QF-PCR for prenatal diagnosis of common aneuploides in women of advanced maternal age

To the Editor: The policy of the Division of Human Genetics (National Health Laboratory Service (NHLS) and University of the Witwatersrand) in respect of prenatal testing for chromosome abnormalities in women of advanced maternal age has changed. The purpose is to accommodate the limited human and financial resources available in South African public health services for such testing.

Advanced maternal age (AMA) screening is undertaken on pregnant women of 35 years or older because of their increased risk of bearing children with the more common autosomal trisomies, namely trisomy 13, 18 and, particularly, 21 (Down syndrome). Once identified, these women should be offered counselling to inform them of their increased risk and the options for its reduction. The options include prenatal testing for trisomies 13, 18 and 21 using fetal material usually obtained by amniocentesis.

Prenatal AMA diagnosis has traditionally been performed by cytogenetic analysis of cultured fetal cells, which is time-consuming (7 - 21 days) and expensive (R2 400, NHLS rate). Quantitative fluorescent polymerase chain reaction (QF-PCR) analysis is now recognised as a viable alternative to cytogenetic analysis for the rapid detection of autosomal aneuploides.[1]

QF-PCR is a molecular (DNA)-based test performed on uncultured fetal cells. Used in the Laboratory of the Division of Human Genetics it is able to detect the common numerical chromosomal abnormalities of chromosomes 21, 18, 13, X and Y. Trisomies 13, 18 and 21 are detected with about 99% accuracy, usually within 48 - 72 hours and at a cost of R1 197 (NHLS rate).

QF-PCR has limitations. It cannot yield accurate results when there is maternal contamination of amniotic fluid or, less commonly, when chromosomal imbalances such as low-level mosaicism (<30%), some types of polyploidy, and structural chromosomal abnormalities (deletions, translocations and ring chromosomes) are present. It detects extra chromosome 21 material present in cells with unbalanced translocations of chromosome 21, but does not identify the problem as a translocation. These shortcomings are, however, put into perspective by a multi-centre audit of 23 genetic laboratories, which found that, in over 98 000 amniocenteses performed after Down syndrome screening, only about 1% of autosomal chromosome abnormalities were not detectable by QF-PCR.[2]

In industrialised countries, newer technologies such as QF-PCR are considered as optional extras to routine cytogenetic analysis for prenatal diagnosis.[1] However, in resource-limited developing nations such as South Africa, we believe that QF-PCR can be the standard diagnostic technique.

Therefore, at the Division of Human Genetics, QF-PCR will now be done instead of conventional cytogenetic analysis in cases where AMA is the only indication. Should abnormalities be detected on sonar or other specific indications, full karyotyping can still be requested and performed. Pretest counselling of AMA women should take this policy change into consideration; a *pro forma* consent form for amniocentesis that does so, is available from the Division of Human Genetics.

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