Mean age (SEM) was 41.1 (1). There was an 8.5% difference in FEV1% between groups A and C, (95% CI (2.6% to 14.4%) p=0.002) and a 29% difference for FE_{NO} between groups A and C, (95%CI (2% to 48%) p=0.034). There was a 1.29 doubling dilution difference in methacholinePC_{20} (95%CI (0.26 to 2.33) p= 0.009) between groups D and F. There was no significant difference between FEV1% when grouped by FE_{NO} (See Abstract P25 Table 1). Applying multiple stepwise linear regression showed that FE_{NO} and FEV1% were both significant predictors of methacholine PC20 (p= 0.002, p<0.001). Only methacholine PC_{20} was a significant predictor of FE_{NO} (p=0.002).

Abstract P25 Table 1 FEV1 are Arithmetic Means and 95%CI and skin prick Median and IQR. Methacholine PC_{20} are Geometric Mean and 95% CI

	Methacholine PC_{20} (mg/ml)		
Outcome	Group A n= 82 ≤0.5	Group B n= 60 >0.5–2	Group C n=66 >2–8
FEV1%	86.5 (82.9–90.1)*	90.4 (87.4–93.5)	95.0 (91.4–98.7)*
FENO	28.1 (23.4–33.8)*	30.6 (24.9–37.6)	39.3 (32.8–47.0)*
No. +ve Skin Pricks	3 (2-5)	3 (2-5)	3 (1-4)
% on ICS	53%	51%	39%
Median BDP dose (ug)	400	400	400
Outcome	Exhaled Nitric Oxide (FENO) (ppb)		
	Group D n=79	Group E n=72	Group F n=57
	≤25	>25-50	>50
FEV1%	89.9 (86.7–93.1)	91.5 (87.8–95.3)	88.9 (85.0–92.9)
Methacholine PC20	0.99 (0.67–1.47)*	0.59 (0.39–0.89)	0.41 (0.26–0.63)*
No. +ve skin pricks	3 (2–4)	3 (2–4)	3 (2–5)
% on ICS	41%	44%	33%
Median BDP dose (μg)	400	400	400

*Significant difference between groups A versus C or between D versus F p<0.05.

Conclusion Our study has highlighted the disconnect between airway inflammation and airway calibre, whilst showing a significant relationship between AHR versus airway calibre and inflammation. Thus, whilst relationships exist between these independent outcomes, the lack of complete concordance highlights the important role that each contributes to the assessment of the asthmatic individual.

P26 HOME SERIAL SPIROMETRY AS AN ADJUNCT IN THE DIAGNOSIS OF VOCAL CORD DYSFUNCTION

doi:10.1136/thx.2010.150961.26

S Y Barnett, B Ziso, S J Quantrill. *Whipps Cross University Hospital NHS Trust, London, UK*

Introduction The diagnosis of vocal cord dysfunction (VCD) is often difficult. Visualisation of the vocal cords using laryngoscopy is the current gold standard method of diagnosis, but may not be diagnostic if carried out when the patient is asymptomatic. An inspiratory flow volume manoeuvre performed during spirometry aids diagnosis, indicating inspiratory flow obstruction when flattened, but is subject to the same problem. Home serial spirometry (HSS), however, may improve diagnostic yield as it can be performed on demand, when the patient experiences symptoms.

Methods A retrospective review was performed of all patients referred to a District General Hospital with symptoms suggestive of VCD, between May 2005 and July 2010. Static spirometry was performed by a lung physiologist within the department. Patients were educated to perform HSS using a Jaeger Spiropro@+ handheld spirometer immediately on experiencing symptoms. Results were downloaded when the machine was returned after a 2-week period. Direct visualisation of the vocal cords via laryngoscopy was performed by a respiratory physician.

Results 54 patients were investigated for possible VCD. A final diagnosis of VCD was made in 31 (57%) cases. Inspiratory loop flattening on static spirometry was present in 48/54 (88%) patients investigated and 28/31 (90%) confirmed cases of VCD. There was evidence of inspiratory loop flattening on HSS in 28/39 (71.7%) patients. 22/39 (56%) who had laryngoscopy were found to have evidence of VCD. 25 patients had both laryngoscopy and HSS performed: 14 of these had evidence of VCD on both tests. 3 of the positive laryngoscopy results were associated with normal HSS. There were eight cases with flattened inspiratory loops on HSS in patients in whom no abnormality was found on laryngoscopy.

Conclusion The nature of laryngoscopy, necessarily performed at one point in time, limits its value in the diagnosis of VCD. HSS is a useful non-invasive test that can increase diagnostic yield in VCD.

