**WS11.5 Newborn screening for cystic fibrosis in Norway**

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**Objectives:** Norway introduced newborn screening for Cystic Fibrosis (CF) in March 2012 based on a three tier immunoreactive trypsinogen (IRT)/DNA/DNA protocol. The cystic fibrosis transmembrane conductance regulator (CFTR) mutation spectrum of Norwegian CF patients as well as mutations previously not seen in the population were included in the mutation panels. We present the results from the first 22 months of nationwide CF screening in Norway.

**Methods:** IRT was measured using GSPTM (Perkin Elmer) and samples above 60 ng/ml were included in 2nd tier testing. This involved Luminex-based analysis of 71 mutations and Sanger sequencing of a local common mutation. If only one mutation was found, 3rd tier testing included sequencing of an additional panel of clinically rare alleles found in Norwegian CF patients. Infants carrying two mutations were reported for diagnostic follow-up.

**Results:** At the end of 2013, 111 648 samples had been screened for CF and 875 children (0.78%) had tested positive in primary IRT screening. 2nd tier DNA assessments revealed 22 samples carrying two CFTR mutations. 3rd tier DNA testing of 86 samples disclosed one child with two mutations. Based on the 23 reported children the most frequent alleles were p.R117H (32.6%) and p.F508del (30.4%). In addition, five infants where no mutation was found were reported due to very high IRT values (>400 ng/ml).

**Conclusion:** We found fewer children with a clear CF genotype than expected, and the CFTR mutations and allele frequencies were different compared to clinical material. This suggests reviewing the IRT cut-off level and continued reporting of p.R117H variants as well as extending the 2nd tier mutation panel.

**WS11.6 Interpretation of nasal potential difference (nPD) measurements in difficult cases of possible cystic fibrosis and the role of published equations**

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**Background:** ECFS guidelines include nPD if diagnostic tests for CF are inconclusive. Equations have been derived that may accurately differentiate CF from non-CF [Wilschanski (eqW)1 and Sermet (eqS)2]. Retrospectively, we analysed nPD traces from our Difficult CF Diagnosis (DCFD) Service to examine agreement between the two equations and with the clinician’s interpretation (CI).

**Methods:** 66 patients underwent nPD testing at a median (range) age of 18.5 (2−67) yrs. nPD traces were also analysed from healthy controls (HC, n = 6) and DF508/DF508 CF patients (n = 10). Proportions of agreement (PA) were calculated.

**Results:** For HC and DF508/DF508 there was perfect agreement (PA = 1) between all 3 analysis methods. In DCFD patients, CI of nPD results in the context of history/investigations led to the following categories: (a) Non-CF: n = 44 (68.2%). eqS was concordant with CI (PA = 1); eqW led to 2 subjects being classified as CF (PA = 0.95); neither has an identified CFTR mutation; (b) Variant/atypical CF: n = 9 (13.6%). 6 were labelled CF by eqS (PA = 0.67) and 3 with eqW (PA = 0.33). Agreement between the two equations was poor (PA = 0.5). On extended CFTR analysis, 2 patients have no CFTR mutations, 1 has one and 6 have two.

**Conclusions:** Both equations work well in classical CF patients and in HC. They were also highly concordant with each other, and CI, in patients referred to the DCFD clinic in whom CF was ruled out. Agreement was poor between the equations in more complex patients with possible variant CF or with traces considered equivocal or adversely affected by inflammation. nPD may be most robust at ruling out CF, particularly as full CFTR gene sequencing becomes more readily available.