NEW PROSPECTS FOR NON-INVASIVE PRENATAL DIAGNOSIS

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Fetal nucleared cells in the maternal circulation constitute a potential source of cells for the non-invasive prenatal diagnosis of fetal genetics abnormalities. Three types of nucleated fetal cells (trophoblasts, lymphocytes and erythrocytes) cross the placenta and circulate within maternal blood. Syncytiotrophoblastic cells may not always reflect the fetal genome and fetal lymphocytes may persist from previous pregnancy. Thus, fetal erythrocytes seem to offer the most potential for non-invasive prenatal diagnosis.

Three steps appear essential to allow non-invasive prenatal diagnosis: 1) distinguishing fetal from maternal cells, 2) enrichment of the fetal cell population, and 3) use of rapid methods of analysis on small number of fetal cells or DNA, respectively. To identify fetal cells several monoclonal antibodies are used, but this is still problematic. Furthermore, the number of fetal cells in the maternal circulation is scarce; in the order of 10-5 to 10-6 or less. Therefore enrichment strategies usingk selective density gradients, magnetic cell sorting (MACS) or fluorescent activated cell sorting (FACS) are required. Rapid analysis can be actueved by tests based on polymerase chain reaction (PCR) or fluorescent in situ hybridisation (FISH). Using these techniques, fetal sexing and fetal aneuploides have been diagnosed in fetal cells recovered from maternal blood, and the diagnoses have been confirmed by conventional invasive methods. Thus, the prospects for non-invasive prenatal diagnosis are promising. However fast and better cell separation techniques are still needed along with further improvements of detection methods. Other major issues to be addressed in the future include the investigation of the presence and frequency of fetal cells in maternal blood throughout gestation, whether there are differences in individual pregnancies, and the persistence and duration of fetal cells in maternal blood after delivery.

FETAL REDUCTION AND SELECTIVE TERMINATION

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Over the course of the past several years, multifetal pregnancy reduction (MFPR) has emerged as a method to reduce the high perinatal morbidity and mortality secondary to iatrogenic multifetal pregnancies created by excessive hormonal stimulation and aggressive assisted reproductive technologies. The experience of a limited number of groups worldwide shows that MFPR is performed mostly as a transabdominal needle insertion into the fetal thorax of potassium chloride. The technical success rate of the procedure approaches 100 %, and in experienced hands, the take-home baby rate is comparable to that of the background expectations for the stopping number of fetuses. In a series of over 1000 cases, most all of which were reduced from higher order of numbers to twins, the percentage of pregnancies reaching viability for 3 to 2 has been 95 %, 4 to 2 90 %, and 5+ to 2 80 %. There are also higher risks for prematuritiy with greater starting and stopping numbers. For second trimester procedures done for fetal abnormalities, referred to as selective termination, there is an inverse correlation between the gestational age at the procedure and the likelihood of fetal loss, with loss rates prior to 16 weeks approximately 5 %, and greater than 17 weeks approximately 15 %. There have been no instances of coagulopathies nor damaged survivors in dizygotic gestations.