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.

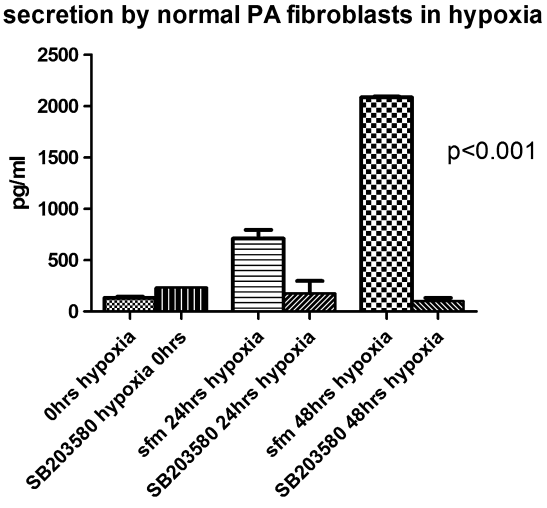
Pulmonary arterial hypertension

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

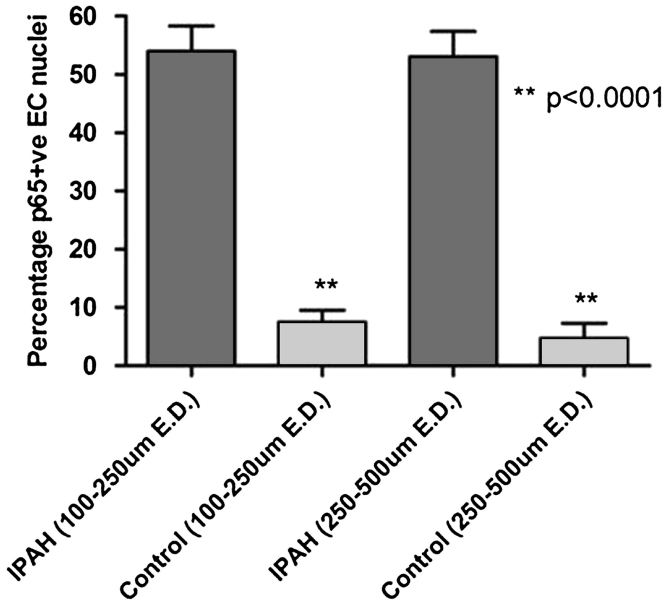
[1]LC Price, [2]G Caramori, [3]P Dorfmuller, [3]F Perros, [4]J Zhu, [1]D Shao, [3]M Humbert, [5]I Adcock, [1]SJ Wort. *[1]National Heart & Lung Institute, Royal Brompton Hospital, London, UK; [2]Università di Ferrara, Via Savonarola 9, Ferrera, Italy; [3]Université Paris-Sud, Faculté de Médecine, Kremlin-Bicêtre, 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

slide performed by a researcher blinded to the groups. Data are expressed as median and IQR, and the groups were compared by the Kruskal–Wallis or Mann–Whitney U test.

Results (1) PAH specimens showed co-localisation of p65 within CD68+ macrophages in 75.4 (64.8–84.6)% of samples. Airway epithelium, neutrophils and lymphocytes were also positive for p65. (2) Pulmonary arterial medial thickness was increased in PAH compared to controls, at 33.7 (18.8–67.9)% in vessels 100–250 mm external diameter (E.D.) and 27.2 (14.8–44.2)% in vessels 250–500 mm ED, vs 17.7 (11.2–30.3)% and 14.9 (11.8–17.8)% in controls ($p<0.0001$ between groups). (3) Nuclear p65 was present in pulmonary artery endothelial cells (EC) but not other vascular cells including pulmonary artery smooth muscle cells in PAH: 53.9 (0–100)% of vessels 100–250 mm E.D. and 53.1 (0–100)% of those 250–500 mm E.D. scored EC p65 positivity in PAH compared to 7.5 (0–25.0)% in 100–250 mm ED and 4.7 (0–21.1)% in 250–500 mm ED in controls ($p<0.0001$ between groups) (Abstract P29 Figure 1).



Abstract P29 Figure 1 Percentage of positive endothelial cell (EC) nuclear p65 immunostaining subdivided according to pulmonary artery external diameter (E.D.).

