determine the extent and distribution of occupational aetiology.

Methods All HP cases identified from a database over a 13 year period were included. The demographic, clinical, exposure history and investigatory Results were reviewed from clinical notes. Cases were categorised in to three groups: occupational, non-occupational and no known cause. Hypothesis testing at the 95% confidence level was used to identify significant differences between the 3 groups.

Results A total of 127 cases (13 occupational; 34 non-occupational; 80 no known cause) of HP were identified. Men were more likely to experience occupational HP ($p=0.029$) compared to the other groups. Occupational HP cases were younger ($p=0.002$), more likely to experience weight loss ($p=0.004$), to have systemic symptoms ($p=0.007$) and a recurrence of symptoms ($p<0.001$). Occupational HP were due to metal working fluids (MWF), birds, mould/fungi, Farmer's lung, and cleaning and treatment sprays. Non-occupational HP were due to birds, mould/fungi in the home and medication. Percentage lymphocyte count in broncho-alveolar lavage (BAL) was significantly raised in occupational HP ($p=0.001$). Where no causative agent was identified, there was a greater absence of exposure history (13.2%–32.5%).

Conclusion Occupations where there is exposure to birds or those working in trades where industrial processes and the use of chemical compounds predominate, are at risk of occupational HP. Birds remain an important cause of non-occupational HP. Clinical features such as weight loss, systemic symptoms and recurrent symptoms should raise a suspicion of an occupational cause of HP. BAL remains an important investigatory tool in HP, especially in occupational HP. An exposure history, especially an occupational history, is mandatory when assessing suspected cases of HP.

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SHOULD RESPIRATORY HEALTH BE ASSESSED AS PART OF A PRE-SEASON MEDICAL EVALUATION IN PROFESSIONAL FOOTBALLERS?

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Introduction and Objectives High rates of exercise induced bronchoconstriction (EIB) are consistently reported in elite endurance athletes, prompting calls to consider screening high risk groups of athletes for respiratory dysfunction.¹ There are currently no robust data examining the prevalence of respiratory symptoms and airway dysfunction (hyper-reactivity and inflammation) in elite footballers. We therefore undertook this prospective study assessing airway health and the impact of treatment in a cohort of professional footballers undergoing squad pre-season screening.

Abstract S107 Figure 1 Relationship between EVH result and presence of respiratory symptoms.

Methods Ninety-seven elite male footballers completed a respiratory assessment including measurement of airway inflammation (FeNO) and screening for EIB using an indirect bronchoprovocation challenge (Eucapnic voluntary hyperpnoea [EVH]). Players demonstrating a positive challenge result (EVH+) were prescribed appropriate standard asthma therapy directed by EIB severity and underwent repeated assessment after 9 weeks of treatment. Eight players (EVH+=3, EVH-=5) also completed a cardiopulmonary exercise test (VO₂ peak) at the initial and follow-up visits (i.e., post-treatment).

Results Twenty-seven players (29%) demonstrated EVH+. Of these, ten (37%) reported no previous history of asthma or EIB. EVH result was not predictable by respiratory symptoms. Seven (24%) of the EVH +players attended for follow-up and demonstrated a reduction in FeNO (pre=85±61 ppb, post=28±11 ppb, $p=0.04$) and a decrease in the fall in FEV₁ post EVH (pre=-22.9±15.4%, post=-9.0±1.6%, $p=0.018$). At follow-up, VO₂ peak was improved by 3.4±2.9 ml.kg⁻¹.min⁻¹ in EVH +players compared to 0.1±2.3 ml.kg⁻¹.min⁻¹ in EVH-players. Magnitude of inference analysis indicated treatment was possibly beneficial (74%) for exercise capacity.

Conclusion Elite footballers have a high EIB prevalence, which remains undetected by a symptom based approach to assessment. Treatment with appropriate standard therapy reduces EIB severity, improves airway inflammation and may improve exercise performance. Therefore, the use of objective tests to screen for EIB in this population would be beneficial.

REFERENCE

1. Dickinson J, Whyte G, McConnell A, et al. Impact of changes in the IOC-MC asthma criteria: A British perspective. *Thorax* 2005;60:629–632. doi:10.1136/thx.2004.037499

Advances in understanding chronic thromboembolic disease and pulmonary hypertension

S108

GENOME-WIDE ASSOCIATION STUDY IN CHRONIC THROMBOEMBOLIC PULMONARY HYPERTENSION REVEALS NEW INSIGHTS INTO AETIOLOGY

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Introduction Chronic thromboembolic pulmonary hypertension (CTEPH) is an infrequent but important complication of acute pulmonary embolism (PE). Thrombophilias and non-O blood groups are genetic risk factors for venous thromboembolism (VTE), however they are not independently associated with CTEPH. Identifying genetic risk factors for CTEPH would provide important insights into pathobiology and might allow risk-stratification following PE. We undertook a genome-wide association study (GWAS) in CTEPH to identify novel disease loci.

Methods To date, 1457 Caucasian CTEPH patients were enrolled from 10 European and US Centres and compared to 1536 healthy Caucasian controls from the Wellcome Trust Case Control Consortium. Genotyping was performed using the HumanOmniExpressExome-8 array. Quality control criteria and statistical analysis are summarised in figure 1.

Results 1250 CTEPH cases, 1492 controls and 7 million single-nucleotide polymorphisms (SNPs) were included after quality control exclusions. Two loci, in chromosomes 4 and 9 were significantly associated with CTEPH (figure 1). The lead SNP in chr9 (rs532436, OR=2.38, $p=4.6 \times 10^{-32}$) is highly correlated with the tagging SNP for the A1 blood group (rs507666, $R^2=0.99$). Reconstructing genetic ABO groups confirmed an over-representation of the A1A1 group in CTEPH compared to controls (7% vs. 2.9%, OR 4.5). Additionally, there were 11 significant SNPs in the chr9 *ADAMTS13* gene locus that is moderately correlated with *ABO* ($R^2=0.33$).

The lead SNP in chr4 (rs13130318, OR=1.4, $p=5.6 \times 10^{-8}$) is highly correlated with a missense variant in *FGG* (rs6050, $R^2=0.89$) associated with decreased fibrinogen protein and increased resistance to fibrinolysis in CTEPH. There were no associations at the *F5* locus, which is highly significant in VTE.

Conclusions We report the first GWAS in CTEPH, identifying at least 2 genetic loci associated with the disease. The *ABO* association is driven by the A1 blood group and represents the largest population attributable genetic risk factor for CTEPH, which is higher than previously reported for VTE. The potential *ADAMTS13* association is a plausible biological candidate, and further work will establish whether it is independent from *ABO*. The lack of associations with other loci found in VTE suggests that *ABO* might have a pathobiological role in CTEPH in addition to its contribution to VTE.

Abstract S108 Figure 1 Manhattan plot of significant loci in chromosome 4 and 9 associated with CTEPH. Quality control exclusion thresholds and chromosome 9 regional association plot shown within figure. Dotted line represents a Genome-wide significance threshold of $p=5 \times 10^{-8}$ (Bonferroni). Imputation was performed from the Haplotype Reference Consortium (Sanger imputation service). An additive model of association was applied using logistic regression with gender and 1 principal component as covariates. HWE (Hardy-Weinberg equilibrium), IBD (identity by descent), MAF (minor allele frequency), PCA (principal component analysis), SNP (single nucleotide polymorphism).