Methods Circulating markers of iron status and erythropoiesis were determined in 135 patients with IPAHA and correlated with clinical indices and survival.

Results Iron deficiency, defined by raised plasma soluble transferrin receptor (sTfR) levels (>28.1 nmol/l) was present in ~63% of patients with IPAHA. Iron, ferritin and transferrin saturation levels were also reduced (Abstract P33 Figure 1); whereas mean haematocrit and haemoglobin levels were similar to healthy controls and red cell distribution width was increased. Levels of the master iron regulator hepcidin, which inhibits the dietary uptake and decreases serum iron, were raised (50.5 vs 34.4 ± 3.0 ng/ml; $p=0.04$) despite the presence of iron deficiency in the majority of patients. Hepcidin correlated inversely with sTfR and erythropoietin (EPO) levels as would be expected, but not with IL-6, the most important inflammatory stimulus for hepcidin expression. After adjusting for iron status, hepcidin levels were significantly higher in IPAHA compared with healthy controls ($p=0.001$). Plasma sTfR levels increased with WHO class ($p<0.05$), showed a weak but significant correlation with 6MWD ($R=-0.25$, $p=0.03$) and growth differentiation factor-15 ($R=0.281$, $p=0.01$) and independently predicted survival after adjustments for 6MWD, WHO class and NT pro-BNP levels ($p=0.022$).

Conclusions A significant proportion of IPAHA patients are iron deficient and this relates to disease severity and outcome. Hepcidin levels are inappropriately high in IPAHA and may be driving iron deficiency.

P34 CHARACTERISING T CELL SUB-POPULATIONS IN PULMONARY HYPERTENSION

doi:10.1136/thx.2010.150961.34

¹AJ Shepherd, ¹K Hopkinson, ²DG Kiely, ²CE Elliot, ²R Condliffe, ³DC Crossman, ¹AG Pockley, ¹A Lawrie. ¹University of Sheffield, Sheffield, South Yorkshire; ²Royal Hallamshire Hospital, Sheffield, South Yorkshire; ³NIHR Cardiovascular Biomedical Research Unit, Sheffield, South Yorkshire

Introduction Pulmonary arterial hypertension (PAH) is characterised by an increase in pulmonary vascular resistance which leads to right ventricular failure and death. Given that PAH is associated with HIV (in which CD4⁺ lymphocytes are depleted), and that athymic rats demonstrate heightened pulmonary vascular remodelling in the SUGEN model, suggests that inflammation plays an important role in disease pathogenesis. T cells might therefore dampen rather than accentuate PAH.

Hypothesis Reduced CD4⁺ T cell numbers and/or an increase in the prevalence, activation and function of naturally-occurring immunoregulatory T (Treg) cells are a "second hit" in the pathogenesis of PAH.

Methodology The T cell subset composition (CD3⁺, CD4⁺, CD8⁺) and prevalence of Treg cells (CD4⁺CD25^{bright}, CD4⁺CD25^{bright}CD127^{dim}, CD4⁺CD25^{bright}CD127^{dim}Foxp3⁺, CD4⁺CD25^{bright}Foxp3⁺) in the peripheral blood of patients with suspected PAH attending the Pulmonary Vascular Disease Unit and corresponding controls (healthy, no PAH at right heart catheterisation with and without SSc) were determined using multiparameter flow cytometry. The activation status (CD69 expression) of T cell subsets was also determined.

Findings Peripheral blood CD3⁺ T cells show heightened activation in patients with PAH compared to controls. The proportion of circulating CD4⁺ T cells is reduced in patients with Idiopathic PAH (IPAHA), and CD4⁺T cells are less activated in patients with limited and diffuse PAH associated with systemic sclerosis (PAH-SSc). The proportion of circulating CD8⁺ T cells is higher in patients with diffuse PAH-SSc, and CD8⁺ T cells are more activated in patients

with IPAHA than in their controls. The proportion of CD4⁺CD25^{high}FoxP3⁺ Treg cells is decreased in patients with limited SSc-PAH compared to controls, and compared with controls, these cells are less activated in IPAHA and limited SSc-PAH.

