

were excluded. 11 healthy volunteers acted as a control group. Serum levels of interleukin (IL) 1 $\beta$ , 2, 4, 6, 8, 10, 12p70 and tumour necrosis factor  $\alpha$  (TNF $\alpha$ ) were measured using a multiplex analyser. A Wilcoxon matched pairs test was used to compare differences between baseline and follow-up samples.

**Results** Patient and control demographics are presented in the Abstract P3 table 1. Levels of IL 2,6,8,10 and TNF $\alpha$  were elevated in the patient group compared to controls. Average time to repeat patient sampling was  $4.7 \pm 1.8$  months. There were no significant differences between the levels of any cytokines between baseline and follow-up in the patients and no overall correlation existed between change in 6MWT and change in any cytokine. When patients who had improved their 6MWT on follow-up were analysed as a separate group, there was a significant ( $p=0.0068$ ) drop in IL6 levels on follow-up.

Abstract P3 Table 1 Patient and control demographics

	Patients	Controls
N	19	11
Male	6 (32%)	3 (27%)
Age (years) (Mean $\pm$ SD)	$58 \pm 14$	$43 \pm 8$
NYHA Class (III/IV)	15 (79%)/4 (21%)	
Aetiology of PH		
IPAH	7 (37%)	
Connective tissue disease	5 (26%) (3 $\times$ SSC, 2 $\times$ MCTD)	
Congenital heart disease	3 (16%) (2 $\times$ Unrepaired, 1 $\times$ Repaired)	
Distal CTEPH	3 (16%)	
Veno-occlusive disease	1 (5%)	
Medication on follow-up		
Endothelin antagonist	8 (43%)	
Prostanoid (Nebulised)	1 (5%)	
Sildenafil	9 (47%)	
Combination	1 (5%)	
mPAP (mm Hg)(Mean $\pm$ SD)	$51.8 \pm 13.5$	
CI (L/min/m <sup>2</sup> )(Mean $\pm$ SD)	$1.89 \pm 0.62$	

CI, Cardiac index; MCTD, Mixed connective tissue disease; mPAP, Mean pulmonary artery pressure; SSC, Scleroderma.

**Conclusions** Several cytokines were elevated in these patients with pulmonary hypertension. The role of cytokines in disease monitoring requires further study and there seems to be little relation with serum cytokines, except IL6, and a change in a patient's clinical state as measured by 6MWT. Replication of results from this pilot study and examination of longitudinal trends in cytokine levels are warranted.

#### P4 THE USE OF SILDENAFIL TO TREAT PULMONARY HYPERTENSION ASSOCIATED WITH SARCOIDOSIS

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**Introduction and Objectives** Pulmonary hypertension (PH) is increasingly recognised as a major contributor to poorer outcomes in pulmonary sarcoidosis. Current treatment guidelines for sarcoidosis associated pulmonary hypertension (SAPH) recommend the optimisation of underlying lung disease and use of oxygen when hypoxaemia is present,<sup>1</sup> however there is insufficient evidence to recommend advanced therapies. Limited data suggest a benefit following treatment with sildenafil in SAPH, although no randomised controlled treatment trials have been reported. We report our experience of patients with SAPH treated with sildenafil.

**Methods** We reviewed 22 patients (mean age  $56 \pm 12$  years; 10 men) with SAPH (mean pulmonary artery pressure  $46 \pm 9$  mm Hg) who

received treatment with sildenafil. Haemodynamic measurements were evaluated by right heart catheterisation in all patients. Serial measurements of brain natriuretic peptide (BNP), pulmonary function testing and functional status were collected.

**Results** The mean duration of follow-up after the commencement of sildenafil was  $21 \pm 14$  months. Six patients died during follow-up, and four patients required the addition of an endothelin receptor antagonist due to worsening pulmonary hypertension. Patients were dichotomised into responders (those maintained on sildenafil monotherapy;  $n=12$ ) or non-responders (those who died or required and escalation of PH therapy during follow-up;  $n=10$ ). Compared to responders, non-responders had a significantly lower % predicted DLco (20% vs 34%;  $p=0.03$ ) and % predicted Kco (46% vs 62%;  $p=0.05$ ) at commencement of sildenafil (Abstract P4 table 1). Within 6 months of commencement of sildenafil, non-responders had a 21% increase in median BNP levels, while responders had a 51% reduction in BNP levels. Sildenafil was ceased in one patient after the development of ocular side-effects attributed to the drug.

