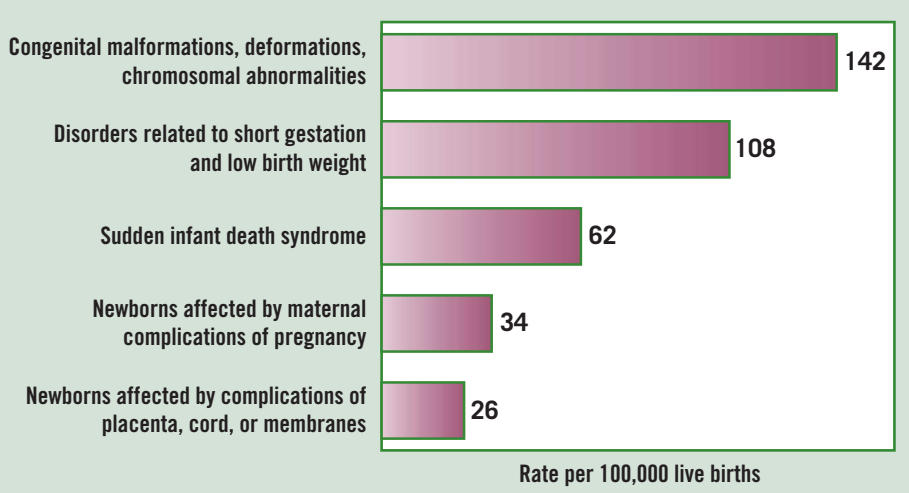
The microarray that was used in the study contains 362 fluorescent in situ hybridization–verified clones that span genomic regions implicated in 55 known human genetic disorders as well as subtelomeric clones of all 41 relevant human chromosome telomeric regions.

"This greatly expands the capability to detect abnormalities in these regions, when compared with conventional prenatal karyotyping," she said during the meeting.

Dr. Eng commented that additional experience will optimize patient education and counseling and yield further insight into the degree of normal variation in these regions. ■

## DATA WATCH

### Birth Defects Were Top Cause of Infant Deaths in 2000




Source: Centers for Disease Control and Prevention

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