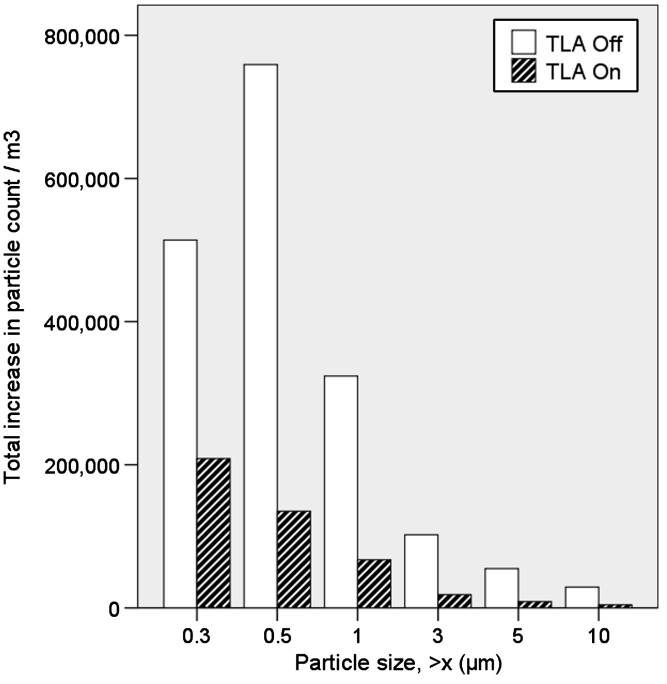
P27 PERSONAL ALLERGEN EXPOSURES ARE INCREASED BY CHANGES IN SLEEP POSITION AND IMPROVED BY TEMPERATURE-CONTROLLED LAMINAR AIRFLOW

doi:10.1136/thx.2010.150961.27

[1]RB Gore, [2]RJ Boyle, [2]H Hanna, [1]A Custovic, [2]C Gore, [3]P Svensson, [2]JO Warner. *[1]University of Manchester, Manchester, UK; [2]Imperial College, London, UK; [3]Airsonett AB, Angelholm, Sweden*

Introduction and Objectives Aeroallergens are released directly from bedding into the breathing zone, and contribute importantly to asthma symptoms. Adults change their sleep position between 3 and 45 times per night. The effect of these turns on inhaled particulate exposures is unknown. We aimed to investigate the effects of changing position on breathing zone particulate exposures and the effect of a novel Temperature-controlled Laminar Airflow (TLA) device on reducing such exposures.

Methods A simulated bedroom was constructed containing bedding from a cat owner. Five healthy volunteers lay recumbent under an active and an inactive TLA device for 175 min. Volunteers made scheduled turns in bed to simulate normal sleep. Real-time total



Abstract P27 Figure 1

particle levels (≥0·5 μm diametre) within the breathing zone were measured by laser particle counting. Inhaled cat allergen exposure was measured by nasal air sampling. Time series analysis was used to evaluate changes in particulate exposures with turning.

Results A greater proportion of larger particles than smaller ones were disturbed by turning over ($F=20.6$, $df=5$, $p<0.001$). With the TLA switched off, 9% (95% CI 4 to 18) of total overhead particles >10 μm diametre were accounted for by turning over, compared with 0.2% (95% CI 0.07 to 0.5) of particles >0.5 μm diameter. TLA treatment reduced total particle numbers (size >0.5 μm) by 3010-fold ($p<0.001$) and significantly reduced the turn-associated increase for all particle sizes (Abstract P27 Figure 1, $p<0.015$). Similar turn-associated increases in nasal air sampler cat particle counts were seen. TLA treatment reduced nasal cat allergen exposures by sevenfold ($p=0.043$).

Conclusions Turning over in bed causes a significant increase in breathing zone exposures to particulates which are within the respirable size range. TLA treatment dramatically reduces overhead breathing zone total particulate exposures and also reduces nasal cat allergen exposure. TLA treatment attenuates the increase in particulate exposures caused by turning over. Treatments which result in better sleep quality and a reduced number of bodily turns may result in a reduction in personal breathing zone particulate exposures in bed.

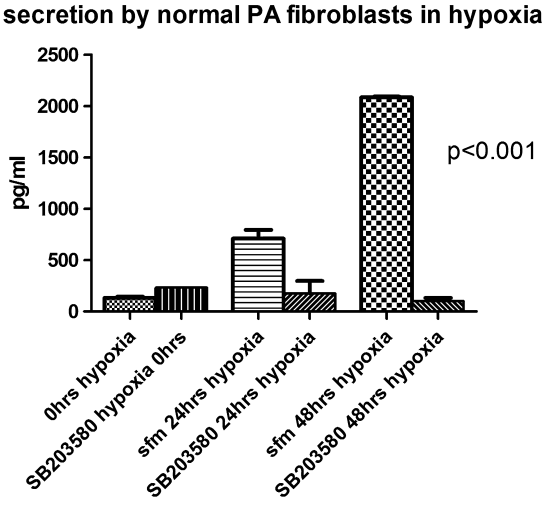
Pulmonary arterial hypertension

P28 INFLAMMATORY PROFILING OF ADVENTITIAL FIBROBLASTS IN PULMONARY HYPERTENSION

doi:10.1136/thx.2010.150961.28

[1]AC Church, [2]A Melendez, [3]RM Wadsworth, [1]AJ Peacock, [1]DJ Welsh. *[1]Scottish Pulmonary Vascular Unit, Glasgow, UK; [2]Department of Immunology, Infection and Inflammation, University of Glasgow, Glasgow, UK; [3]Department of Pharmacology, University of Strathclyde, Glasgow, UK*

The concept that inflammation is important in the pathogenesis of pulmonary hypertension (PH) is gaining credence. Studies have suggested that Interleukin-6 (IL-6) and -1 are involved in the development of PH and that IL-6 can stimulate smooth muscle cell proliferation. The adventitial fibroblast has been suggested as a potential source of mitogens and inflammatory mediators which contribute to the development of PH.



