Addressing service challenges such as lack of time, prioritisation of achieving QOF indicators and increasing workload demands, as well as the cultural challenges created by professional hierarchies may allow HCP to deliver quality SM more consistently and effectively.

Severe lung disease progression and transplantation

P109 CIRCULATING MMP ACTIVITY AND LUNG REMODELLING IN LAM

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LAM is characterised by the progressive accumulation of lung cysts. It is possible increased proteolysis causes extra-cellular matrix breakdown leading to cyst formation. Matrix metalloproteinases (MMPs) are expressed in the lungs and serum of patients with LAM and can break down the extracellular matrix. Here we examined MMP expression and activity patients with LAM and healthy women and related MMP activity to extent and activity of lung disease.

59 patients with LAM and 32 healthy controls were recruited. Ethical approval was obtained and all gave informed consent. Serum was collected in separator tubes and processed within 30 minutes, urine was centrifuged at 4°c and all samples were stored in aliquots at –80°c. MMP-2 and –9 were measured by ELISA and gelatin zymography. Urine results were normalised against creatinine concentration prior to analysis. Lung function data was obtained from clinical records. Cyst volume was measured on a Philips MX8000 IDT 16 slice spiral CT scanner using density mask software on a Philips Healthcare Q19.5 Extended Brilliance™ Workspace. The trachea and large airways were excluded, cysts were defined as having a threshold density of <-900 Hounsfield units and cyst volume expressed as a percentage of total lung volume. Rate of decline for FEV_1 was estimated from symptom detection to current lung function. Data were analysed using non parametric Mann-Whitney U tests and linear regression.

Total serum MMP-2 ($p<0.01$), total MMP-9 ($p<0.001$) and active MMP-9 ($p<0.05$) assessed by zymography were greater in patients than controls. Urine MMP-9 did not differ. Total serum MMP-2 was associated with preserved FEV_1 ($p<0.01$, $r^2= 0.040$). Cyst volume was correlated with reduction in FEV_1 and FEV_1/FVC ratio but not with any MMP measurement. Median FEV_1 decline was 108.5ml/year (range 0–840): no measurement of MMP expression or activity was correlated with rate of decline.

Total and active MMP-9 were raised in serum from LAM patients but were not associated with clinical course. Surprisingly, higher serum MMP-2 was associated with preserved lung function. It is not clear if circulating MMP levels reflect the situation in the lung and further analysis of MMPs as a therapeutic target for LAM is required.

P110 INTERLEUKIN-33 IN CHRONIC LUNG DISEASE

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Background IL33, a member of the IL-1 superfamily has been implicated in the pathogenesis of asthma and postulated to play an aetiological role in several non-pulmonary fibrotic diseases. IL-33 expression has predominantly been reported in mucosal surfaces. We hypothesised lung epithelium might act as a source of IL33 release into the microenvironment as a damage associated molecular pattern (DAMP); propagating pro-inflammatory/fibrotic pathways.

We evaluated tissue expression of IL-33 from a range of chronic lung diseases and assessed release in response to airway epithelial damage *in vitro*. Finally, we determined if IL-33 was detectable in BAL of lung transplant patients developing Bronchiolitis Obliterans Syndrome (BOS).

Methods Expression of IL-33 in chronic lung disease was evaluated by immunohistochemistry from patients with IPF(n=3), COPD(n=3), Bronchiectasis(n=3) and CF(n=3). Epithelial damage was induced in Primary Bronchial Epithelial Cells and 16HBE14o-cells by oxidative stress or freeze/thaw and release of IL33 evaluated by ELISA and Western Blot. BAL was prospectively collected(n=207) from post lung transplant patients(n=26) and IL-33 concentration measured by ELISA. BAL samples were classified as Non – BOS(n=116) or BOS(n=91) on the basis of histological and clinical data. Co-existing presence of infection was identified by standard microbiological culture.

Results IL33 was strongly expressed in airway epithelia with a predominant nuclear location. This was more marked in chronic lung diseases with an infective aetiology (CF and bronchiectasis). IL33 was not detectable in response to airway epithelial cell injury *in vitro*. However, IL-33 levels were elevated in BAL of individuals with BOS($p=0.011$). Longitudinal analysis of 26 individuals spanning the time frame of initial BOS diagnosis demonstrated a trend towards increased concentration of IL-33 in BAL in the immediate period following BOS diagnosis. There was a strong association between elevated IL-33 levels and the presence of BOS with concomitant infection($p<0.001$).

Conclusion IL33 is strongly expressed in the airway epithelium in chronic respiratory diseases but does not appear to be passively released as a DAMP in airway epithelial cell damage. Elevated IL33 with infection in the post transplant population suggests sources other than epithelium may be important but further work is required to evaluate the relevance and significance of these observations.

P111 BRONCHOALVEOLAR LAVAGE DOES NOT AFFECT THE ACUTE INFLAMMATORY RESPONSE FOLLOWING BRONCHOSCOPY AND MEDIASTINOSCOPY

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Objective Bronchoalveolar lavage (BAL) may be used to investigate acute inflammation following thoracic surgery. However, BAL has previously been found to induce an acute phase response in healthy and critically-ill patients complicating research analysis (1,2). We sought to examine the impact of BAL in thoracic surgery patients hypothesising that BAL would not lead to a significant additional acute inflammatory response.

Methods Seventeen patients undergoing lung cancer staging bronchoscopy and mediastinoscopy were randomly assigned to have 220mls 0.9% NaCl BAL before surgery (n=10) or no BAL (n=7). Blood samples were taken pre-operatively followed by 6 and 24 hours post-operatively. Exhaled nitric oxide (eNO) was also measured at a flow rate of 50mls/sec at these times. All patients had a CXR at 24hrs and were evaluated for evidence of SIRS using predefined criteria.

