213* Progression of pulmonary hyperinflation and trapped gas associated with genetic factors in children with cystic fibrosis (CF)

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Functional deterioration in CF is best reflected by increased degree of ventilation inhomogeneities (Am J Respir Crit Care Med 2005; 171: 371–8). A clinically similarly important mechanism is gas trapping, known to impair gas exchange dramatically. We aimed to determine which lung physiological factors (airway resistance, ventilation inhomogeneities, pulmonary hyperinflation) or genetic factors dominantly influence these mechanisms in CF. Serial annual lung function tests, performed in 164 CF-children (81 males; 83 females; age: 6–18 y), provided data pertaining to functional residual capacity (FRCpleth, FRCMBNW), lung clearance index (LCI), volume of trapped gas (VTG), effective specific airway resistance (sReff), and forced expiratory indices (FEV1, FEF50). Pulmonary hyperinflation (FRCpleth > 2SDS) was already present in 43% of patients at age 6–8 yrs, increasing to 84% at age 20 yrs. The proportion of patients with VTG increased from 41% to 83%. All lung function parameters showed age-related progression. Children with severe pulmonary hyperinflation and gas trapping at the age 6–8 yrs have the worst progression of their disease over time. Gas trapping was more associated with airway obstruction than with ventilation inhomogeneities and significantly associated with the CFTR genotype. Similar to the tracking of lung function in asthma, tracking in CF starts very early whereby genetic factors play an important role. Thus, early assessment of pulmonary hyperinflation, ventilation inhomogeneities and trapped gas in conjunction with CFTR genotypes will help to monitor functional disease progression in CF.

214 Airway reactivity in Cystic Fibrosis

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Variability in responsiveness to bronchodilator drugs is one of the features of inflammation in cystic fibrosis (CF). A subpopulation of CF patients (pts) demonstrates airway reactivity. Bronchial reactivity may be considered one of the markers of poor prognosis.

Aim of the study was to asses the reversibility of FEV1 after bronchodilator (Salbutamol) and the bronchial hyperreactivity after histamine aerosols in our CF pts followed in one CF Center from Bucharest.

Methods and Results: 27 CF pts, age range 5–20 years (mean age 10.6 years), 18/27 chronically infected with *Pseudomonas aeruginosa* or *Staphylococcus aureus* were enrolled in the study. Baseline FEV1 values was used to define three groups of pts. First group (12 pts) demonstrate normal FEV1 (mean value 103.48% of predicted). The second group (9 pts) had moderate decrease of FEV1 (mean value 64.9% of predicted) and a third group (6 pts) had a severe decrease of FEV1 (mean value 45.5% of predicted). All the children were tested for response to bronchodilator aerosols and positive response was defined as $\geqslant$12% change in FEV1 from baseline value.13/27 (48.7%) had a positive response represented by an increase in FEV1 (11.5% to 17.5%). The bronchodilator response was negative in all the pts from the third group (mean increase FEV1 of 0.4% of predicted). The bronchial reactivity was assessed in 7 pts with FEV1 $\geqslant$80% of predicted. The percentage of fall FEV1 and FEF50 from baseline was determined. Decrease of FEV1$\leqslant$12% and of FEF50 $\leqslant$15% was considered significant. The hyperresponsiveness was found in 6/7 cases.

Conclusions: Our results confirm the data from previous studies regarding variability of airway reactivity in CF pts due to the chronic bronchial inflammation. The follow-up prospective study of our cases may demonstrate correlation between bronchial reactivity and deterioration of respiratory function.

Abreviations: FEV1 = forced expiratory volume in one second. FEF 50=forced expiratory flow at 50% of vital capacity.

215 Baseline pulmonary function as a predictor of blood oxygenation while breathing a normobaric, hypoxic gas mixture in adults with Cystic Fibrosis

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Study objective: To develop a Pre-Flight assessment for adults with cystic fibrosis to predict the need for in-flight oxygen supplementation.

Subjects: Sixty ambulatory and clinically stable adults with cystic fibrosis with a mean FEV1 of 52.6% (range 22–112%) predicted.

Methods: The study contained two parts. Part one was the routinely pulmonary function test in our lungfunction laboratory. Part two was the inhalation of a normobaric, hypoxic gasmixture (15% O_2 in 85% N2) with finger-probe pulse-oximetry and on-line breath-by-breath registration for the simulation of air travel or the remaining at an altitude of 2,438 m (n-HAST).

Results: None of the subjects had a baseline oxygen saturation lower than 90%. In all subjects there is a significant lower O_2-sat (%) during n-HAST whereas heart rate and minute ventilation are significant higher.

Baseline O_2-sat correlated best with O_2-sat during n-HAST. None of the subjects who were not at risk (FEV1 $\geqslant$50% predicted) had clinically significant desaturations, O_2-sat <85%, during n-HAST. In the at risk group, subjects with an FEV1 <50% predicted, six subjects had dangerous desaturations. In three of them n-HAST was ended prematurely when their O_2-sat reached a value of <80%.

Conclusions: We conclude that all patients with an FEV1 < 30% predicted and baseline O_2-sat $\leqslant$95% require in-flight oxygen. Patients with an FEV1 < 30% predicted and baseline O_2-sat > 95% and patients with an FEV1 30–50% predicted and baseline O_2-sat $\leqslant$95% are at risk when exposed to a hypoxic challenge such as an altitude simulation test or air travel. In these patients further assessment in order to predict necessity of in-flight oxygen is highly recommended.

216 Compact and portable gas mixing measurements using a photoacoustic analyzer

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Background: Evidence is increasing that a simple index of ventilation inhomogeneity (lung clearance index; LCI) derived from a multiple-breath inert gas washout is a more sensitive measure of airway dysfunction in children with CF than spirometry. To date, this has required a mass spectrometer (MS), which is both expensive and complex to maintain. Innocor is a photoacoustic gas analyzer that has been designed to measure cardiac output by inert gas rebreathing. Its capacity to measure sulfur hexafluoride (SF6) means that it can be adapted to measure LCI.

Aims: To compare the performance of Innocor to a MS, the current gold standard for measuring LCI.

Methods: Using a specially constructed syringe, instantaneous step changes in flow and gas concentration were generated. Speed of response is given as the 10–90% rise and fall time. We also compared the signal:noise ratio of the two devices during LCI measurements. Signals from both machines were sampled at 100Hz.

Results: Innocor can measure SF6 concentrations as low as 0.005% with minimal noise compared to a MS. Both MS and Innocor track changing SF6 concentrations similarly, but the Innocor signal is slower (rise time 150 msecs compared to MS rise time of 80 msecs). During LCI measurement, this leads to a small but acceptable difference of 4% in the calculated total expired volume of SF6.

Conclusions: The modified Innocor device provides a promising alternative to the MS in assessing ventilation inhomogeneity. The device is both much smaller and less expensive, and has excellent signal resolution down to below 0.005% SF6. The signal rise time is slower, but this is unlikely to cause major error in the calculation of lung volumes or LCI during normal breathing.