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.