Introduction The bleomycin mouse mode can be used as a model of pulmonary fibrosis. The Influenza A virus can infects epithelial cells leading to cell death and injury. Acute exacerbations of Idiopathic Pulmonary Fibrosis (IPF) are characterised by epithelial cell apoptosis with unknown cause. The role of infection in acute exacerbations of IPF is unclear. The aim of this study is to investigate the effect of influenza infection on bleomycin-induced pulmonary fibrosis.
Materials and Methods 60 U of bleomycin was instilled into lungs of 6–8 week old male C57Bl/6 mice. After 28 days mice were exposed intranasally with 10, 20 Units of influenza virus 'x31' or PBS, and lungs harvested 5 or 21 days later. Lung tissue harvested for mRNA analysis, histology and hydroxyproline levels. Animal studies were ethically reviewed and carried out in accordance with Animals (Scientific Procedures) Act 1986 and the GSK Policy on the Care, Welfare and Treatment of Animals.
Results Influenza infection increased in lung collagen levels: COL1 mRNA but not COL3 was increased. There was also an increase in matrix deposition on Masson's trichrome staining. There were increased hydroxyproline levels in influenza infected mice with fibrotic lungs due to bleomycin administration, compared with mice exposed only to bleomycin. Non-fibrotic, influenza- infected mice showed apoptosis on histological TUNEL staining. CCNA2 mRNA in influenza infected mice with fibrotic lungs was increased compared to fibrotic mice alone indicating an increase in epithelial apoptosis.
Conclusion These data suggest that influenza infection may enhance the fibrotic response in the lung by promoting epithelial apoptosis and fibrogenesis.

P145 S100A12 AS A BIOMARKER FOR NEUTROPHIL MEDIATED INFLAMMATION IN PATIENTS UNDERGOING CARDIAC SURGERY NECESSITATING CARDIOPULMONARY BYPASS

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Cardiac surgery necessitating cardiopulmonary bypass (snCPB) is often associated with the systemic inflammatory response syndrome (SIRS) and insufficient post-operative oxygenation, transiently fulfilling the criteria for acute lung injury (ALI); for a minority, SIRS becomes severe with an inherent mortality risk. SIRS is characterised by a marked increase in the production of neutrophils and their recruitment into the circulation. S100A12 (calgranulins C, EN-RAGE) is the predominant endogenously expressed neutrophil associated S100 protein. Its presence in plasma suggests utility as a biomarker of inflammation given that S100A12 was the first S100 protein shown to bind to the pro-inflammatory receptor for advanced glycation end-products (RAGE). We therefore undertook this study to ascertain whether increased release of S100A12 following snCPB is associated with aspects of the operative procedure and also levels of other established biomarkers of inflammation/ neutrophil activation in this patient population.
Methods 39 patients undergoing complex cardiac surgery necessitating CPB were recruited for the study. Peripheral blood was collected pre-operatively and immediately post-CPB and plasma was isolated. Enzyme-linked immunosorbent assays were used to measure myeloperoxidase (MPO), S100A12, IL-6 and IL-8 in these samples. In addition a series of clinical patient variables were recorded. Statistical analysis was performed using GraphPad Prism v.5, USA. One way ANOVA followed by post-hoc Dunn's test was used and a p value of <0.05 was considered significant. Correlation between variables was assessed using the nonparametric Spearman test.
Results Plasma levels of S100A12 were significantly increased following snCPB (from 8.52 ng/ml, IQR 4.1–13.1 to 144.6 ng/ml, IQR 86.7–206.7). Post-snCPB levels of S100A12 correlated, positively with post-snCPB levels of MPO ($r = 0.418$, $p = 0.01$), white cell count ($r = 0.322$, $p = 0.01$) and neutrophil count ($r = 0.363$, $p = 0.027$), as well as CPB time ($r = 0.399$, $p = 0.013$), but not with length of ICU and hospital stay.
Conclusion The study shows that surgery-necessitating CPB results in the release of S100A12. Associations found suggest that S100A12 may be a biomarker for neutrophilia and neutrophil activation related to the onset of SIRS in this population.

P146 CAN EXHALED HYDROGEN SULPHIDE AND HYDROGEN CYANIDE BE USED TO DIAGNOSE PNEUMONIA IN THE INTENSIVE CARE UNIT?

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Introduction Hydrogen sulphide (H_2S) and hydrogen cyanide (HCN) have been proposed as biomarkers of infection and inflammation, and therefore may be useful in the Intensive Care Unit (ICU) to diagnose or monitor pulmonary infection. Our aims were to monitor breath H_2S and HCN concentrations in intubated, ventilated patients with pulmonary infiltrates on CXR and correlate them with clinical features and serum H_2S and HCN concentrations.
Methods Adult patients ventilated on controlled modes with new pulmonary infiltrates on CXR were recruited from Christchurch Hospital ICU. Once daily end-tidal breath samples were collected and analysed off-line by selected ion flow tube mass spectrometry (SIFT-MS). Initial breath samples and concurrent arterial blood samples were obtained after intubation.
Results Twenty-eight patients were recruited (17 male), median age 61.5 years (range 26–85 years). Median breath H_2S concentration of all samples was 0.96 ppb (range 0.22–5.12 ppb, median intra-subject CV 9.97%) and HCN concentration 0.76 ppb (range 0.31–11.5 ppb, median intra-subject CV 8.53%) collected over a median of 3 days (range 1–8 days). In general, there was little variation in breath volatile concentration over time. There was a weak relationship between breath and blood HCN concentrations ($r_s = 0.39$, $p = 0.04$). Breath concentrations were not significantly higher than inspired concentrations. Inspired and exhaled volatile concentrations were related (H_2S $r_s = 0.83$, $p < 0.0001$; HCN $r_s = 0.66$, $p < 0.0001$). Breath H_2S and HCN concentrations could not be used to differentiate between patients with pneumonia and those with pulmonary infiltrates due to conditions other than pneumonia. Exhaled volatile concentrations could not separate patients with SIRS or sepsis from those without SIRS or sepsis.
Conclusions As far as we are aware, this is the first study to explore breath H_2S and HCN concentrations in ventilated ICU patients. There was no difference in breath volatile concentrations between patients with pulmonary infiltrates caused by

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