

New Molecular Techniques for the Prenatal Detection of Chromosomal Aneuploidy

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techniques and the evidence supporting their use in prenatal diagnosis. These methods are reliable and cost-effective for detecting the targeted fetal aneuploidies, but are limited in their ability to detect non-aneuploid chromosome abnormalities, some of which are clinically significant.

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Summary Statements

1. Currently available methods for rapid aneuploidy detection (RAD) include fluorescence in situ hybridization (FISH) and quantitative fluorescence polymerase chain reaction (QF-PCR). Multiplex ligation-dependent probe amplification (MLPA) is a newer technology under investigation.
2. FISH and QF-PCR are known to, and MLPA is proving to, have similar sensitivity and specificity to full cytogenetic karyotyping (the current "gold standard") for the detection of fetal aneuploidy (for chromosomes 13, 18, and 21 and the sex chromosomes). Advantages of QF-PCR and MLPA over full karyotype include substantially reduced turnaround time and automation and batching of samples resulting in reduced cost per sample. FISH is not amenable to automation and remains more costly than PCR-based techniques.
3. The main disadvantage of current RAD methods is the failure to detect chromosome aberrations that are not aneuploid for the targeted chromosomes. Some of these aberrations are predicted to have clinical morbidity.
4. In the future, RAD alone may be a suitable tool for prenatal diagnosis for a subset of women undergoing invasive testing solely for an increased risk of fetal aneuploidy. It would not be suitable for those women with other risk factors such as structural fetal abnormalities on ultrasound or a personal or family history of a chromosomal rearrangement (such as a balanced translocation). These women should always have a full cytogenetic karyotype analysis.
5. The introduction of new techniques for prenatal diagnosis should include analysis of benefits versus risks and cost effectiveness. RAD may be a suitable alternative to full karyotype when amniocentesis is undertaken primarily to exclude fetal aneuploidy. However, a counterargument is that an invasive procedure puts a pregnancy at risk, thereby justifying the most "complete" test available. It is likely that further development of prenatal molecular techniques will allow for improved detection of more chromosomal disorders at lower cost.

Abstract

Objective: To review the molecular genetic techniques currently available for rapid prenatal diagnosis of fetal aneuploidy, as well as those still under investigation.

Options: Limited to introductory discussion of rapid aneuploidy detection methods.

Evidence: Medline was searched for articles related to the topic that were published after 1992. This document represents an abstraction of the information.

Values: This update was prepared by the Genetics Committee of the Society of Obstetricians and Gynaecologists of Canada approved by the Executive and Council of the Society of Obstetricians and Gynaecologists of Canada.

Benefits, Harms, and Costs: This update provides information about methods of rapid aneuploidy detection using molecular

Key Words: Prenatal diagnosis, genetic screening, chromosome aberrations, aneuploidy, fluorescence in situ hybridization, polymerase chain reaction

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