FIVE THINGS TO KNOW ABOUT ...

Noninvasive prenatal testing from cell-free DNA

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Noninvasive prenatal testing uses a maternal blood sample to screen for specific fetal chromosomal aneuploidies

The test analyzes fragments of DNA derived from the placenta circulating in maternal blood. The sensitivity and specificity of noninvasive prenatal testing depend on the chromosome being analyzed and also vary by testing laboratory. For trisomy 21 (Down syndrome), both sensitivity and specificity of the tests tend to be greater than or equal to 99%.¹⁻⁵ Most studies to date do not provide positive or negative predictive values. Of note, authors of most published studies have commercial affiliations with testing laboratories.

Physicians need to ensure that women receive counselling before and after testing to allow informed decision-making

Pre- and posttest counselling should include a discussion of the limitations of this testing.³ Most noninvasive testing only addresses aneuploidies of chromosomes 21, 13 and 18, with optional analysis of the sex chromosomes. No information is provided about other genetic conditions, congenital anomalies or other parameters of fetal or maternal health. Test failure can occur when there is insufficient fetal DNA, which can be related to maternal weight, gestational stage, or technical or sampling issues.⁵ This testing has not been well studied in multiple gestations.³

Noninvasive prenatal testing may be considered in pregnancies at high risk for aneuploidy

Current guidelines recommend that this testing is only an option in pregnancies at high risk for aneuploidy.^{2,3} Although the definition of high risk varies among centres, it often includes, but is not limited to, advanced maternal age, abnormal aneuploidy screening results, ultrasound findings suggestive of the aneuploidies detected, and personal or family history of trisomy. More data on test performance in low-risk pregnancies are becoming available;^{6,7} however, the use of this test in such populations is currently controversial.

Noninvasive prenatal testing is not a replacement for invasive testing

False-positive results may occur because of several factors. One major reason is that the DNA analyzed is believed to originate from the placenta and a discrepancy between fetal and placental karyotypes is a well-documented phenomenon.^{2,5} The gold standard for diagnosis and confirmation of fetal chromosomal aneuploidies remains amniocentesis or chorionic villus sampling for karyotype analysis.^{2,3} No irrevocable action should be taken without confirmatory invasive testing.

In Canada, some provincial health insurance programs will pay for noninvasive prenatal testing under certain circumstances

Currently, private laboratories outside of Canada perform the analysis on samples drawn in Canada. Costs and services offered vary among test providers, and accessibility varies by jurisdiction.

Resources

- The Society of Obstetricians and Gynaecologists of Canada practice guideline: <http://sogc.org/guidelines/detection-of-down-syndrome-trisomy-18-and-trisomy-13-using-cell-free-dna-in-maternal-plasma>
- International Society for Prenatal Diagnosis position statement on aneuploidy screening: www.ispdhome.org/public/news/2013/PositionStatementAneuploidy4apr2013.pdf

For references, please see Appendix 1, available at www.cmaj.ca/lookup/suppl/doi:10.1503/cmaj.131551/-/DC1

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