Abstract P109 Figure 1 Mean VAS ratings of cough severity, throat discomfort and voice change according to diagnosis.

P110 FEASIBILITY OF CONTINUOUS LARYNGOSCOPY DURING PROVOCATION IN THE ASSESSMENT OF INDUCIBLE LARYNGEAL OBSTRUCTION

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Introduction Inducible laryngeal obstruction (ILO) is typically provoked by a range of stimuli, including perfumes and exercise, and characterised by transient throat tightness, dyspnoea and stridor. Central to the diagnosis of ILO is paradoxical adduction of laryngeal structures on inspiration. Continuous laryngoscopy during exercise (CLE) is now established as the gold-standard diagnostic test for exercise-ILO, but diagnosis of other forms of ILO is currently dependent on non-continuous laryngeal visualisation, where crucial diagnostic behaviour of the larynx may be missed. We report the first application of continuous laryngoscopy during provocation (CLP).

Methodology Fifteen female patients (aged 36–58) suspected of having ILO and referred from the RBH specialist upper airway clinic underwent CLP, using self-selected provocation agents to elicit their typical symptoms. Three patients had a prior confirmed diagnosis of asthma. The flexible nasendoscope (CMOS, Karl Storz) was passed without anaesthetic and secured on specialist headgear (figure 1). Patients entered a sealed provocation booth, where they were exposed to the agents they had selected, unable to see the monitor. On elicitation of upper airway symptoms, the specialist SLT initiated laryngeal control strategies with visual biofeedback. The test ended when the patient's typical symptoms had been generated or when exposure exceeded the point of previous symptom provocation.

Results All patients tolerated continuous placement of the scope and confirmed that exposure in the chamber had been sufficiently concentrated to provoke typical symptoms. Only one patient exhibited classical paradoxical glottic movement. Pre-exposure, the vocal cords were closely adducted in three (20%) patients and fully adducted during unintentional breath-holding in three patients (20%). All patients subsequently attended a review with the specialist SLT to consolidate understanding of CLP findings and use of control strategies.

Conclusion CLP is a safe and well-tolerated method for evaluating laryngeal movement during provocation and negates repeated passage of the nasendoscope. Continuous monitoring

throughout provocation testing improves diagnostic accuracy by capturing the presence or absence of paradoxical movement and may be linked with software that tracks laryngeal movement digitally. Further work is needed to develop standardised CLP protocols and identify clinical phenotypes of ILO.

Abstract P110 Figure 1 Demonstration by first author of nasendoscope placement for CLP.

Infected lung: from bench to bedside

P111 EXHALED BREATH BIOMARKERS IN PULMONARY ASPERGILLOSIS

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Introduction Pulmonary aspergillosis has a substantial global health burden, and is difficult to diagnose and treat. *Aspergillus* metabolism Results in measurable changes in volatile organic compounds (VOCs) and these may be detectable in the breath. In this pilot study, we sought to measure the abundance of VOCs in the breath samples of patients with pulmonary aspergillosis, and identify any difference in VOC profile between patients with and without *Aspergillus* in their airway.

Methods Patients were recruited while attending the National Aspergillosis Centre and University Hospital South Manchester, and categorised as *Aspergillus* positive or *Aspergillus* negative on the basis of high volume sputum culture. Lower airway breath samples were collected from patients and analysed by thermal desorption gas chromatography mass spectrometry (TD-GC-MS). A target library based upon previous literature reports of *Aspergillus*-related VOCs was used to deconvolve the raw GC-MS data. Peak area on the chromatogram for each sample was calculated as a measure of VOC abundance. Potentially discriminating compounds between the groups were identified by univariate analysis.

Results 18 patients were recruited, and were allocated to the following groups: culture-positive (n=7), and culture-negative

Abstract P111 Figure 1 Box-and-whisker plots of relative VOC abundance in culture-positive and culture-negative groups.