Conclusion NF-kB activation is present in macrophages and pulmonary arterial endothelial cells in pulmonary arteries of 100–500 mm ED in patients with PAH.

P30 THE CHANGING FACE OF PULMONARY HYPERTENSION: THE ROLE OF HEART AND LUNG DISEASE

doi:10.1136/thx.2010.150961.30

SF Crawley, MK Johnson, AJ Peacock. *Scottish Pulmonary Vascular Unit (SPVU), Glasgow, UK*

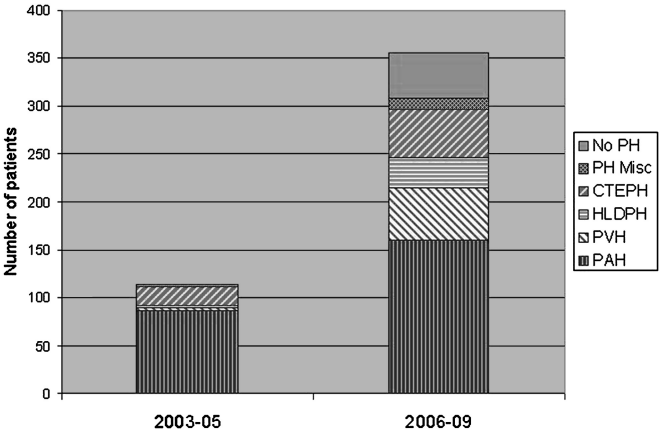
Introduction The advent of disease-targeted therapy for pulmonary arterial hypertension (PAH) has led to an increased awareness of this condition within the general cardiology and respiratory communities. More patients are being referred to specialist centres for diagnostic assessment, however there is concern that many will have pulmonary hypertension (PH) due to underlying lung disease or left heart disease.

Aim The aim of the study was to review the outcome of diagnostic admissions to the Scottish Pulmonary Vascular Unit (SPVU) before (2003–2005) and after (2006–2009) the introduction of disease-targeted PAH therapy.

Methods 470 new patients with suspected PH were admitted between January 2003 and December 2009 for diagnostic assessment including right heart catheterisation (RHC). Demographic and haemodynamic data from these patients were retrospectively reviewed. Following RHC patients were diagnosed with:

– Group 1. PAH;
– Group 2. Pulmonary venous hypertension (PVH) due to left heart disease;
– Group 3. PH due to hypoxic lung disease (HLDPH);
– Group 4. Chronic thromboembolic PH (CTEPH);
– Group 5. PH due to unclear multifactorial mechanisms (PH Misc);
– No PH.

Results In 2003–2005, 114 patients underwent diagnostic assessment, and 112 had PH. Of these 77.7% had PAH and 18.8% had CTEPH. Only 2.7% of patients had PVH and 0.8% had HLDPH. In 2006–2009, 356 patients underwent diagnostic assessment, and 308 had PH. Of these only 51.9% had PAH and 15.9% had CTEPH. However, now 17.9% of patients had PVH, and 10.4% had HLDPH. 48 patients had No PH at the time of RHC (Abstract P30 Figure 1).



Abstract P30 Figure 1 Outcome of diagnostic assessment in the pre and post-treatment era.

Conclusion Prior to admission all referrals are screened by an SPVU consultant, but despite this there are a significant number of patients proceeding to RHC who will have PH due to left heart or lung disease. This highlights the importance of fully assessing all patients with suspected PH, as per ESC/ERS 2009 guidelines, before instituting expensive and potentially dangerous PAH therapy. We need to improve our non-invasive screening methods so that fewer patients proceed to RHC who do not have PAH.

P31 DISEASE TARGETED THERAPIES AND EFFECT ON SURVIVAL IN IDIOPATHIC, HERITABLE AND ANOREXIGEN-ASSOCIATED PULMONARY ARTERIAL HYPERTENSION (PAH)

doi:10.1136/thx.2010.150961.31

Y Ling, M Johnson, A Peacock. *Scottish Pulmonary Vascular Unit, Glasgow, UK*

Introduction The median survival of idiopathic PAH was 2.8 years before the availability of modern therapies. Substantial progress has been made over the past 20 years. Currently available disease targeted therapies have been shown in clinical trials to improve symptoms, exercise capacity and survival. Combination therapies