Methods Circulating markers of iron status and erythropoiesis were determined in 135 patients with IPAH 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 IPAH. 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 IPAH 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 IPAH patients are iron deficient and this relates to disease severity and outcome. Hepcidin levels are inappropriately high in IPAH and may be driving iron deficiency.

P34 CHARACTERISING T CELL SUB-POPULATIONS IN PULMONARY HYPERTENSION

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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 (IPAH), 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 IPAH 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 IPAH 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 ofthese 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

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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 ± 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 ± 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 ± 0.44	2.74 ± 0.27	<0.001
Haemoglobin g/dl	10.1 ± 1.4	8.3 ± 1.3	0.001
LDH U/l (0–175)	403 ± 97	463 ± 154	0.66
Bilirubin µmol/l (0–17)	51 ± 31	32 ±10	0.11
ADMA µmol/l	0.778 ± 0.137	1.007 ± 0.239	0.012
SCF pg/ml	167.6 ± 81.5	313.6 ± 156.7	0.013
IL 8 pg/ml	12.96 ± 4.01	35.80 ± 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

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pathogenesis of PH associated with SCD. The roles of IL 8 and SCF warrant further investigation.

P36 FUNCTIONAL CLASS AND GAS TRANSFER ARE USEFUL TOOLS IN THE ASSESSMENT OF PULMONARY HYPERTENSION ASSOCIATED WITH SICKLE CELL DISEASE

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Introduction and Objectives WHO Functional class (FC) is an important tool in the management of patients with pulmonary arterial hypertension. There is an increasing awareness of pulmonary hypertension (PH) as a complication of Sickle cell disease (SCD). We wished to evaluate functional class and gas transfer (diffusion capacity DLCOc, KCOc) in patients with SCD (HbSS) with and without PH based on trans thoracic echocardiogram.

Methods 32 patients were reviewed and their functional class was determined. Trans thoracic echocardiograms were reviewed in these patients for evidence of PH (defined as a tricuspid regurgitation jet velocity TRV ≥ 2. 5 m/s). Haematological and lung function data were also reviewed. Only patients in steady state and without a crisis in the preceding 2 weeks were included.

Results Of patients with PH 36% (5/14) were FC ≥3 compared to 6% (1/18) without PH. There was a significant difference in functional class in patients with and without PH on echocardiogram ($p<0.05$). There was a significant correlation between TRV and WHO functional class ($p=0.002$, $r= 0.54$). The correlation between TRV and functional class remained significant after correction for haemoglobin. Mean haemoglobin was 8.3±1.3 g/dl in those with PH and 10.1±1.4 g/dl in those without PH ($p=0.001$). Neither PH nor FC was associated with parenchymal abnormalities visible on CT and/or chest radiograph. PH was also associated with a lower diffusion capacity (DLCOc mmol/min/kPa: 3.60±0.79 vs 7.60±2.66, $p=0.034$) and a lower diffusion capacity corrected for alveolar volume (KCOc mmol/min/kPa/l: 1.04±0.31 vs 1.96±0.3, $p=0.034$). TRV was significantly correlated with DLCOc only ($p=0.036$ $r= -0.79$).

Conclusion Although patients with Sickle cell disease may have a number of reasons to account for their breathlessness, functional class and measurements of gas transfer may be useful markers in screening patients for pulmonary hypertension regardless of low steady state anaemia.

P37 FLYING—SAFER THAN WE THOUGHT? A QUESTIONNAIRE-BASED STUDY OF 156 INDIVIDUALS WITH HEREDITARY HAEMORRHAGIC TELANGIECTASIA; 95 WITH PULMONARY AVMS

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Introduction Flight has become an integral part of modern life: 65.9 million passengers used Heathrow airport in 2009.[1] Flight, however, exposes us to a unique environment with a reduced FiO_2–, increased humidity and relative immobility. Although guidelines have been published,[2] there are relatively limited published data regarding flight safety. Patients with particular conditions may provide high risk models for the general population regarding the safety of the flight environment. Here we report the results of a questionnaire-based study in individuals with hereditary haemorrhagic telangiectasia (HHT), a condition that leads to recurrent nosebleeds, but more importantly for respiratory physicians, frequent pulmonary arteriovenous malformations (PAVMs) that result in a right to left shunt, hypoxaemia, and risk of paradoxical embolic stroke.[3]

Methods PubMed searches identified no studies into the effect of flight in HHT or PAVM patients. With ethical approval (NRES 10/H0806/8), patients with definite HHT who had attended our hospital's HHT clinic, were sent a questionnaire. Participants were asked to document flights they had taken, and to list any symptoms they experienced during or shortly afterwards. Responses were correlated with physiological variables in their hospital records.

Results 156 replies were received from 308 questionnaires (response rate 50.6%). 145 individuals (95 [65%] with pulmonary AVMs), had flown, reporting 18 943 flight hours in 3950 flights. The median number of flights per patient was 17 short haul, and 8 long haul. There was no difference in erect SaO_2 between those who reported breathlessness and those who did not (median 93 (range 85–96)% vs median 94 (84–99)% respectively. Individuals who reported breathlessness stated that in-flight oxygen was of benefit (Abstract P37 Table 1).

Abstract P37 Table 1 All six patients reporting dyspnoea had PAVMs

	Asymptomatic	Nosebleed	Dyspnoea	Deep venous thrombosis	Ischaemic Stroke
All flights					
Patients (n (%))	111 (77)	26 (18)	6 (4)	2 (1)	1 (<1)
Short haul (<6 h)					
Patients (n (%))	130 (89)	14 (10)	3 (2.1)	0 (0)	0 (0)
Flights taken (n (%))	2864 (96)	78 (3)	39 (1)	0 (0)	0 (0)
Long haul (≥6 h)					
Patients (n (%))	120 (83)	20 (14)	6 (4)	2 (1.4)	1 (0.7)
Flights taken (n (%))	837 (86)	112 (12)	17 (2)	2 (<1)	1 (<1)

Conclusion These data suggest that even in a population group expected to be more susceptible to complications, flying appeared safe for the vast majority of individuals. A minority of HHT patients did experience adverse symptoms. These were difficult to predict based on clinic measurements.

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P38 WHICH PATIENTS WITH PULMONARY ARTERIOVENOUS MALFORMATIONS ARE DYSPNOEIC? RETROSPECTIVE ANALYSIS OF A SINGLE CENTRE 2005–2010 COHORT

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Introduction/objectives Pulmonary arteriovenous malformations (PAVMs) are aberrant connections between pulmonary arteries and veins, creating a right-to-left shunt. Hypoxaemia is common,[1] but dyspnoea is usually not the presenting complaint.[2] We hypothesised this may be relevant to dyspnoea mechanisms in the general population.

Methods With ethical approval, new patients presenting with CT-proven PAVMs between June 2005 and July 2010 were studied retrospectively. Based on self-reported exercise tolerance at presentation, and blinded to physiological measurements, two

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