(n=11). Analysis of patient demographics and potential breath contaminants revealed no significant difference between groups. The targeted analysis incorporated 35 VOCs. Of these, 2 were found to be significantly more abundant (figure 1) in culture-positive than culture-negative patient samples. These compounds most likely represent limonene ($p=0.017$) and alpha-terpinene ($p=0.007$).

Conclusion This pilot study has identified differences in the exhaled VOC profile of patients with sputum culture-positive and culture-negative pulmonary aspergillosis. The finding of elevated levels of terpenoids in the breath of culture positive patients concurs with current understanding of the *Aspergillus* volatome *in vivo* and *in vitro*. A larger study using multivariate analysis should be performed to identify discriminating exhaled VOC signatures in patients with aspergillosis for future clinical use.

Abstract P112 Figure 1 *Achromobacter* spp. antibiotic sensitivities in CF (above) and non-CF Bronchiectasis (below) patients.

P112 INCIDENCE AND CLINICAL OUTCOMES OF PULMONARY INFECTION WITH ACHROMOBACTER SPP

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Background *Achromobacter* is considered an emerging Gram-negative pathogen in cystic fibrosis (CF) although its pathogenic potential is controversial and its impact in other patients groups largely unknown.

Methods All *Achromobacter*-positive respiratory samples analysed at our institution from 2007–2016 were identified. Antibiotic susceptibility was tested using the disc-diffusion method. Clinical data were collected from medical records. The Leeds criteria were adapted to define chronicity of infection.

Results 48 patients were identified, with a diagnosis of CF in 25, bronchiectasis in 16 and miscellaneous other conditions in 7. Median (IQR) number of samples provided was 4 (1–16), 1.5 (1–2.25) and 1 (1–1.5) in the CF, bronchiectasis and other groups respectively. In the CF group, the median age at first *Achromobacter* isolate was 22.3 years (IQR 17–30) and mean BMI 21.8 kg/m² (SD 4.1). Baseline FEV₁%-predicted in the CF population was 50.4% (SD 22.6%). Among bronchiectasis patients, median age at first isolate was 61 years (IQR 58–78)

and FEV₁ 1.35 L/s (SD 0.75). During the study period, the yearly rate of detection of *Achromobacter* infection increased across all groups, with 4 cases in 2007 rising to 25 in 2016 and a mean of 9.9 cases/year. In any given year during the period 2012–2016, the mean proportion of CF patients with chronic, intermittent and cleared infection was 25%, 54% and 29% respectively, whilst in the bronchiectasis group it was 11%, 37% and 57%. Co-infection with *Staphylococcus aureus* was seen in 20% of samples from CF patients. Equivalent figures for other pathogens were: *Pseudomonas aeruginosa* 14%, *Aspergillus* 11% and non-tuberculous mycobacteria 7%. In the bronchiectasis group, co-infection was mainly seen with *Pseudomonas aeruginosa* (15%). Antibiotic resistance was significantly greater in the CF group compared to the bronchiectasis group, particularly to meropenem (57% of CF isolates vs 0% of bronchiectasis isolates), piperacillin-tazobactam (31% vs 0%) and colistin (20% vs 0%); $p<0.05$.

Conclusions Detection of *Achromobacter* spp from respiratory samples increased over the study period with CF patients more likely to develop chronic infection. *Achromobacter* spp isolates from CF patients had greater levels of antibiotic resistance than those from patients with bronchiectasis.

P113 ANTIMICROBIAL PEPTIDES IN INFLAMMATORY PHENOTYPES OF COPD

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Introduction Antimicrobial peptides act to defend the host from microbial action and colonisation. Patients with COPD and neutrophilic inflammation experience bacterial colonisation more frequently than other COPD phenotypes. Here we assess the levels of five antimicrobial peptides in peripheral blood and sputum in relation to their inflammatory phenotype. We hypothesise that patients with neutrophilic inflammation have lower antimicrobial peptide levels than other COPD inflammatory phenotypes and that the presence of non-typeable haemophilus influenzae (NTHi) is associated with low antimicrobial peptide levels.

