22* Retrospective analysis of stored dried blood spots (Guthrie cards) using IRT measurements to detect clinically diagnosed children with cystic fibrosis in Switzerland

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Aims: To evaluate whether the planned two step newborn screening for cystic fibrosis (IRT − 7 most common DNA mutations) would have retrospectively detected all clinically diagnosed children with CF in Switzerland in the last 3 years. **Methods:** A questionnaire was mailed to all CF centres to collect all names of children who were diagnosed with CF based on clinical symptoms and two positive sweat tests (or 2 gene mutations) since 1st January 2006, when general newborn screening was centralised in Switzerland. Afterwards, IRT was measured in stored dried blood spots from the 4th day of life (Guthrie cards) of these children using AutoDELFIA Neonatal IRT-Kit (PerkinElmer, Finnland).
Results: 57 children with clinically diagnosed CF were reported from the CF centres. From 45 we have received the permission to analyse their Guthrie card. 29 children had IRT-values above 60 ng/ml (2009: 4/4, 2008: 5/8, 2007: 10/17, 2006: 10/16). Fifteen children had a value between 30 and 60 ng/ml. All these values were much higher compared to IRT-measurements from Guthrie cards of the control group (8–10 healthy children from the same day of each patient: mean IRT 15.4 ng/ml). There was only one false negative IRT result: This child was diagnosed with atypical CF in the first week of life using molecular diagnostic (F508 del/R31c) as both parents were known heterozygous CF carriers. The child is pancreatic sufficient and would have been missed in the proposed algorithm as the IRT was identical to the control group (9.72 vs. 9.68 ng/ml) and the sweat test was normal (Cl=15 mmol/l).
Conclusions: All children (but one with an atypical CF) would have been detected with the planned two step protocol.

23 Cystic fibrosis newborn screening − clinical findings at date of diagnosis

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Background: From June 1996 until December 2007 a two-step IRT/DNA-screening was performed in eastern saxony, Germany. 160674 neonates have been screened and 38 children with cystic fibrosis (CF) have been diagnosed. We wanted to show that even if the diagnose is confirmed in the first month of life, most children with CF show already clinical symptoms.
Methods: In all patients with CF we reported birth weight and length, weight and length at date of diagnosis, clinical pulmonary and gastrointestinal symptoms reported by the parents at the first contact, clinical examination and stool elastase.
Results: Birth weight and length was significant lower than birth weight and length of healthy children in Germany (p = 0.015 for birth weight and p = 0.00 for birth length). In 50 % of the cases weight and length at date of diagnosis was on a lower percentile than at birth. In 22% of the cases parents already recognized pulmonary symptoms like cough or bronchitis and gastrointestinal symptoms like diarrhea, abdominal pain or insufficiant weigth gain. In 24% clinical examination showed pulmonary symptoms as well and in 81% we found already at that time pancreas insufficiency.
Conclusions: Children with cystic fibrosis in most cases already have clinical symptoms even if they are diagnosed early by newborn screening. Especially insufficiant weight gain and growth and pancreas insufficiency are often not noticed by parents at that stage of illness and should be treated. Therefore newborn screening is a nessecary tool for a better treatment in early life of children with cystic fibrosis.

24 Experience with harmonizing the neonatal CF screening (NSCF) management via model IRT/PAP/DNA in the Czech Republic

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IRT/DNA/IRT is nationwide NSCF since 10/2009. Although efficacy confirmed during pilot study (2005–6), high number of healthy carriers discovered (1:15.4 in selected group). CF more specific IRT/PAP/DNA now runs in parallel. In comparison with IRT/DNA/IRT is cost effective but requires higher amount of sweat tests (ST) (~1%).
Detection of PAP or IRT+PAP increase (at ~3 wks of life) is followed by a ST laboratory referral. As this moment brings psychological burden to the family, we prefer contact via the family paediatrician (FP) who has got most up-to-date information about child and family. Parents sign informed consent with blood spot DNA analysis at the moment of ST. The ST result notification is administered on the same day by phone. The first information about diagnosis (DG) is provided by CF medical specialist together with psychologist who both follow up the family. To minimize extreme stress a telephone hot line with a CF psychologist and social worker is available for parents, personal meeting possible to arrange. Four-day stay in CF centre is fixed up for intensive airway clearance training, pancreatic enzyme administration and other instructions coming from all CF team members (social worker, hygiene rules specialist, geneticist, CF nurse).
Although basic information about NSCF is provided at the maternity unit there is generally low public awareness about CF. Learning about CF is therefore very stressful. The education should be positively structured with a focus on importance of early treatment on positive prognosis, improving life quality and survival expectancy.

25* Sweat chloride (SC) concentration and CFTR mutation class among infants identified by newborn screening (NBS) in California (CA)

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In 2007 CA began CF NBS using an algorithm that includes full CFTR gene analysis (via scanning-sequencing technology), minimizing the false positive rate. Infants with 2 mutations detected are referred to CF Centers (CFCs) for evaluation and confirmatory SC testing. While a positive SC test represents definitive diagnostic criteria for CF, individuals with CF could have SC outside of the diagnostic range. We are currently conducting a prospective study of SC in infants identified by CA CF NBS. Here we present the SC results of infants identified in the first 2 years of CF NBS by CFTR genotype. CFTR mutations were categorized according to their class into Groups A (classes I, II, III), B (classes IV, V) or C (Unclassified). Median SC results were analyzed by genotype groups (mutation1/mutation2: A/A, A/B, A/C, B/C, C/C). 429 newborns had positive results; 95% (N = 406) had $\geqslant$1 SC test performed. Among screen positive infants meeting the inclusion criteria (N = 285), the A/C mutation group was the most prevalent (45%) followed by the A/A group (33%). Median initial SC (mmol/L) was highest among infants in group A/A (94.5) and lowest among infants in group C/C (13.5). Despite low SC in all groups but A/A, the percentage of infants in each group with a final diagnosis of CF was significant (A/A 90%, A/B 42%, A/C 20%, B/C 29%, C/C 19%). By initial SC category, 6% of infants with a diagnosis of CF had values $\leqslant$29, 12% between 30–59 and 71% $\geqslant$60 mEql/L. 11% did not have a SC test. Although genotype and SC are correlated, neither is a perfect predictor of final diagnosis. This study emphasizes the importance of longitudinal follow up at CFCs regardless of initial SC results.