Results IL-6 and CRP increased post-operatively peaking at 6hrs and 24hrs respectively however there was no statistically significant difference between the increase for BAL and non-BAL patients ($p>0.05$). There was no significant increase or variation between the groups for IL-2, IL-4, IL-10, TNF-α or IFN-γ ($p>0.05$). eNO tended to decrease in the BAL group and increase in the non-BAL group at 6hrs although there was no significant difference between the groups ($p=0.167$). Post-operative CXR atelectasis developed in 3 patients (2 BAL). One patient in each group developed SIRS.

Conclusion BAL has minimal impact on acute inflammation following bronchoscopy and mediastinoscopy. It may therefore be used to safely and reliably obtain samples for research or microbiology purposes in thoracic surgery patients.

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P112 THERAPEUTIC WHOLE LUNG LAVAGE FOR SILICOSIS – FIRST APPLICATION IN THE UK

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Silica is a highly fibrogenic dust and this is reflected in the low amounts of dust found in the lungs of those with fatal silicosis – approximately 3g in total. Despite a low workplace exposure limit for respirable silica, new cases of silicosis continue to be diagnosed. There is no effective pharmacological treatment. In China, whole lung lavage (WLL) has been performed for silicosis with evidence of improved dyspnoea at 6 months. To our knowledge the technique has not previously been attempted in the UK.

We carried out WLL in 2 stonemasons with silicosis. Patient A presented aged 41 in 2007 with MRCP dyspnoea score 3, FVC 3.27L (60% predicted), and radiographic features of extensive silicosis (Category 3R, ILO classification). To determine if mineral could be removed from his lungs, a bronchoscopic lavage was performed using 180ml saline. The lavage fluid contained 4.8g/l of mineral. WLL was then performed with 7L saline on the right, and a month later 12L on the left. Each procedure lasted approximately 1 hour and the patient was discharged without complication within 24 hours. The washings contained 0.66g/l mineral. The total removed was approximately 7.9g, 50% of which was silica, (silica content was determined by transmission electron microscopy with energy dispersive x-ray spectrometry). On review at 6 months there had been no clinical or radiological changes.

Patient B presented aged 31 with MRCP dyspnoea score 2, FVC 3.96L (65% predicted), and radiographic features of silicosis (Category C). A 9L right WLL produced considerably less mineral (0.09g/l: total approximately 0.1gm). 21% was silica.

These cases demonstrate that WLL is acceptable and safe in patients with silicosis in the UK, and that substantial quantities of mineral can be removed from the lungs. It is postulated that reducing the silica burden will slow the rate of disease progression, but there is no evidence in support of that. Evidence will be difficult to adduce given the variable nature of silicosis and its relatively slow rate of progression. In the meantime, we suggest that WLL is considered for younger patients with advanced silicosis.

P113 SECRETED LYSYL OXIDASE IS ELEVATED IN THE BRONCHOALVEOLAR LAVAGE FLUID OF PATIENTS WITH IDIOPATHIC PULMONARY FIBROSIS

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Background Idiopathic pulmonary fibrosis (IPF) is a chronic progressive fibrotic lung disease for which there are no effective treatments. As a result the prognosis is poor, with a median survival of 3 years from the onset of symptoms. The key feature of IPF is formation of 'fibroblastic foci', accumulations of highly active, proliferative fibroblasts and myofibroblasts that lay down vast quantities of collagen and other extracellular matrix proteins. Lysyl oxidase (LOX) is a secreted enzyme involved in cross-linking of collagen and implicated in several fibrotic conditions. Increased cross-linking due to LOX upregulation in IPF may contribute to decreased lung compliance. Further, LOX may represent a biomarker that can be used to detect early responses or 'proof-of-mechanism' in clinical trials for new IPF drugs. We hypothesized that levels of LOX protein were higher in bronchoalveolar lavage (BAL) fluid from IPF patients compared to healthy controls.

Methods BAL fluid was collected from patients with IPF or volunteers following ethical approval and informed consent. A quantity of BAL fluid determined to contain 20μg protein was concentrated with Strataclean resin and resuspended in 2x sample buffer. LOX protein content was determined by SDS-PAGE and western blotting followed by densitometry.

Results LOX can be detected in BAL fluid from patients with IPF. Both pro and active forms of the LOX enzyme are significantly elevated in IPF compared to healthy controls, with active LOX detected in 12/25 IPF patients compared to 1/9 healthy controls.

Conclusions There is increasing evidence for a role of LOX in fibrosis. Here we suggest LOX may be involved in IPF pathogenesis, and demonstrate that it is possible to detect secreted LOX in BAL fluid from patients with this condition. LOX may therefore represent a biomarker that could be used in clinical trials for IPF. Further work would be required to validate and optimise assays for clinical use.

P114 PULMONARY FUNCTION PROGRESSION IN LANGERHANS CELL HISTIOCYTOSIS

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Langerhans Cell Histiocytosis (LCH) is a rare, dendritic cell disorder commonly involving the lungs either alone, (PLCH) or as part of multi-system disease (MSLCH). The natural history is variable, ranging from spontaneous resolution to progressive respiratory failure and death. Until recently there were no large follow up series containing lung function data (Tazi A et al, ERJ 2012; 02107–2011).

We retrospectively compared pulmonary function over time in patients with PLCH and in MSLCH with lung involvement from our database of 83 adult LCH patients. 46 patients were male; mean age at diagnosis was 34 (range 16–76) years (y). 9/83 patients, 4 male, mean age 32 y, had PLCH. 21/83 13 male, mean age 28y, had MSLCH with lung involvement.

All PLCH had smoked with mean 14 pack-y. 7 continued smoking after diagnosis. Initial lung function (n=8) at a mean of 1 (–1 to