Method Plasma and sputum supernatants from 8 healthy donors, 18 COPD patients and 10 non-eosinophilic asthmatics were tested for SLPI, osteopontin, lysozyme, elafin and beta defensin-1 by ELISA. Patients were stratified into eosinophilic and neutrophilic groups with a 3% sputum eosinophil cut-off. NTHi was measured in sputum plugs by qPCR of the *Omp P6* gene.

Results Levels of antimicrobial peptides in plasma and sputum showed no difference between those with eosinophilic and neutrophilic COPD. Between disease groups, beta defensin-1 levels are higher in plasma of COPD patients (median: 10.92 ng/ml (IQR: 4.137–18.09)) than healthy individuals (median: 3.665 ng/ml (IQR: 2.59–4.549), $p=0.0033$) and non-eosinophilic asthmatics (median: 4.984 ng/ml IQR: 3.334–7.208), $p=0.0442$) (figure 1). No antimicrobial peptide correlated with NTHi levels in the sputum plug.

Conclusions Similar levels of SLPI, osteopontin, lysozyme, elafin and beta defensin-1 in sputum and plasma between COPD phenotypes suggests that defence against pathogens by these antimicrobial peptides is not lacking in differential inflammatory COPD phenotypes. The role antimicrobial peptides play in NTHi colonisation remains to be determined.

Abstract P113 Figure 1 Concentrations of beta defensin-1 in plasma from healthy individuals, asthmatics and COPD patients.

P114 GLUCOCORTICOID RECEPTOR α AND β EXPRESSION IN BRONCHIAL EPITHELIAL CELLS INFECTED WITH NTHI

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Introduction Steroids act through the glucocorticoid receptor (GR), of which the alpha-isoform (GR α) is most abundant. Neutrophilic COPD is associated both with resistance to steroids and with airway bacterial infection, most commonly by non-typeable Haemophilus influenzae (NTHi). We hypothesised that NTHi downregulates GR α or upregulates its inhibitory beta-isoform (GR β) in bronchial epithelial cells, thereby inhibiting their response to steroids.

Method Bronchial epithelial cell line Beas-2B were treated with the corticosteroid Fluticasone propionate (0, 1 nM or 100 nM) for 2 hours prior to infection with 1.5×10^4 , 1×10^6 and 1.5×10^7 CFU/ml NTHi (low, medium and high load respectively). 6 hours post-infection supernatants were collected and RNA extracted from cells. RNA was reverse transcribed to cDNA in which levels of GR α , GR β and GAPDH were determined by SYBR Green PCR and expression calculated using the Pfaffl method relative to untreated cells.

Results GR α expression in Beas-2B was enhanced by corticosteroid treatment in a stepwise manner for 1 nM (median fold increase from untreated: 1.491, IQR: 1.305–1.668), and 100 nM (median: 1.742 fold, IQR: 1.51–1.9) ($p \geq 0.05$ for both). Increasing load of NTHi showed no effect on GR α expression. GR β expression showed little fluctuation from levels of untreated cells upon infection with NTHi alone or high dose corticosteroid, however the two showed a trend to synergistically decrease in GR β expression when treated with high corticosteroid and high load of NTHi (median fold change from untreated cells: 0.542 (IQR: 0.453–0.578) ($p=0.25$) (figure 1).

Conclusions Corticosteroid treatment shows a trend to increased GR α expression on Beas-2B cells. Increased NTHi load has no effect on GR α expression of Beas-2B cells. GR β expression appears not to be affected by NTHi infection alone, however with corticosteroid shows a trend to decreased expression. The experiments are to be repeated in primary bronchial epithelial cells to determine whether they follow the trend seen here in a cell line.

Abstract P114 Figure 1 Expression of GR β in Beas-2B cells relative to untreated cells normalised to GAPDH.