

Offer Early Genetic Screening, Prompt Disclosure

BY JANE SALODOF MacNEIL
Southwest Bureau

SCOTTSDALE, ARIZ. — Noninvasive genetic screening has a higher detection rate when done in the first trimester of pregnancy and should be offered with prompt disclosure of results, Joe Leigh Simpson, M.D., said at the annual meeting of the Central Association of Obstetricians and Gynecologists.

An offer of amniocentesis or chorionic villus sampling (CVS) to every pregnant woman regardless of age also should be considered, according to Dr. Simpson, chairman of obstetrics and gynecology at Baylor College of Medicine, Houston.

"I believe a good case could be made for universal invasive screening," he said. "I believe amniocentesis and CVS are much safer than generally touted. The 1-in-200 [loss rate] figure we have told our patients is doing them a disservice, because it is not a valid figure in 2005."

He predicted karyotyping will become obsolete as a diagnostic tool within the next 5-10 years. Chromosomal microarrays currently in development are more accurate than karyotypes, and should soon be able to detect many common

Mendelian disorders, Dr. Simpson said after describing ongoing research at Baylor, where he also is a professor in the department of molecular and human genetics.

"I don't think there is any question the public will demand this approach and not karyotypes," he said. "Karyotypes have a limited future in terms of the diagnostic field."

The American College of Obstetricians and Gynecologists is reviewing the current guideline for invasive and noninvasive screening, adopted in 1996, according to Dr. Simpson. He predicted a revision with a "cafeteria of options" will be announced early next year.

Among the noninvasive options he listed are sequential first and second trimester screening with various serum analytes, nuchal translucency ultrasound, and nasal bone inspection.

"Noninvasive first-trimester screening shows clear improvement, 5%-10%, over second-trimester screening, and is more applicable to multiple gestations," he said,

citing recent results from a new analysis of data from the First and Second Trimester Evaluation of Risk for Aneuploidy (FASTER) trial. "Successful incorporation with nasal bone [screening] could yield over 90% detection."

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Dr. Simpson said nuchal translucency ultrasound in the first trimester is especially useful in women with multiple gestations, as it allows assessment of individual fetuses. With serum testing alone, he said, detection rates in this population can dip as low as 25% with second-trimester screening.

First-trimester screening for absence of nasal bone was not successful in a 2003 report from the FASTER trial, but other studies have reported Down syndrome detection rates as high as 73%, according to Dr. Simpson. He advocated using nasal bone inspection with other noninvasive tests rather than as the sole measure.

In two recent studies from the United Kingdom, he said 30,564 women and 15,822 women, respectively, were screened

by four measures: pregnancy-associated plasma protein A (PAPP-A), human chorionic gonadotropin (hCG), nuchal translucency, and nasal bone inspection. The detection rates were 93% and 97%, respectively.

"Early is better for issues of privacy and access to management, but it is also [better] for sensitivity," Dr. Simpson said.

Addressing the controversy over disclosure of first-trimester results before a woman returns for second-trimester screening, he warned of the potential for litigation if the patient fails to return or is somehow lost to follow-up without learning she is at high risk.

"What if you have someone who would have had a procedure if you told her the results in the first trimester, and she just did not get around to coming back to you, or there is a hurricane or whatever?" he said, adding that second-trimester detection rates have been shown not to decline as feared when high-risk women were advised of first-trimester results.

As for invasive procedures, Dr. Simpson said the fetal loss rates are "probably no more than 1 in 500." He cited several large studies showing fetal loss rates as low as 1 in 667 amniocentesis procedures. ■

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Risk of CVD High in Women With Placental Syndromes

BY MARY ANN MOON
Contributing Writer

Women who have placental syndromes are at high risk for premature cardiovascular disease, particularly if there is associated fetal compromise, according to Joel G. Ray, M.D., of the University of Toronto, and his associates.

The level of cardiovascular risk conferred by a placental syndrome—preeclampsia, gestational hypertension, placental abruption, or placental infarction—is comparable with that of such conventional risk factors as hypertension, obesity, diabetes, and dyslipidemia. "We believe that maternal placental syndrome should be considered an additional risk factor for cardiovascular disease in women, especially when the woman's fetus is adversely affected," Dr. Ray, of the division of obstetrics and gynecology at the university, and his associates said (*Lancet* 2005;366:1797-803).

They assessed outcomes in a population-based study of Ontario residents who gave birth between 1990 and 2004. The mean maternal age at delivery was 28 years. Of 1,026,265 subjects, 75,380 (7%) were diagnosed as having a placental syndrome.

After a mean of 8.7 years' follow-up, cardiovascular events occurred in more than twice as many women with placental syndromes as in women without placental syndromes, irrespective of the presence of potential confounders such as diabetes. The rate of events was 500/million person-years among those with placental syndromes, compared with 200/million

in those without placental syndromes.

The women's mean age was 38 years at the time of the first cardiovascular event. These included coronary, cerebrovascular, or peripheral artery events, or the need for a revascularization procedure.

The risk for cardiovascular events was even higher if the placental syndromes led to fetal growth restriction or intrauterine fetal death. It was higher still in women who had preexisting cardiovascular risk factors when they became pregnant, such as smoking or various features of the metabolic syndrome.

The findings do not imply placental disorders cause cardiovascular events to occur in the near future, the investigators said. "Rather, a more plausible explanation relates to a woman's abnormal metabolic milieu that predates her pregnancy and continues after delivery. This chronic state of dysmetabolism might create an inhospitable environment during the development of the placental spiral arteries, which can adversely affect fetal health, while negatively affecting the large arteries of a woman's heart, brain, and extremities over a broader period of time," they noted.

Physicians "should try to ensure that women are a healthy weight before they enter their reproductive years." This should reduce their risk for placental syndromes and fetal compromise as well as for cardiovascular disease, the researchers said.

It remains unknown whether women who have had placental syndromes might lower their risk of premature cardiovascular disease by making lifestyle changes, they added. ■