58 Ability of ultrasonography to detect cystic fibrosis in utero

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Objective: Sonographic finding of fetal echogenic bowel (FEB) has been associated with several pathologies such as chromosomal abnormalities, congenital infections or cystic fibrosis (CF). The aim of this study was to assess the ability of ultrasonography to detect CF in utero.
Method: This study relied on the experience of Brittany (western France) where CF is frequent. Such a study was possible in our region because a newborn screening (NBS) program is set up since 1989 and because analysis of the CFTR gene following a FEB diagnosis is also effective since the early 1990s. Combination of the data from these two programs enabled to assess the proportion of CF fetuses that were diagnosed by ultrasonography over the study period (period 1993–2007).
Results: Over the 15-year period, our NBS program screened 539,479 newborns and identified 186 CF patients (incidence: 1/2900). A diagnosis of FEB had been made in utero in 5 of them. Over the same time, 14 other pregnancies, in which a diagnosis of FEB was made, were terminated because the molecular analysis revealed CF. Consequently, among the 200 (186+14) CF cases over the study period, 19 (14+5; 9.5%) presented a FEB and were therefore diagnosed in utero by ultrasonography.
Conclusion: This study reveals that ultrasonography has led to identify close to 10% of the CF cases over the study period in our region. These findings are of first importance for clinicians who order testing for CF following a FEB diagnosis. They highlight the efficiency of ultrasonography as a screening tool for CF in utero, what contributes to modify the incidence of CF.
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59 First results of preimplantation genetic diagnosis of cystic fibrosis in Russia

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Preimplantation genetic diagnosis (PGD) is an alternative for prenatal diagnosis that makes it possible to perform the diagnosis of monogenic disorders at the preimplantation embryo level. Cystic fibrosis is one of the monogenic diseases for which PGD can be performed.
In our study we report 8 cases of PGD for this particular disorder over a 3-year period. 79 blastomeres underwent embryo biopsy in 8 IVF+ICSI cycles. After PGD for CF mutations and PGS for common aneuploidies 19 of them were transfered and 4 clinical pregnancies were achieved (pregnancy rate – 50%). 5 healthy babies have been born already and there is one ongoing pregnancy. No misdiagnosis was recorded.
We conclude that PGD is an effective alternative to prenatal diagnosis for couples with an ethical or a religious objection to pregnancy termination and for infertile patients carrying a genetic disorder. In our case pregnancy rate was 50%s, half of all women that underwent their first PGD cycle achieved a birth or ongoing pregnancy.

60 Preimplantation genetic diagnosis for cystic fibrosis

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For couples at risk of having children affected with Cystic Fibrosis (CF), preimplantation genetic diagnosis (PGD) is an alternative to prenatal diagnosis (PND) thus avoiding selective termination of affected pregnancies. PGD is a procedure in which one or two blastomeres from embryos obtained through in vitro fertilization are analysed, after which embryos shown to be free of the disease under investigation are transferred to the maternal uterus to initiate pregnancy. We report our experience with PGD for CF.
From April 2002 to December 2008, 58 couples inquired about PGD for CF at our center. Molecular analysis was performed for 34 families. Thirty PGD cycles were initiated for 16 couples including couples with heterozygous partners carrier of a severe CFTR gene mutation (n = 11), CF-affected male partners (n = 2), and congenital bilateral absence of the vas deferens in males (n = 3). One to 3 genetically unaffected embryos were selected for transfer in 19 cycles resulting in 7 clinical pregnancies (36.8% per transfer): 1 was spontaneously aborted, 4 produced 5 unaffected live births, 1 twin pregnancy is still ongoing and 1 unaffected pregnancy confirmed by PND was selectively terminated because of an abnormal karyotype.
Over the years, we have constantly updated the technologies used and have now evolved to a rapid and efficient fluorescent multiplex PCR protocol allowing the simultaneous analysis of nine sequences either located within the CFTR gene (F508del mutation, IVS1CA, IVS8CA, D7S677, IVS17bTA and IVS17bCA markers), or on each side of the gene (D7S486, D7S23 and AFM320vb5 polymorphisms). This protocol is applicable to >95% of the couples requesting PGD for CF, broadening the range of prenatal testing options for these families.

61 Trisomy 21 – possible cause for false positive sweat test?

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Aim of study: to evaluate the possible influence of 21 trisomy on sweat test result in cystic fibrosis.
Material and Method: 5 month old female infant was admitted to hospital for evaluation of particular phenotype. Clinical examination at admission revealed hypotrophy, particular phenotype (epicanthic skin folds, eyelid slit, low-seat ears, hypertelorism, epicanthus, a slightly open mouth with tongue protrusion, simian crease, "sandal sign"), pallor, hypotonia, no pathological change in lungs at auscultation; on cardiac auscultation: systolic murmur of III /VI degree, abdominal muscular diastasis. The phenotype was assimilated to a Langdon-Down syndrome.
Results: The kariotype has confirmed a structural chromosomal abnormality of robertsonian translocation type between acrocentric chromosomes 21 and 22, and a numerical chromosomal abnormality consistent with a total trisomy 21 type, the cytopenic formula being: 46, XX, –22, +21, trob (21;22). The sweat test was positive; NaCl 86 mmol/l and 98 mmol/l the second test. The genetic analysis for cystic fibrosis was negative for the 29 most common mutations for central-eastern european area. Echocardiography revealed a common atrioventricular canal complete form. An abdominal ultrasonography showed several images interpreted as cholelithiasis.
Conclusion: The question is if there is an association between trisomy 21 and cystic fibrosis or another condition is the leading cause of false positive sweat test still has to be answered.