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## 30 Sixteen years of newborn screening for cystic fibrosis using the IRT/IRT strategy in Buenos Aires Province, Argentina

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**Introduction:** Newborn Screening (NBS) for Cystic Fibrosis (CF) is today an unquestionable tool for the public health system. It allows an early diagnosis, a timely treatment, a better quality of life, and growth improvement. It also offers the best scenario for genetic counseling and family planning. Although, NBS for CF is mandatory in Argentina since 1994, it was not until 2008 that the law was regulated in Buenos Aires Province (BA). Moreover, since Jul/10, NBS is part of the Diagnosis and Treatment for Congenital Diseases Program (PRODyTEC), Ministry of Health (BA). Before then, NBS scope was limited mostly to private sector and made mainly upon request.
**Objective:** To present NBS for CF results for the period Jul/95-Dec/11 using IRT/IRT and sweat test as confirmation.
**Materials and Methods:** IRT measurements were performed using DELFIA technology (cut off value 70 ng/ml). Since the strategy did not consider searching for mutations, genetic testing was carried out only after sweat test confirmation.
**Results:** Along the first 15 years, 1.168.524 newborns (NB) were screened, 85% being BA natives and the rest from other provinces. In 2011, 200.463 NB (86.7% from BA) were tested, reaching coverage of 60% of total NB. 166 NB were confirmed with CF, giving an incidence rate of 1:7.039. 13 of these NB corresponded to false negative, but only 5 were true cases, the remaining presented meconium ileus (MI) at birth.
**Conclusions:** Recall rate, sensitivity (excluding MI) and specificity were 0.55%, 96.8% and 99.96% respectively. Similar values are reported in the literature for IRT/IRT.

## 31 Comparative study for the evaluation of a new technology for cystic fibrosis screening

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**Objectives:** Cystic fibrosis (CF) is one of the most frequently diagnosed autosomal-recessive diseases in the Caucasian population. Screening for Cystic Fibrosis Transmembrane conductance Regulator (CFTR) gene mutations, including poly T, is strongly recommended in infertile couples planning a pregnancy by assisted reproductive technology (ART). This study evaluated the performance of the new Nanochip CF70 kit (Savyon Diagnostic, Israel), a microarray assay, and compared it with the Innolipa kits (Innogenetics, Belgium).
**Methods:** From January to July 2012 we analyzed 392 blood samples with Innolipa and Nanochip technologies that identify respectively 70 and 56 CFTR mutations. Both tests include the most common Italian mutations and the poly-T screening. Discordant results were analyzed with the Devyser CFTR Core Kit (Devyser, AB, Sweden), MLPA (MRC Holland), Direct Sequencing (DS) on the 3730 DNA Analyzer (AppliedBiosystems), and Sequenom's MassArray system (Diatechpharmacogenetics, Italy).
**Conclusion:** Innolipa and NanoChip were concordant for 371/392 samples. 21/392 (0.5%) discordant results were tested with the aforementioned technologies: DS confirmed Innolipa results in 18/21 samples and Nanochip results in 1/21, while Devyser and Sequenom did not recognize some mutations not included in their panels. DS was essential for the identification of two different homozygous deletions; although they were not present in Innolipa panels, in 2/21 samples Innolipa indicated a mutation with the warning no interpretation possible
In this study the Innolipa assay confirmed its reliability and Nanochip showed that it could become competitive with slight changes to the software.

## 32 Uptake of genetic counseling and analysis of DNA testing outcomes following newborn screening for cystic fibrosis: Experience of the Prague centre

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**Objectives:** Within the nationwide cystic fibrosis (CF) neonatal screening (NBS) scheme we assessed the uptake of post-NBS genetic counseling (GC), together with DNA testing assessment. Within the "IRT/DNA/IRT" NBS scheme GC is proactively offered to the parents of an ascertained newborn with 1 or 2 *CFTR* mutations.
**Methods:** GC reports and our internal CF database were used for data collection.
**Results:** Since August 2009, 201 newborns with 1 or 2 mutations were identified of which 35 suffered from CF, 5 had equivocal diagnosis of CF (EDG), including detection of 161 carriers. Parents of 179 cases (90.0%; i.e. one or both parents) underwent GC. Provision of GC was not documented in 5 instances (2.5%), while 15 (7.5%) families declined GC. Altogether DNA testing was performed in 156 (77%) cases. Both parents were tested in 129 newborns (comprising 26 CF patients, 3 EDG cases and 100 carriers), only mothers were tested in 26 newborns (3 CF patients, 1 EDG and 22 carriers), including father of a carrier. In the parents of CF carriers DNA testing revealed a couple with the 25% risk of CF and 6 highly likely cases of non-paternity, i.e. with no mutation identified. The "obligate" carrier status of each parent of the 29 children with 2 mutations found within CF NBS was confirmed.
**Conclusions:** The uptake of GC is high. However, deceased infants with 1 *CFTR* mutation and no sweat test result, children with EDG and revelation of non-paternity in parents of CF carriers demonstrate some of the difficult GC issues in CF NBS. Implementation of the IRT/PAP/DNA protocol would reduce the number of DNA tests and thus decrease DNA testing-related CF NBS burden.

## 33 High rate of false-positive results in cystic fibrosis newborn screening among a Spanish population of Maghribian origin

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**Background:** A wide variety of physiological or medical conditions have been associated with hypertrypsinaemia in the neonatal period. A slightly higher immunoreactive trypsin (IRT) concentrations has been reported in babies of North African parentage than in babies of North European origin.
**Objectives:** To analyze the IRT levels and the rate of Cystic Fibrosis Newborn Screening (CF NBS) false positives (FP) in Maghribian newborns as compared with babies of other ethnic groups in a ethnically diverse Spanish Region (Murcia).
**Methods:** A three-stage (IRT1/IRT2/DNA) protocol, using the sweat chloride concentration for discriminating between false and true positives, has been performed in Murcia since March 2007. T-student and $Chi^2$ tests were used to assess differences between both populations regarding FP ratio and IRT levels.
**Results:** In last 6 years, 106 infants (21 North Africans, mostly from Morocco, and 85 of other ethnic groups) with a FP result of the NBS have been referred to our CF unit. According to current population census in Murcia, it means that the rate of FP is 6.08 per 100,000 inhabitants among non-Maghribians and 27.8 per 100,000 inhabitants among Maghribians; OR 4.56 (IC95% 2.83; 7.35). Mean IRT1 level was 81.8±26.6 ng/ml in the first group and 106.7±101 ng/ml in the second one (p 0.055); mean IRT2 level was 61.2±15.3 ng/ml in the first group and 96.3±79 ng/ml in the second one (p 0.0003).
**Conclusions:** In our population, the rate of FP and IRT levels (mainly the second tier) are much higher in newborns of Maghribian origin as compared with those of other ethnic groups. Maybe, we should adjust IRT cut-off to ethnic origin.