Abstract P4 Table 1 Demographic and baseline clinical characteristics of patients with sarcoidosis associated pulmonary hypertension receiving treatment with sildenafil\*

	Non-responders (n=10)	Responders (n=12)	p Value
Age (years)	53.5 (14)	58.5 (10)	NS
Gender, M:F	5:5	5:7	
Follow-up (months)	23 (16)	20 (12)	NS
Baseline			
mPAP (mm Hg)	50 (10)	43 (8)	NS
PaO <sub>2</sub> (kPa)	7.8	8.2	NS
DLco % predicted	20	34	0.03
Kco % predicted	46	62	0.05
$\Delta$ BNP at 6 months	+21%	-51%	

\*Values are given as mean (SD) or median (range).

**Conclusions** Our observations suggest that sildenafil is safe and well tolerated in SAPH. At commencement of sildenafil, a lower % predicted DLco and Kco, and an increasing BNP level within the first 6 months of therapy, was associated with increased risk of death or requirement for additional PH therapy. Controlled trials are warranted before therapeutic recommendations can be made.

#### REFERENCE

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#### P5 PULMONARY HYPERTENSION IN A MOUSE MODEL WITH REDUCED MACROPHAGE NUMBER (MACLOW)

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**Introduction and Objectives** Pulmonary arterial hypertension (PAH) is a devastating condition with high morbidity and poor life expectancy. Pathologically PAH is characterised by the medial thickening of the small distal pulmonary arteries. Early endothelial cell (EC) dysfunction and apoptosis, and the subsequent abnormal proliferation and migration of pulmonary artery smooth muscle cells are thought to be a major contributing factor. Macrophages are proposed to play an important role in regulating these processes and are recruited to remodelled pulmonary arteries but the exact role of

macrophages, and whether they are required for this remodelling remains unclear. We have recently developed a mouse model (*MacLow*) where approximately 50% of macrophages are depleted and now aim to investigate whether *MacLow* mice would demonstrate a reduced pulmonary hypertension phenotype in response to hypoxia, when compared to non-macrophage ablated littermates.

**Methods** Macrophage ablation was induced in CD68-rtTA-eGFP/tetDTA double transgenic mice (*MacLow*) where macrophage-specific (CD68) induction of the cytotoxic diphtheria toxin A chain (DTA) is achieved by administration of doxycycline containing chow diet (doxy-chow). Mice were divided by sex and then fed either regular or doxy-chow for 2 weeks prior to either 2 weeks exposure to hypoxia (10% oxygen), or room air. All mice were phenotyped for PH by echocardiography followed by closed chest cardiac catheterisation. Heart and lung tissue were harvested for morphological, immunohistochemical and biochemical analyses.

**Results** Doxy-chow fed mice displayed the expected 50% reduction in macrophages (liver) compared to controls. *MacLow* mice with the induced ablation of macrophages were not protected from hypoxia induced pulmonary hypertension although females displayed a trend for higher RVSP after hypoxia (34 mm Hg vs 29 mm Hg). Interestingly male *MacLow* mice with induced macrophage ablation displayed a spontaneous PAH phenotype (33 mm Hg), in normoxia, that was not further increased by hypoxia. The changes in RVSP were accompanied by appropriate changes in RVH.

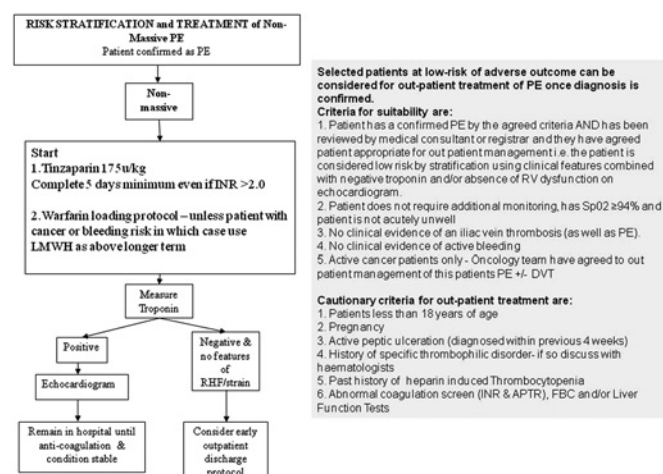
**Conclusion** These data suggest that macrophages play a modulating role in pulmonary vascular remodelling but further work is required to explore the mechanisms involved in this phenotype, and to fully assess the change in macrophage number within the lungs of these mice.

