The 31st ECFS Conference in Prague, Czech Republic, June 11, 2008

We started with a brief report from Dr Carlo Castellani on the new consensus on CF diagnosis which is now published in the Journal of Pediatrics. It is a guideline by the Cystic Fibrosis Foundation for the CF diagnostic route in both infants with positive NBS results and older patients presenting with an indistinct clinical picture. Their recommendations involve a combination of clinical presentation, laboratory testing, and genetics to confirm a diagnosis of CF.

Dr Martin Schwarz gave an overview of the importance of polymorphisms in CF diagnosis. There are over 1500 sequence variants in the CFTR gene, but only about 2% with evidence for functional consequences. For the majority of CFTR mutations evidence for changed function is only empirical. Moreover, many are private variants and the assessment of pathogenicity is difficult. The term 'polymorphism' is falling out of favour. Alternative names are sequence variant, unclassified variant, or mutation of unproven or uncertain clinical relevance. Examples of such sequence variants are: T5 (and TG repeat), G576A (+/- R668C), S1235R (+/- T5), M470V and I148T. 'Polymorphisms' may be of significance in atypical presentations. They have poor predictive value, but may help in determining if a clinical presentation is CFTR-related. The collation of clinical and molecular genetic data is urgently required.
Dr Peter Middleton from Sidney, Australia, presented his results on nasal potential difference measurements. For assessment of the presence of chloride secretion he used a superfusion solution with low chloride concentration (6mM) versus a zero chloride solution (both in the presence of Amiloride). The zero chloride solutions gave responses about 2mV larger than the 6mM solution. In addition, he tested the influence of 0 mM, 10 mM and 20 mM glucose concentrations on basal PDs and there were no differences between these solutions.
Dr Isabelle Sermet from Paris, France, showed her results on the presence of CFTR as assessed by immunodetection in nasal ciliated cells in correlation with nasal transepithelial potential difference. She showed that there is also CFTR expression in F508del and stopcodon patients. However, it did not aid to solve the diagnosis in cases with intermediate nasal PD values. In summary, she does not use this method for diagnosis, but for follow-up and characterisation of the disease phenotype.

Dr Inez Bronsveld presented the evaluation of the different nasal PD methods used in the different CF centres in Europe, and the question whether there is a need for standardisation. She showed that there are many differences, smaller and larger, between the methods used in different centres. There is variation in voltmeter; the anatomic site for measurement; exploring catheter width and site of the holes; reference electrodes being either calomel or Ag/AgCl; skin bridges being either ECG electrodes with abrasion or agar bridges and subcutaneous needle; the connections to the electrodes appeared to vary between almost all centres having their own custom made connections; perfusion solutions; perfusion sequence and timing; registration by chart recorder or computer; the interpretation of the results taking the best reading or the mean of both. The aim is to find out whether the differences in methods are important for test result and which are most important to standardise. With the standardization we aim to minimize variability between operators and study sites and want to get consistent results to compare between various CF centres and participate in multi-centre studies.