371 Evaluation of nonclassic CF: interpretation of sweat test methods in correlation to ICM and CFTR genotype

N. Derichs[1], C. Stolpe[1], C. Müller[1], J. Sanz[2], S. Gallati[2], M. Ballmann[1]. [1]*Pediatric Pulmonology, CF-Center, Medical School Hannover, Hannover, Germany;* [2]*Human Genetics, University Hospital, Bern, Switzerland*

Evaluation of nonclassic CF is complicated by inhomogeneous standardisation of sweat test methods despite the presence of consensus criteria. Aim of this study was to investigate the interpretation of sweat test parameters and its correlation to intestinal CFTR chloride secretion and CFTR genotype.
In n = 103 patients (mean age 11±1 yrs.) with mild pulmonary symptoms, PS and 0–1 mutations in CFTR mutation screening a non-standardised sweat test (Cl– concentration without sweat amount/Na+ concentration/conductivity) in the collaborating center had been interpretated as pathological/borderline, in part due to ignorance of reference values. We compared these data with a standardised sweat test and both intestinal current measurement (ICM) (n = 103) and extensive CFTR genotype analysis (exon 1–27) (n = 29).
Present sweat test results (Cl– standardised 40±2 mmol/l) differed significantly from previous recordings: Cl– non-standardised 61±3 mmol/l ($p < 0.001$), Na+ 70±5 mmol/l, NaCl 74±3 mmol/l. On the basis of ICM and CFTR genotype analysis the diagnosis nonclassic CF was made in n = 7 individuals with rare mutations. Interestingly, in all n = 14 patients who already had been diagnosed and treated for CF for up to 30 years before inclusion into this study, a revision of the diagnosis CF was necessary.
These data underline the problem of non-standardised sweat test performance and the importance of adequate result interpretation. This could avoid unnecessary extended diagnostics and misdiagnosing of CF. ICM helps to overcome diagnostic dilemmas by exclusion or confirmation of nonclassic CF when needed.

372* Outcome of the pregnancies with an echogenic bowel detected by ultrasonography: the 15 year-experience of Brittany (western France)

V. Scotet[1], I. Duguépéroux[1], M.P. Audrezet[1,2], M. Blayau[3], P. Boisseau[4], P. Parent[5], H. Journel[6], C. Férec[1,2]. [1]*Inserm U 613, Brest, France;* [2]*Dept of genetics, Brest, France;* [3]*Dept of genetics, Rennes, France;* [4]*Dept of genetics, Nantes, France;* [5]*Unit of medical genetics, Brest, France;* [6]*Unit of medical genetics, Vannes, France*

This study aimed to describe the outcome of the fetuses in whom an echogenic bowel was detected at routine ultrasound examinations of pregnancies in Brittany over a 15-year period (1991–2005). We registered all the diagnoses of echogenic bowel made in pregnant women living in Brittany and who were referred for a CFTR gene analysis (n = 269). A questionnaire was sent to the gynaecologists to know the pregnancy outcome and the pathologies diagnosed. We calculated the CF frequency, described the other pathologies and assessed the ability of ultrasonography to detect CF in utero. Among the 269 fetuses, 21 were diagnosed with CF, leading to a CF incidence of 7.8%. The pregnancy outcome was documented for 212 of the non-CF fetuses (85.5%) and an other pathology was evidenced in 46 of them (21.7%). A karyotypic abnormality was diagnosed in 21.7% of these fetuses (n = 10 including 7 Trisomy 21), a congenital viral infection in 19.6% (n = 9 including 4 CMV) and a cardiac malformation in 15.2% (n = 7). The other diagnoses were: atresia (n = 4), toxemia gravidis (n = 3) and other (n = 13 including 7 abdominal problems). Finally, by combining these data with those of the newborn screening, we showed that ultrasonography enabled to diagnose 10.2% of the CF cases over the study period. These findings are of first importance for clinicians who order testing for CF following the diagnosis of an echogenic bowel. They show that a pathology was diagnosed in 28.8% of such fetuses and highlight the ability of ultrasonography to detect CF in utero.
Supported by: Association "Vaincre La Mucoviscidose".