## P6 MANAGING ACUTE PULMONARY EMBOLISM IN THE OUTPATIENT SETTING: INITIAL EXPERIENCES AND OUTCOMES IN A UK DISTRICT GENERAL HOSPITAL

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**Introduction and Objectives** Outpatient (OP) management of low risk cases of pulmonary embolism (PE) can be as effective as inpatient (IP) management and reduce length of stay (LOS) (1). Concerns exist regarding the safety of this strategy, with a wide range of adverse outcomes reported (2). In our hospital a treatment



Abstract P6 Figure 1 Pathway to identify low risk individuals diagnosed with PE suitable for OP management.

pathway was implemented to identify low risk individuals diagnosed with PE suitable for OP management, based on the European Society of Cardiology PE Guidelines (2008) (Abstract P6 figure 1). The aim of this study was to retrospectively review all cases of acute PE in a 6-month period, to determine appropriateness of management as OP and assess LOS, venous thromboembolism (VTE) recurrence and anticoagulation related adverse events.

**Methods** Episodes of PE occurring between January and June 2010 were identified through clinical coding (ICD-10: I26). Clinical notes were reviewed and data collected for LOS, time to diagnostic investigation, risk stratification (troponin, echocardiography and adverse clinical features), IP/OP management, recurrence of VTE, bleeding events, respiratory clinic follow-up and mortality.

**Results** 102 cases were identified of which 90 had acute PE. 81 sets of clinical notes were available. 24 (29.6%) patients were managed as OP. This group was younger than those treated as IP ( $59.30 \pm 3.84$  vs  $64 \pm 2.12$ ,  $p < 0.05$ ). The LOS was significantly shorter for OP: ( $1.87 \pm 0.27$  vs  $8.79 \pm 0.77$  days;  $p < 0.0001$ ). There were no episodes of recurrent VTE or bleeding events at 90 days in either group, and only one readmission for anticoagulation related events (high INR; IP group). Three patients (3.7%) died within 90 days (1 from sepsis, 1 from metastatic carcinoma and 1 from congestive cardiac failure). We identified a number of patients with low risk who were not treated as OP for a various reasons. All patients with OP management were subsequently followed by Respiratory team.

**Conclusions** Out patient management of diagnosed PE in a carefully selected group is practical, safe and decreases LOS using existing OP DVT services. The use of risk stratification assists identification of safe OP management.

## REFERENCES

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## P7 ARE WE SCREENING SURVIVORS OF PULMONARY EMBOLISM (PE) FOR CHRONIC THROMBOEMBOLIC PULMONARY HYPERTENSION (CTEPH)?

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**Background** Incidence of CTEPH following idiopathic PE has been reported as 4%. The British Thoracic Society recommends that patients with massive or submassive PE should undergo echocardiography 6–12 weeks following the index event.

**Aim** To investigate local practice in the follow-up of patients with acute PE to devise management guidelines.

**Methods** A retrospective study of 110 patients diagnosed with acute PE at our hospital between 2007 and 2008 was conducted. Mean age was 68.6 years (range 27–100), 40 (36%) were male and 18 (16%) had previous venous thromboembolism. In 51 (46%) patients PE was idiopathic.

**Results** All patients diagnosed with PE were normotensive and 27 (25%) had in-patient echocardiography (ECHO). In 5 (18%) patients scan confirmed RV dilatation and 2 of them had repeated ECHO within 2 months. Subsequently one patient was diagnosed with CTEPH and underwent pulmonary endarterectomy. In the group of patients with acute PE but without in-patient echocardiography 40 of 83 (48%) received a follow-up appointment (mean 4 months) and 10 (25%) had follow-up ECHO. Two more patients were diagnosed with CTEPH during this period (mean 34 months) with an overall incidence of 2.9%.

**Conclusion** Recorded outcome, literature review and the BTS/ERS guidelines resulted in the development of local protocol for the screening acute PE survivors for CTEPH. [Abstract P7 figure 1].