

P249 IT IS POSSIBLE TO DETECT ACTIVE NEUTROPHIL ELASTASE IN EXHALED BREATH CONDENSATE OF PATIENTS WITH CYSTIC FIBROSIS

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Introduction CF is characterised by chronic progressive respiratory decline punctuated with periods of acute pulmonary exacerbations (PEX). Given the relationship between PEX number and chronic rate of decline and that ~25% of PEX patients fail to regain their baseline FEV₁, there remains a need for a reliable biomarker to predict PEX and/or monitor responses to treatment. Several biomarkers have been explored, including sputum Neutrophil Elastase (NE). However, any sputum-based biomarker will only be suitable for patients able to expectorate, whereas significant disease begins earlier in life. Previously, our group (Thorax 2013;68: 532–9) reported the change of physiological, functional and structural markers over a PEX within which we collected exhaled breath condensate (EBC). These samples were analysed with a newly-developed immunoassay; detection of NE would offer the potential to detect airway inflammation in non-expectorating subjects.

Methods EBC was collected using an Ecoscreen condenser, stored at –80°C, and then analysed using the ProteaseTag® Active Neutrophil Elastase Immunoassay (ProAxis Ltd).

Results 35 EBC samples from 19 participants were available. Participants were 12–44 years; 10 female. Median FEV₁% predicted was 52.5% (IQR 43.75%–74.8%). All had chronic *Pseudomonas aeruginosa* infection apart from 1 who had chronic *Burkholderia cepacia* complex infection. NE could be detected (\geq LLD 7.2 ng/ml) in 28 of 35 samples (80%). For

the whole group, median concentration was 15.45 ng/ml (IQR 10.36–19.02 ng/ml).

Discussion This was a small, pilot study seeking to demonstrate the feasibility of measuring active NE in EBC and successfully reporting, for the first time to our knowledge, detectable levels of this inflammatory marker. However, levels were near the lower end of detection of the immunoassay; therefore development of a more sensitive assay could be helpful. Further work is needed to establish CF/non-CF differences and the relevance of levels to accepted measures of airway disease. The use of EBC could allow monitoring of airway inflammation at the early stages of CF lung disease when patients cannot expectorate sputum, and during a period in their disease progression when the potential impact of interventions on long term outcomes may be greatest.

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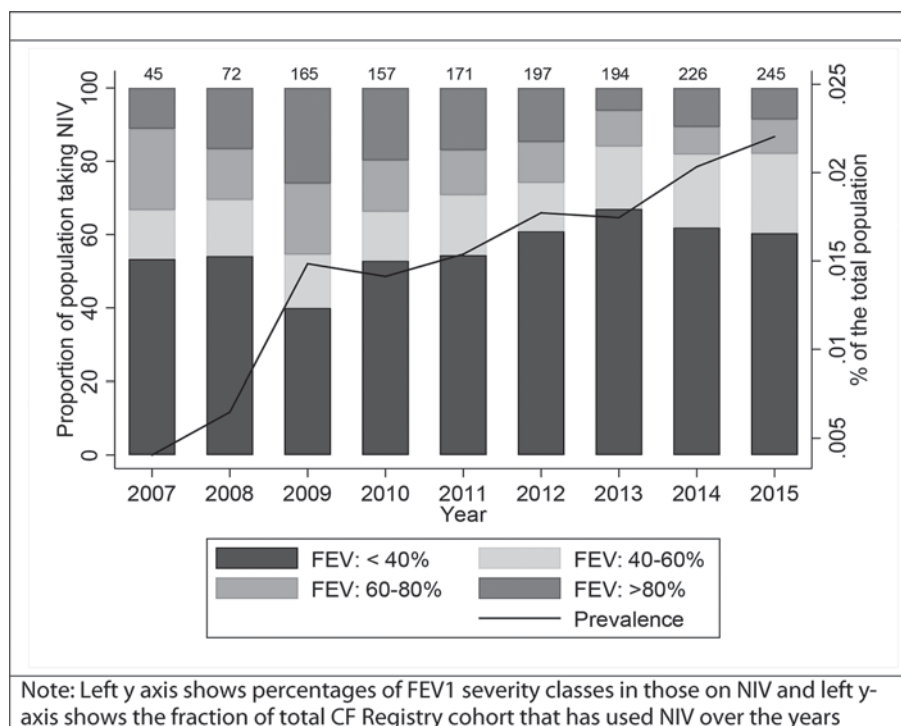
P250 A NATIONAL STUDY OF NON-INVASIVE VENTILATION AND CLINICAL OUTCOMES IN CYSTIC FIBROSIS

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Introduction/Objectives Non-invasive ventilation (NIV) is often used as a ‘bridge’ to transplantation, for symptom control or as an adjunct to physiotherapy. Whether or not NIV is being appropriately used in UK patients with CF, successfully targeting those who will benefit most, is unknown; nor is there information on the life expectancy of those who start on NIV.

Methods The present study is part of the CF-Epidemiological Network (CF-EpiNet project) and uses data from the UK Cystic Fibrosis Registry to describe the patterns of NIV use by



Abstract P250 Figure 1 Lung function distribution across years and prevalence of NIV use.

patients in the UK. We examined the records of 11 120 patients and assembled a longitudinal, retrospective cohort from those seen between 2007 and 2015. We used Cox proportional hazard models to assess the survival of patients on NIV.