373* Respiratory exacerbations in childhood associated with compound heterozygote CFTR genotype ΔF508/R117H on a background of 7T polythymidine tract at intron 8

T.W. Lee[1], S.P. Conway[1,2], D. Peckham[2], K.G. Brownlee[1]. [1]*Leeds Regional Paediatric Cystic Fibrosis Centre, St James's University Hospital, Leeds, United Kingdom;* [2]*Leeds Regional Adult Cystic Fibrosis Centre, Seacroft Hospital, Leeds, United Kingdom*

Debate continues regarding the clinical implications for compound heterozygotes identified with ΔF508 and R117H/7T mutations of the CFTR gene. Consequently it remains unclear whether R117H/7T mutations should be screened for, how intensive monitoring and treatment should be, and what information about prognosis should be given.
Previous reports regarding children with this genotype have shown that pathogenic organisms such as *Pseudomonas aeruginosa* and *Staphylococcus aureus* are commonly isolated from respiratory secretions [1,2] and there is one recent report of a pulmonary exacerbation in childhood associated with ΔF508/R117H/7T [2].
We report extensive and prolonged right middle lobe and right lower lobe collapse and bilateral patchy consolidation in a 4 year-old child with this genotype. Bronchoscopy two months after the start of the illness demonstrated extensive pus in the right main stem bronchus. Culture of respiratory secretions was positive for *Staphylococcus aureus*. Symptoms and chest X-ray changes resolved after three weeks treatment with physiotherapy and intravenous antibiotics. Subsequently *Pseudomonas aeruginosa* has been isolated from her sputum during a mild respiratory exacerbation.
Taken together with recent published data [1,2] this case would suggest that this compound heterozygote CF mutation should not be considered benign in childhood.

References

[1] Lording A, et al., J of Cystic Fibrosis 2006; 5: 101–104.
[2] O'Sullivan BP, et al., Pediatrics 2006; 118: 1260–1265.

374 ^{18}FDG-PET/CT in CF: correlation with both inflammatory markers and FEV_1

M. Cohen-Cymberknoh[1], M. Klein[2], S. Armoni[1], D. Shoseyov[1], M. Orevi[2], R. Chisin[2], E. Kerem[1]. [1]*CF Center, Hadassah Medical Centers, Jerusalem, Israel;* [2]*Nuclear Medicine, Hadassah Medical Centers, Jerusalem, Israel*

Progressive pulmonary disease associated with chronic bacterial infection and inflammation is the major cause of morbidity and mortality in cystic fibrosis (CF) patients. Identifying markers of inflammation that correlate with lung injury may be useful in monitoring disease progression and response to therapy. High resolution computed tomography (HRCT) is used to monitor changes in lung structure but does not permit differentiation between acute and chronic lesions. We have previously shown that positron emission tomography (PET) with ^{18}fluoro-deoxy-glucose (FDG) allows visualization of focal inflammation or infection and therefore appears to be a promising tool to quantify new processes.
The purpose of this study was to determine whether biomarkers of systemic inflammation correlate with FDG-PET/CT findings.
14 patients with CF (12 male, 2 female, age 14–40 y) performed FDG-PET/CT. PET and CT images were interpreted by a nuclear medicine physician/radiologist, blinded to the clinical data. We correlated the PET severity score (PSS), reflecting the number and intensity of FDG uptake of lung foci with FEV_1, CRP, WBC, % and total neutrophils and sputum bacteriology.
The best correlation was detected between PSS and total neutrophils ($R^2 = 0.4$), no correlation was noted between PSS and CRP ($R^2 = 0.1$), WBC ($R^2 = 0.19$), % neutrophils ($R^2 = 0.06$) or FEV_1 ($R^2 = 0.2$).
Our findings suggest that the focal changes observed in FDG-PET correlate with increased total neutrophils count, reflecting active neutrophilic inflammation. Larger studies, currently carried out at our center, are needed to validate these results. Confirmation may add FDG-PET/CT as a method to predict the severity of disease progression in patients with CF.