P115 CIGARETTES SMOKE EXTRACT INDUCES INFLAMMATORY GENE EXPRESSION IN HUMAN BRONCHIAL EPITHELIAL CELLS

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Background Chronic obstructive pulmonary disease (COPD) is an inflammatory disorder of the respiratory tract characterised by airflow obstruction. It is increasingly recognised that the innate immune pattern-recognition receptors may contribute to airway inflammation in COPD in response to environmental factors such as cigarette smoke (CS). One pattern-recognition receptor that has recently come to attention in chronic airway disease is the cell surface receptor for advanced glycation end products (RAGE). RAGE also exists as a soluble form (sRAGE) that primarily functions as receptor decoy and an endogenous inhibitor of RAGE signalling. Clinical studies show that smokers with or without COPD have significantly greater levels of RAGE expression in airway epithelial cells compared with never smokers. However, the role of RAGE in mediating CS-induced inflammatory gene expression has not been understood. We hypothesise that CS can induce RAGE expression, sRAGE reduction, and inflammatory gene expression in human bronchial epithelial cells (BEAS-2B).
Method Confluent BEAS-2B cells were treated with different concentrations of Cigarette Smoke Extract (CSE) (1%, 2.5%, and 5%) for 24 hours. Western blotting was used to assess protein expression of RAGE in cell lysate. ELISA was used to measure interleukin 6 (IL-6), CXCL1 (GRO-α), CXCL5 (ENA-78), CXCL8 (IL-8), CXCL10 (IP-10), CCL11 (eotaxin), and sRAGE in culture medium.
Result We found that IL-6 and CXCL8 releases were markedly increased by CSE in a concentration-dependant manner, but CXCL-1, CXCL5, CXCL10 and CCL11 could not be detected in both untreated and CSE-treated cells. Interestingly, RAGE was highly expressed in untreated cells and CSE treatment did not further increase its expression. Furthermore, sRAGE was also undetectable in both untreated and CSE-treated cells.
Conclusion These findings suggest that CSE can induce inflammatory gene expression in BEAS-2B cells. Further experiments are being conducted to explore the effect of CSE on other inflammatory gene expression and to investigate the role of RAGE in mediating CSE-mediated inflammatory response in BEAS-2B cells.

P116 NEATSTIK® – A NOVEL POINT OF CARE TEST FOR THE MEASUREMENT OF ACTIVE NEUTROPHIL ELASTASE IN PATIENTS WITH RESPIRATORY DISEASE

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Introduction and Objectives Sputum levels of active neutrophil elastase (NE) are frequently elevated in respiratory diseases, such as bronchiectasis, chronic obstructive pulmonary disease (COPD), and cystic fibrosis (CF). Increased NE levels have been demonstrated to inversely correlate with pulmonary function, and risk of exacerbations. Active NE is also recognised as a biomarker of subclinical infection; however, no tools presently exist for its routine monitoring at home or in the clinic. Translation of the ProAxsis NE Activity Based Immunoassay (ABI) to a Point of Care (PoC) device, would facilitate routine monitoring of those patients at highest risk of upcoming exacerbations; enabling pre-emptive medical intervention, and mitigating the patient's risk of developing serious complications.
Methods Active NE levels in sputum samples (n=10) were determined using the NE ABI (ProAxsis Ltd, Belfast), in accordance with manufacturer's instructions; followed by assessment using the NEATstik PoC test (threshold 10 µg/ml in sputum). For measurement of NE using NEATstik, sputum was diluted x10, gently rotated for 1 min, an aliquot (70 µl) was then transferred onto the test sample port of the device and allowed to develop for 10 min, after which the signal intensity at the test-line was visually graded (0–10).
Results NE ABI analysis of sputum revealed that 7 out of 10 samples under investigation contained active NE at levels above the NEATstik test threshold. All 7 samples were found to produce a strong positive test line on the PoC device. Moreover, no test line was visible for the remaining samples with active NE concentrations below 10 µg/ml.
Conclusion Availability of NEATstik, the first highly sensitive and specific PoC test for the rapid detection of active NE in complex clinical samples, should enable the proactive management of multiple chronic respiratory diseases. It has the potential to assist in the identification of patients at highest risk of imminent exacerbations, and thus allow closer monitoring by their clinical team and/or pre-emptive treatment to avoid/minimise the impact of such exacerbations. Additionally, for those presenting with an ongoing exacerbation, the test facilitates patient stratification, with those most likely to respond to antibiotic therapy identified and their response to treatment assessed.

