these levels differ over an exacerbation time course. We sought to investigate the effects of *Haemophilius influenzae* cell-interaction upon airway inflammation and whether the levels of *H. influenzae* bacteria and cell-dissociated bacteria differ over an exacerbation time course.

**Methods** Cell differential counts were carried out on sputum samples as per standard protocol. Bacterial DNA was extracted and *H.influenzae* was quantified using qPCR from the sputum plug (contains cell-associated and dissociated bacteria) and the sputum cell-free supernatant (cell-dissociated bacteria only). Inflammatory mediators (IL-1α, TNF-α, IL-8 and neutrophil elastase (NE)) were measured in the sputum supernatant using commercial assays.

**Results** 63 patients (77% male; average age of 69 (45–88); $FEV_1$ percentage predicted of 53%; mean percentage neutrophil count in sputum of 65%) at stable state were analysed. Levels of *H. influenzae* in the supernatant only correlated with the sputum total cell count (r=0.38; p=0.03). Levels of *H. influenzae* in the plug correlated with inflammatory mediators (sputum neutrophil percentage r=0.42, p=0.01; sputum macrophage percentage r=−0.35, p=0.04; IL-1α r=0.36, p=0.03; IL-8 r=0.49, p<0.01; NE r=0.40, p=0.02). The exacerbation time course in 10 paired COPD subjects was examined. There was no significant difference in *H. influenzae* levels in the plug (p=0.89) (figure 1A). However, there was a significant increase in levels in the supernatant over the exacerbation time course (p=0.05) (figure 1B).

**Conclusion** *H. influenzae* levels in the sputum plug appear to have much more of an effect on airway inflammation than levels of cell-dissociated *H. influenzae* suggesting that cell-associated bacteria may be a driver of airway inflammation in COPD. Further investigation into this highly complicated relationship needs to be conducted.

## S117 THE EFFECT OF CIGARETTE AND ELECTRONIC CIGARETTE VAPOUR ON BACTERIA IN CHRONIC LUNG INFECTION

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10.1136/thoraxjnl-2017-210983.123

**Introduction** Cigarette smoke is a risk factor for the development of several chronic lung diseases, e.g., Chronic Obstructive Respiratory Disease (COPD) and bronchiectasis. This study aims to determine the effect of cigarette smoke and electronic cigarette vapour, on key bacteria involved in the progression and exacerbation of chronic lung disease.

**Methods** Cigarette smoke extract (CSE) and electronic cigarette vapour extract (ECVE) were prepared using a modified syringe driver apparatus and bubbling through appropriate growth media. Reference isolates [*Haemophilus influenzae*, ATCC49766 (HI), *Streptococcus pneumoniae* ATCC49619 (SP), *Staphylococcus aureus* ATCC29213 (SA) and *Pseudomonas aeruginosa* ATCC 27853 (PA)] were grown in broth +/- CSE or ECVE. Biofilm formation and survival in the *Galleria mellonella* infection model, following bacterial exposure to CSE/ECVE were determined. Levels of IL-8 and TNFα secretion from A549 cells, following infection by bacteria+/-CSE/ECVE and addition of cell-signalling inhibitors, were measured by ELISA.

**Results** A trend towards increased biofilm formation following exposure to either CSE or ECVE was observed, which reached statistical significance with SP and PA +CSE (p=0.0047 and 0.0043, respectively) and SA+ECVE (p<0.001). There was decreased survival of *Galleria mellonella* following infection with bacteria+CSE/ECVE vs. bacteria only, suggestive of increased virulence; this was statistically significant in the case of HI (p=0.016) and PA (p=0.0005) +CSE. Statistically significant increases in IL-8 secretion in A549 cells were observed for HI and PA +CSE and SA +ECVE, and in TNFα, with SP and SA+ECVE. However, a clear trend towards increases in both cytokines following CSE/ECVE exposure was evident, with little difference observed between CSE/ECVE. Addition of pathway inhibitors following A549 cell infection with bacteria+CSE/ECVE resulted in a decrease in IL-8 or TNFα via the same pathways as with bacteria alone.

**Conclusion** Exposure of bacteria involved in the pathogenesis of chronic lung infection to both CSE and EVCE resulted in increased virulence, biofilm formation, and inflammation, and may contribute to establishment of chronic infection and persistence. Further work is required to determine the clinical effects of ECVE.

# Of mice and men

## S118 ELK1 GENE DELETION LEADS TO SPONTANEOUS EARLY FIBROTIC CHANGES IN THE AGEING LUNG

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10.1136/thoraxjnl-2017-210983.124

**Rationale** Idiopathic pulmonary fibrosis is a chronic fibroproliferative disease with a median survival of approximately 3 years. αvβ6 integrins are upregulated in lung fibrosis and are associated with increased activation of the profibrotic cytokine TGF-β. The transcription factor Elk1 can repress gene expression of β6. We therefore hypothesise that animals lacking functional Elk1 ($Elk1^{-/0}$) will develop age related pulmonary fibrosis.

**Methods** Elk1 knock-out ($Elk1^{-/0}$) and wild-type ($Elk1^{+/0}$) mice were allowed to age for 365 days. At 365 days old mice were sacrificed and their lungs harvested for evaluation of collagen gene expression, lung hydroxyproline concentration and histological assessment.

**Results** Lungs were extracted and lung wet weights were measured in $Elk1^{-/0}$ mice and wild-type ($Elk1^{+/0}$) controls and no significant difference between the two genotypes was shown (175.7 mg, 161.8 mg respectively n=6–8). However, assessment of total lung hydroxyproline established that there was significantly more hydroxyproline in $Elk1^{-/0}$ mice compared with $Elk1^{+/0}$ controls (852.3, 758.4 μg/lung set, respectively, n=5–8, p=0.0346). Assessment of Masson's trichrome stained $Elk1^{-/0}$ lung tissue sections found a small number of fibrotic lesions were present. Furthermore, there was a trend towards increased alveolar wall median thickness in $Elk1^{-/0}$ mice compared with $Elk1^{+/0}$ animals (5.94 vs 5.56 μm respectively). In a small number of 12 week old mice we identified a trend towards increased α-smooth muscle actin (αSMA) mRNA expression in the lungs of $Elk1^{-/0}$ mice compared with