IL-6 release from pulmonary artery fibroblasts is stimulated in hypoxia and inhibited by p38 MAPK inhibitor

Abstract P28 Figure 1 IL-6 secretion by normal PA fibroblasts in hypoxia. IL-6 release from pulmonary artery fibroblasts is stimulated in hypoxia and inhibited by p38 MAPK inhibitor.

Methods Rat pulmonary artery fibroblasts (RPAF) were isolated from normal Sprague–Dawley rats, rats exposed to 2 weeks of hypobaric hypoxia. Cells were cultured by explant technique. Normal RPAF were quiesced for 24 h in serum free media (SFM) and then exposed to periods of prolonged acute hypoxia or maintained in normoxia. The conditioned media was collected and stored at −70°C. RPAF from the chronic hypoxic and monocrotaline models were exposed to 1% serum or maintained in SFM and conditioned media collected. The effect of p38 MAPK blockade using SB203580 (an alpha-isoform specific inhibitor) was examined. The conditioned media was analysed using cytokine array technology and ELISA.

Results In normoxic conditions after 48 h, conditioned media from normal fibroblasts showed release of TIMP-1 and low levels of VEGF-A. The expression profile changed with 48 h exposure to hypoxia showing increased levels of VEGF-A and immunomodulators such as IL-6 (see Abstract P28 Figure 1), MIP-3α (CXCL20), LIX, CINC-1, sICAM-1. The secretion of these mediators were blocked by the addition of SB203580 suggesting an important role for p38MAPK in the control of these proteins. TNF-α was not released from these cells under the conditions studied. With the chronic hypoxic RPAF after 48 h of 1% serum stimulation in normoxia, the cytokine profile mirrored that of normal RPAF in acute hypoxia. Again this was blocked using SB203580.

Conclusion Pulmonary artery fibroblasts release mediators in response to hypoxia, which have been implicated in both recruitment of inflammatory cells and the proliferation of pulmonary artery smooth muscle cells. We have demonstrated that inhibition of the p38MAPK-alpha isoform can block the secretion of these mediators. This may have therapeutic implications for the treatment of hypoxia related pulmonary hypertension.

P29 ENDOTHELIAL CELL NF-KB ACTIVATION IS INCREASED IN HUMAN IDIOPATHIC PAH

doi:10.1136/thx.2010.150961.29

[1]LC Price, [2]G Caramori, [3]P Dorfmuller, [3]F Perros, [4]J Zhu, [1]D Shao, [3]M Humbert, [5]I Adcock, [1]SJ Wort. *[1]National Heart & Lung Institute, Royal Brompton Hospital, London, UK; [2]Università di Ferrara, Via Savonarola 9, Ferrera, Italy; [3]Université Paris-Sud, Faculté de Médecine, Kremlin-Bicêtre, F-94276; AP-HP, Centre National de Référence de l'Hypertension Pulmonaire Sévère, Service de Pneumologie et Réanimation Respiratoire, Hôpital Antoine Béclère, Clamart, F-92140, Paris, France; [4]Lung Pathology Unit, Imperial College London, Royal Brompton Hospital, London, UK; [5]Department of Cell & Molecular Biology, Airways Disease Section, National Heart and Lung Institute, Faculty of Medicine, Imperial College London, London, UK*

Background Pulmonary arterial hypertension (PAH) is associated with pulmonary vascular inflammation, and several of the inflammatory genes involved are regulated by nuclear factor-kB (NF-kB). NF-kB is a heterodimer of p65 and p50 subunits which, upon activation, translocate into the nucleus and binds to target gene promoters. NF-kB activation in PAH has not been examined in detail to date. We assessed NF-kB activation by immunohistochemical analysis of nuclear p65.

Methods Samples were obtained from South Paris University from patients with severe idiopathic PAH (IPAH) following lung transplantation (n=10) and from control subjects undergoing lobectomy or pneumonectomy (n=10). Tissue blocks were fixed and paraffin-embedded, 4-mm thick sections underwent immunoperoxidase double staining for macrophage (CD68+)/p65, using mouse anti-human CD68 (Dako; 1:100 dilution) and rabbit anti human p65 (Santa Cruz Biotechnology; 1:50 dilution), before detection with chromogen fast red and counterstaining with haematoxylin. Vessels of interest were defined and quantitative scoring of nuclear p65 immunostaining of ten randomly selected pulmonary arteries per