P117 NEUTROPHIL CHEMOTAXIS IN THE SZ FORM OF ALPHA-1 ANTITRYPSIN DEFICIENCY

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Introduction Alpha-1 antitrypsin deficiency (AATD) is a genetic disorder which predisposes to the development of lung disease. The PiSZ phenotype is associated with a lower risk of disease and a pattern of emphysema more characteristic of patients with chronic obstructive pulmonary disease (COPD) than the PiZZ phenotype. Aberrant migration of neutrophils has been observed in stable COPD, possibly contributing to the pathogenesis. Neutrophils from PiZZ patients show a migratory phenotype similar to that of healthy controls and the migratory characteristics of PiSZ neutrophils have not been investigated.
Methods The chemotaxis of peripheral blood neutrophils in PiSZ patients was characterised using an Insall chamber and time-lapse video microscopy. Migratory characteristics of the neutrophils were compared with existing data from PiZZ and usual COPD patients. A marker of neutrophil elastase activity known as Aα-Val^{360} was compared between patient groups and the relationship between patient characteristics and neutrophil migration was examined.
Results PiSZ neutrophils moved with a reduced velocity compared to cells from PiZZ patients in the presence of IL-8

(Mean (SEM): 0.156 (0.036) vs 0.308 (0.045); p=0.016). No difference was apparent in migrating velocity between PiSZ and PiMM neutrophils (Mean (SEM): 0.692 (0.150) vs 0.868 (0.344); p=0.6480). The PiMM COPD patients had higher levels of Aα-Val^{360} when compared to PiSZ (Median (IQR): 25.3 (22.6) vs 14.2 (7.75); p=0.015) and PiMM (Control) patients (Median IQR: 25.3 (22.6) vs 15.9 (12.1); p=0.018). A correlation between alpha-1 antitrypsin level and migrating velocity was observed (r^2=0.410, p=0.003).

Conclusion Neutrophils from PiSZ patients exhibited a migratory phenotype intermediate between PiZZ and usual COPD patients. Higher levels of Aα-Val^{360} in COPD patients suggest that they have elevated levels of neutrophil elastase activity.

P118 PROCALCITONIN CAN REDUCE ANTIBIOTIC USAGE IN PATIENTS WITH SUSPECTED RESPIRATORY INFECTIONS IN AN ACUTE RESPIRATORY SERVICE

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Introduction Procalcitonin (PCT) guidance can help safely decrease antibiotic exposure in patients with suspected or confirmed respiratory infections.[1] Its use however across UK hospitals remains limited. We set out to see if utilising it in an acute respiratory service will aid consultant decision making and reduce unnecessary antibiotic usage.

Methods A case series of 222 patients with suspected respiratory infections were consecutively included over 3 months. Their records where examined retrospectively. A PCT result of <0.25 µg/L would have suggested no potential need for antibiotics.

