Tests that use DNA from mother's blood to determine sex of fetus often effective

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As a noninvasive method of determining the sex of a fetus, tests using cell-free fetal DNA obtained from the mother's blood after 7 weeks gestation performed well, while urine-based tests appear to be unreliable, according to a review and analysis of previous studies, reported in the August 10 issue of *JAMA*.

Noninvasive prenatal determination of fetal sex could provide an important alternative to invasive cytogenetic determination, which is currently the gold standard for determining sex and single-gene disorders. Amniocentesis has small but measurable rates of procedure-related pregnancy loss; and sonography can be performed as early as 11 weeks' gestation to determine fetal sex, although not reliably, according to background information in the article. "The availability of a reliable noninvasive alternative to determine fetal sex would reduce unintended fetal losses and would presumably be welcomed by pregnant women carrying fetuses at risk for disorders," the authors write.

Using cell-free fetal DNA as a noninvasive method for prenatal determination of fetal sex provides an alternative to invasive techniques for some heritable disorders. In some countries, such as the Netherlands, the United Kingdom, France, and Spain, this testing has already transitioned to routine clinical care despite the absence of a formal assessment of its performance. "More recently, companies have begun offering this technology directly to the consumer over the Internet. The tests are marketed for nonmedical use to curious parents-to-be with promises in some cases of accuracy as high as 95 percent to 99 percent

at as early as 5 to 7 weeks' gestation," according to background information in the article.

Stephanie A. Devaney, Ph.D., of the National Institutes of Health, Bethesda, Md., and colleagues performed a systematic review and meta-analysis of previous research to examine the analytic validity of cell-free fetal DNA testing, which describes the test's ability to detect Y chromosome sequences within maternal samples, as well as the clinical validity of the test, as indicated by its ability to correctly identify fetal sex. The researchers selected 57 studies (which included 80 data sets [representing 3,524 male-bearing pregnancies and 3,017 female-bearing pregnancies]) for inclusion in the analysis.

The researchers found that the overall performance of the tests had sensitivity of 95.4 percent, specificity of 98.6 percent, positive predictive value, 98.8 percent, and negative predictive value, 94.8 percent. Performance was high using maternal blood. DNA methodology and gestational age had the largest effects on test performance, with real-time quantitative polymerase chain reaction (RTQ-PCR) outperforming conventional PCR. Test performance was high if performed using RTQ-PCR on a blood sample taken at a time during pregnancy when sufficient cell-free fetal DNA was present (7 weeks' gestation or later), with the best performance after 20 weeks' gestation. Testing performed prior to 7 weeks' gestation using blood, and all tests using urine, were found unreliable.

"The improved performance with later gestation is likely attributable to the increased concentration of cell-free fetal DNA within maternal blood as the fetus and placenta develop. This would explain the poor performance of the test prior to 7 weeks' gestation and the near-perfect performance in the third trimester," the authors write.

The researchers suggest that this "technology can be useful in clinical

settings for early detection of fetuses at risk for sex-linked disorders requiring follow-up testing."

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