Conclusions These data indicate that circulating T cell subset profiles are altered in patients with PAH and a changing T cell subpopulation profile might therefore be a potential biomarker of disease or provide insight into future therapeutic targets. Studies to determine the influence of disease progression on T cell subpopulations, the functional properties of Treg cells in patients with PAH and the interaction of these cells with pulmonary artery endothelial cells in vitro are currently underway.

P35 ELEVATED TRICUSPID REGURGITATION JET VELOCITY ON ECHOCARDIOGRAM IN SICKLE CELL DISEASE IS ASSOCIATED WITH RAISED INFLAMMATORY MEDIATORS AND LOW STEADY STATE HAEMOGLOBIN BUT NOT OTHER MARKERS OF HAEMOLYSIS

doi:10.1136/thx.2010.150961.35

¹H Ranu, ¹E Connell, ¹C Hunt, ¹F Boa, ²J Lee, ²L Brown, ¹F Willis, ¹H Buyck, ¹BP Madden. ¹St George's Hospital, London, UK; ²St George's Medical School, London, UK

Introduction and Objectives Pulmonary hypertension (PH) in Sickle cell disease (SCD) is defined as tricuspid regurgitation jet velocity ≥ 2.5 m/s on trans thoracic echocardiogram. It is an important complication of SCD and is associated with significant mortality. Haemolysis with impairment of the nitric oxide pathway is felt to play a major part in its pathogenesis. We have examined the association of haemolytic markers and inflammatory cytokines in haemoglobin SS (HbSS) adults with PH (TRV ≥ 2.5 m/s) and without PH (TRV < 2.5 m/s). Cytokines studied included interleukin 8 (IL-8), which may have a role in promoting adhesion of sickled red cells to vascular endothelium and stem cell factor (SCF), which acts on erythroid progenitor cells.

Methods 32 adult HbSS patients (mean age 37 years $\pm$ 11.6, median 37 years) were recruited at steady state defined as 2 weeks or more following an acute crisis. Serum levels of haemolytic markers (haemoglobin, lactate dehydrogenase LDH, bilirubin), asymmetric dimethylarginine (ADMA a naturally occurring nitric oxide synthase inhibitor), SCF and IL 8 were measured.

Results Results are given in Abstract P35 Table 1 and expressed as mean $\pm$ SD. TRV was significantly correlated with Hb ($p=0.003$ $r=-0.51$), ADMA ($p<0.05$, $r=0.35$), IL 8 ($p=0.009$, $r=0.48$) and SCF ($p=0.006$, $r=0.51$).

Abstract P35 Table 1 Values for haemolytic and inflammatory markers in SCD patients with TRV < 2.5 m/s and TRV ≥ 2.5 m/s

	No PH (TRV < 2.5 m/s)	PH (TRV ≥ 2.5 m/s)	p value
TRV m/s	1.88 $\pm$ 0.44	2.74 $\pm$ 0.27	<0.001
Haemoglobin g/dl	10.1 $\pm$ 1.4	8.3 $\pm$ 1.3	0.001
LDH U/l (0-175)	403 $\pm$ 97	463 $\pm$ 154	0.66
Bilirubin μ mol/l (0-17)	51 $\pm$ 31	32 $\pm$ 10	0.11
ADMA μ mol/l	0.778 $\pm$ 0.137	1.007 $\pm$ 0.239	0.012
SCF pg/ml	167.6 $\pm$ 81.5	313.6 $\pm$ 156.7	0.013
IL 8 pg/ml	12.96 $\pm$ 4.01	35.80 $\pm$ 32.16	0.015

Conclusion PH in SCD is associated with lower haemoglobin and ADMA but not other markers of haemolysis. There is a significant association of TRV with IL 8 and SCF, which has not been previously described in adults. Inflammatory mediated endothelial dysfunction is likely to also play an important role in the