Results

- 75 patients (34%) with a COPD exacerbation; 45 (20%) a lower respiratory tract infection; 34 (15%) community acquired pneumonia; 17 (8%) asthma exacerbation; 13 (6%) Hospital acquired pneumonia; 11 (5%) Exacerbation of bronchiectasis; 10 (4%) aspiration pneumonia; 17 (8%) with other conditions, not a primary respiratory infection.
- 172 patients (77%) had a PCT of<0.25 µg/L and 50 (23%)≥ 0.25 µg/L.
- In 96 patients (56%) with a low PCT, consultants decided not to prescribe antibiotics: stopped in 56 (33%) and not started in 40 (23%).
- In 76 patients (44%) the consultant prescribed antibiotics: continued in 32 (19%); started in 28 (16%) and in 16 (9%) switched to another antibiotic.
- Bronchiectasis and Aspiration pneumonia patients were more likely to get Antibiotics despite low PCT, 6 patients in both groups (54%) and (60%) respectively.
- Lower respiratory tract infections and Hospital acquired pneumonia patients were less likely to be given antibiotics if the PCT was low, 9 patients (20%) in the first group and 3 (23%) in the second.
- In Patients with a PCT level≥0.25 µg/L 45 (90%) received antibiotics.

Conclusion Low levels of Procalcitonin can reduce antibiotic usage in patients admitted with respiratory infections. This could have an effect on reducing the risk of antimicrobial resistance and costs associated with antibiotic prescriptions. Apprehension remains among respiratory physicians in utilising it as expressed in the number of patients who had antibiotics despite low PCT levels. The validation of the test in conditions like Bronchiectasis and aspiration pneumonia requires further evidence.

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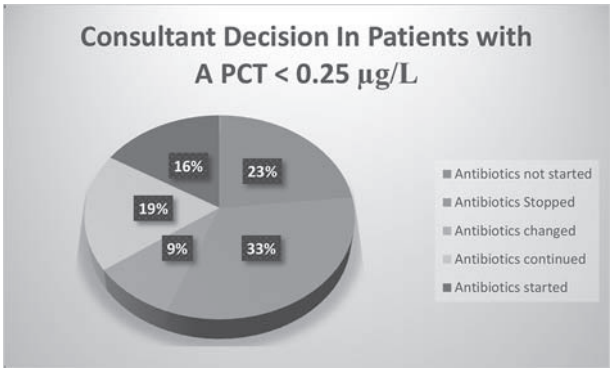

Abstract P118 Figure 1

P119 PICKING UP A BUG BY PICKING YOUR NOSE HAND TO NOSE TRANSMISSION OF STREPTOCOCCUS PNEUMONIAE IN HEALTHY PARTICIPANTS – PILOT STUDY

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Introduction and Objectives *Streptococcus pneumoniae* (pneumococcus) is a leading cause of morbidity and mortality worldwide, causing community acquired pneumonia (CAP), otitis media, bacterial meningitis and septicemia. Respiratory illnesses are reduced by handwashing, but for pneumococcus, the importance of non-aerosolised modes of spread is unknown. Our objective was to investigate the modes of transmission of *S.pneumoniae* from the hands to nose that are able to cause colonisation.

Methods This study examines "hand-to-nose" transmission using a modification of our established controlled human infection model: healthy volunteers were administered pneumococcus (serotype 6B) onto their fingertip or back of their hands in a wet or dry dot, and asked to either sniff the bacterial residue, or make direct contact with the nasal mucosal surface (pick/poke their nose). Colonisation was defined as pneumococcal culture at any time point between day 2 and 9 post exposure.

Results Colonisation rates were highest in those participants who poked their nose with wet pneumococcus ('wet poke group' 4/10, 40%), and who sniffed the wet bacteria from the back of the hand ('wet sniff group' 3/10, 30%). Drying of the bacteria on the skin before "sniff" or "poke" was associated with low colonisation rates (1/10 and 0/10 respectively). The 'wet sniff' technique was further investigated to improve precision of rates, extending the group to 33 participants, of which 6 were positive (18%).

Correction: *P117 Neutrophil chemotaxis in the sz form of alpha-1 antitrypsin deficiency*

Vayalapra S, McGuinness AJA, Stockley RA, *et al*. P117 Neutrophil chemotaxis in the sz form of alpha-1 antitrypsin deficiency. *Thorax* 2017;72:A146–7. doi:10.1136/thoraxjnl-2017-210983.259.

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