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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different conditions. Using this breath collection method, there is no role for the use of breath H_2S or HCN in the diagnosis or monitoring of pneumonia in critical illness.

Abstract P146 Table 1. Causes of pulmonary infiltrates as determined by clinical factors, radiological and microbiological results, and initial breath volatile concentrations for each condition.

Cause of pulmonary infiltrates	Number of patients (%)	Median H_2S concentration (range) (ppb)	Median HCN concentration (range) (ppb)
Pneumonia	12 (43)	1.18 (0.61–3.47)	1.13 (0.50–1.41)
Pulmonary oedema	6 (21)	1.32 (0.30–2.57)	1.09 (0.42–3.87)
Aspiration lung injury	4 (14)	1.31 (1.09–1.54)	0.85 (0.63–2.73)
Atelectasis	3 (11)	0.74 (0.42–2.51)	1.57 (0.47–10.11)
ARDS (cause other than pneumonia)	2 (7)	0.76 (0.54–0.98)	0.62 (0.50–0.75)
Other	1 (4)	0.22	0.42

P147 CURRENT SMOKERS FACE INCREASED RISK OF ACUTE LUNG INJURY POST OESOPHAGECTOMY COMPARED TO FORMER SMOKERS- IMPLICATIONS FOR THERAPY AND TRIAL DESIGN?

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Introduction Patients undergoing oesophagectomy have ~25% risk of developing post-operative Acute Lung Injury (ALI). A recent meta-analysis showed that smoking cessation prior to an operation reduces the risk of respiratory complications [1]. We hypothesised that current smokers would have an increased risk of ALI post-oesophagectomy compared with former smokers.

Methods We analysed data from 14 current smokers and 37 former smokers recruited to the translational sub-study of the BALTI prevention trial. Extravascular Lung Water Index (EVLWI) and Pulmonary Vascular Permeability Index (PVPI) were measured using PICCO. Plasma and Bronchoalveolar lavage fluid (BALF) cytokine levels were measured by ELISA.

Results Current smokers were significantly younger and had a lower BMI than former smokers. Current smokers were more likely to develop post-operative ALI which required ventilation but there was no difference in the rate of respiratory infection. PVPI was significantly higher immediately post op and on day 1 post op and EVLWI was significantly higher on day 1 post op in current smokers (see table).

Plasma levels of FAS ligand were significantly lower in current smokers pre-op, post-op and on day 1 post-op. Pre-op plasma levels of sICAM1 were significantly higher in current smokers but there was no difference in post-op levels. Plasma levels of IL-17 were lower pre-op, post-op and on day 1, although only the post-op difference reached significance. In BAL, levels of VEGF were significantly lower and levels of IL1ra and TNFR1 were significantly higher in current smokers (see table).

Conclusion Current smokers have a higher risk of Acute Lung Injury following oesophagectomy than former smokers. This finding is supported by higher post-operative levels of extravascular lung water and pulmonary vascular permeability and differences in both plasma and BAL cytokines in current smokers. Our data highlights the importance of encouraging patients to stop smoking prior to major surgery as well as the need to control for smoking history in trials aiming to ameliorate lung injury in this patient group.

REFERENCES

1. Wong, J. *et al*. Short-term preoperative smoking cessation and postoperative complications: a systematic review and meta-analysis. *Can J Anaesth*, 2012. 59(3): 268–79

Abstract P147 Table 1. Differences between current smokers and former smokers undergoing oesophagectomy. Data is expressed as median values except where specified.

		Current Smokers (n = 14)	Former Smokers (n = 37)	P-value
Age (Years)		48	65	**<0.001**
BMI (kg/m^2)		22	26	**0.002**
Developed ALI - n (%)		6 (43)	6 (16)	**0.045**
Developed respiratory infection - n (%)		5 (35)	12 (32)	0.824
EVLWI (ml/kg)	Pre-op	8.3	7.8	0.520
	Post-op	11.0	9.3	0.191
	Day 1	9.8	7.9	**0.040**
PVPI	Pre-op	2.13	1.74	0.151
	Post-op	2.43	1.97	**0.050**
	Day 1	2.09	1.69	**0.008**
Fas Ligand(pg/ml)	Pre-op	21.85	36.78	**0.001**
	Post-op	17.62	30.73	**0.001**
	Day 1	9.05	18.38	**<0.001**
sICAM-1 (ng/ml)	Pre-op	103.52	56.95	**0.005**
	Post-op	51.38	43.01	0.199
	Day 1	100.38	88.00	0.226
IL-17A (pg/ml)	Pre-op	8.42	55.66	0.088
	Post-op	2.64	36.84	**0.043**
	Day 1	8.26	83.57	0.084
VEGF (pg/ml)	BAL	94.05	153.40	**0.016**
IL1ra (pg/ml)	BAL	50.99	9.83	**0.007**
sTNFR1 (pg/ml)	BAL	270.5	168.5	**0.042**

P148 ASPIRIN THERAPY IS ASSOCIATED WITH REDUCED MORTALITY IN PATIENTS WITH ACUTE LUNG INJURY

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Introduction Platelet activation has a role in the pathogenesis of ALI. Observational data suggests aspirin treatment may prevent the development of ALI in critically ill patients. However, it is unknown if aspirin usage alters outcomes in patients with established ALI.

Methods All patients with ALI were identified prospectively in a single large regional medical and surgical ICU between December 2010 and July 2012. Demographic, clinical, and laboratory variables were recorded. Aspirin usage, both pre-hospital and during Intensive Care Unit (ICU) stay, was included. The primary outcome was ICU mortality. We used univariate and multivariate analyses to assess the impact of these variables on ICU mortality.

Results Two hundred and two patients with ALI were included. 56 (28%) of these received aspirin either pre-hospital, in ICU,

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