Results 1077 patients (715 adults and 362 children <16 years) had reported use of NIV recorded at least once. Usage increased after 2012 (figure 1). At the first recorded use of NIV the median (IQR) age was 21 years (14, 28), BMI 18.4 kg/m² (16.8, 22.7), 49.2% were male, 90.3% on PERT, 75.1% growing *Pseudomonas*, 54.6% homozygous F508del; the mean FVC_{pp} was 64.5% and FEV₁ pp 47.2%. At this time 68.8% of patients had a FEV₁ pp <60%; 52% were <40%, while in adults this percentage reached 61%. In children there was a higher proportion starting treatment with better lung function ie ≥60% (33.8%). The median survival of patients who start NIV is 3.47 years. The hazard ratio for NIV use was 3.90 (95% CI: 3.06–4.96).

Conclusions Not surprisingly, patients start NIV when their lung function is significantly impaired. Yet, increased proportions of people with FEV₁ pp ≥40% on NIV were also identified. The higher lung function at the start of NIV for children may reflect that it is used for purposes other than a bridge to transplant in this group; the registry only collects a yes/no variable for NIV use and not the reason for use. Survival after initiation of NIV is poor; this is likely reflect that NIV is a marker of disease severity but further analysis will be needed to explore this.

P251 ENVIRONMENTAL FUNGAL SAMPLING IN A CYSTIC FIBROSIS CENTRE

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Objectives *Aspergillus* is a ubiquitous organism and CF lungs are vulnerable to infection. *Aspergillus* is known to be found in high numbers in organic matter and during building works. We commenced environmental fungal air sampling prior to and during building work carried out adjacent to our CF unit to evaluate and monitor our air quality.

Methods An SAS Microbial air sampler sampled 1 cubic metre of air over 5 min in assigned locations throughout our ward on a weekly basis. Outdoor samples were taken during this time for comparison. Each plate was cultured for 4 days at 30°C.

Results The predominant organism was *Aspergillus fumigatus*, the second *Penicillium* Spp. Site 1, outdoor air: revealed a maximum yield of 59 colony forming units (CFU) *A. fumigatus* (range 0–59 CFU, median 9), and 8 CFU *Penicillium* (0–8, median 0). Site 2, ward corridor: 29 CFU *A. fumigatus* (0–29 CFU, median 2.5), 15 CFU *Penicillium* (0–15, median 0.5). Site 3, patient room: 12 CFU *A. fumigatus* (0–12 CFU, median 2), 9 CFU *Penicillium* (0–9, median 0). Site 4, positive pressure anteroom: 2 CFU *A. fumigatus* (0–2 CFU, median 0), 1 CFU *Penicillium* (0–1 CFU, median 0). Site 5, patient room: 58 CFU *A. fumigatus* (0–58 CFU, median 4.5), 5 CFU *Penicillium* (0–5 CFU, median 2.5). There was a clear rise in

Aspergillus yield demonstrated during the summer months in all areas except our positive pressure anteroom which persistently yielded negligible fungal growth.

Conclusions High levels of *A. fumigatus* were persistently yielded from sites 1, 2, 3 and 5, both at baseline and during building works, with peak counts being found in the summer months. Fungal ingress onto the ward was demonstrated in all sites except in our positive pressure anteroom, with ≥10 air changes per hour, leading to isolation rooms. This gives doubts about the efficacy of our ventilation system in the majority of locations throughout our ward and needs to be clinically correlated with patient outcomes.

P252 CLINICAL PROFILE OF INFANTS WITH CYSTIC FIBROSIS SCREEN POSITIVE, INCONCLUSIVE DIAGNOSIS (CFSPID) IN THE WEST MIDLANDS

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Background The introduction of newborn screening for cystic fibrosis (CF) has resulted in up to 10% of infants with the positive result but inconclusive diagnosis. The European cystic fibrosis consensus group has defined CFSPID as newborn screened infants with elevated immunoreactive trypsinogen and normal sweat chloride and two CFTR mutations, at least one with unclear phenotypical consequences OR infants with intermediate sweat chloride with one or no CFTR mutations (Munck:2015). The majority will remain well and have no long-term health implications. However, a small percentage of these infants may develop the disease by three years.

Aim To study the prevalence, clinical characteristics and clinical course of children who meet the CFSPID criteria within a large UK regional paediatric CF centre

Methods Retrospective data review of children identified on newborn screening who met the ECFS CFSPID criteria using CF registry, regional screening centre notification and the local network database.

Results Between October 2006 to December 2016, 148 infants were CF screen positive. 9 children (6.08%) met CFSPID diagnostic criteria. The median follow up period was 25 months (range 6–95 months). Median age at repeat sweat test was 3 years (range 1.5–5 year). All patients were heterozygous for ΔF508. The second mutation identified included R117H in 6 children, D1152H in one child and Arg810Ser in 2 siblings. 2 patients had *Staph aureus* and *Haemophilus influenzae* once on cough swabs. None of them was positive for *Pseudomonas aeruginosa*. All were pancreatic sufficient. All children in the group remained nutritionally well. None had chronic isolates of significant respiratory pathogens common in cystic fibrosis and repeat sweat test remained normal in all patients.

Conclusion Early outcomes for CFSPID are good. National guidance on information provided to families at diagnosis, frequencies of clinic follow up are necessary. In addition assessment of the psychological impact of the diagnosis to the families would be valuable. National data collection possibly through a UK CF registry based study to inform long term outcomes in children with a diagnosis of CF SPID is needed.