improved management of respiratory failure. This study examined outcomes and prognostic factors for HIV-infected patients admitted to our ICU over a 10-year period.

Methods Retrospective study of HIV-infected adults admitted to a UK University-affiliated hospital ICU between January 1999 and March 2009. Information collected included patient demographics, receipt of HAART (no patient began HAART while on the ICU), reason for ICU admission and hospital course. Outcomes were survival to ICU and hospital discharge. Comparison was made against outcomes for general medical patients admitted to the same ICU. Multivariate analysis was used to assess prognostic factors.

Results 192 HIV-infected patients had 222 admissions to the ICU. Among these 192 patients, 116 required mechanical ventilation and 43 renal replacement therapy. Their ICU admission was due to an HIV-associated diagnosis in 113 patients; 37 patients had *Pneumocystis* pneumonia. Survival to ICU discharge and hospital discharge was 78% and 70%, respectively, compared with 75% and 68% among 2065 general medical patients admitted to the ICU on 2274 occasions over the same time period. HIV infection was newly diagnosed (on this hospital admission) in 42 patients; among this group ICU and hospital survival was 69% and 57%, respectively. Factors associated with ICU survival were age (OR=0.97, 95%CI 0.93 to 1.00, per 10 year increase), haemoglobin (OR=1.33, 95%CI 1.07 to 1.65, for an increase of 1 g/dl), APACHE II score (OR=0.56, 95%CI 0.39 to 0.90, per 10 unit increase), receipt of HAART (OR=2.88, 95%CI 1.29 to 6.42) and need for mechanical ventilation (OR=0.18, 95%CI 0.07 to 0.43).

Conclusions In the era of HAART the outcome from ICU for HIV-infected patients was comparable to that among general medical patients. These data infer neither HIV infection itself, nor an HIV-associated diagnosis should preclude referral to the ICU. The poorer outcome among those with newly diagnosed HIV infection underscores the need to encourage HIV testing outside of Genitourinary Medicine clinics.

Pathophysiological mechanisms in childhood asthma

S83 PRESCHOOL WHEEZING PHENOTYPES IN A REPRESENTATIVE UK BIRTH COHORT

doi:10.1136/thx.2010.150938.34

¹J M Harris, ²A Bush, ²N Wilson, ¹P Mills, ¹C White, ¹S Moffat, ¹L Shread, ¹P Cullinan. ¹Occupational & Environmental Medicine, Imperial College (NHLI), London, UK; ²Paediatrics, Imperial College (NHLI), London, UK

Introduction and objective The 2008 ERS Task Force¹ recommended that preschool wheezing be classified as episodic (viral) wheeze (EVW) or multiple trigger wheeze (MTW). We investigated the relationship between these phenotypes and reported wheeze and medication use in later childhood.

Methods Between 1993 and 1995, 658 consecutive mothers attending for routine ante-natal care (93% of those eligible) were recruited; they subsequently gave birth to 642 children. Detailed respiratory data were collected annually until the child reached the age of 5½ years (n=602; 94%). Further information was collected at age 8 (n=593; 92%) and 14 (n=497; 77%) years. EVW was defined as occasional wheeze in the past 12 months which occurred when the child had a cold or other infection; all other reported wheeze was defined as MTW. Using data from birth to age 5½, children were categorised as never wheezing (n=238); only EVW wheeze (n=208); both EVW and MTW wheeze (n=100) and only MTW wheeze (n=56).

Results The prevalence of EVW fell from 32% at age 0–1 to 7% at age 4–5½; MTW prevalence was approximately 10% each year. Compared with never wheezers, in each wheezing group there was a higher proportion of boys (54%, 65%, 61%), (48%); p=0.02, higher

exposure to ETS, and a greater prevalence of maternal and paternal asthma (p<0.001, p<0.001, p=0.06, respectively). Respiratory outcomes at 8 and 14 years were higher amongst the three wheezing groups, especially for those with MTW (see Abstract S83 Table 1). There was a higher prevalence of current wheeze and medication use at 8 and 14 years for those with a higher frequency of wheezing between birth and age 5½; and a lower prevalence of the same outcomes for those who only wheezed between birth and age two, compared to those who wheezed later.

Abstract S83 Table 1

Wheezing phenotypes: birth to age 5½ years					
	Never (n=238)	Only EVW (n=208)	Both EVW & MTW (n=100)	Only MTW (n=56)	p-Value* p Value†
Age 8 years					
Current wheeze	7 (3%)	21 (10%)	33 (35%)	18 (36%)	<0.001 <0.001
Atopic (2 mm cut-off)	42 (19%)	26 (14%)	21 (25%)	15 (31%)	0.02 <0.001
Any current medication	1 (0.4%)	9 (4%)	18 (19%)	14 (27%)	<0.001 <0.001
Age 14 years					
Current wheeze	15 (7%)	17 (10%)	24 (32%)	15 (41%)	<0.001 <0.001
Atopic (3 mm cut-off)	55 (32%)	29 (19%)	24 (39%)	14 (50%)	0.001 <0.001
Any current medication	5 (3%)	5 (3%)	11 (15%)	11 (30%)	<0.001 <0.001

*Comparisons between all four groups.

†Comparisons between three wheezing groups.

Conclusion At 8 and 14 years of age, never wheezers and pure EVW had lower prevalences of atopy, wheeze and current medication use than those with any MTW. These data provide external validity to the ERS phenotypes, and suggest that they provide useful prognostic information.

REFERENCE

1. Brand, et al. *Eur Respir J* 2008;**32**:1096–1110.

S84 CHILDHOOD INCIDENT ASTHMA AND PHYSICAL ACTIVITY: A SYSTEMATIC LITERATURE REVIEW AND META-ANALYSIS WITH HETEROGENEITY ASSESSMENTS

doi:10.1136/thx.2010.150938.35

L Lochte, R Granell, J A C Sterne, A J Henderson. *University of Bristol, Bristol, UK*

Introduction and Objectives Physical activity (PA) has been found to be associated with prevalent childhood asthma but evidence from cross-sectional studies is inconclusive; demonstrating both positive and negative associations of PA with asthma. The aim of this study was to systematically review and meta-analyse the literature on PA and incident or “new-onset” childhood asthma.

Methods Medline, Embase, and the Cochrane Library were searched for articles on the associations between PA and asthma, restricted to age group 0–18 years and publications 1995–2010. PA was searched by ‘physical fitness, exercise, physical exertion’ and asthma additionally qualified by FEV₁, BHR, EIA, EIB, exercise test and wheeze. Summary ORs and 95% CIs were estimated by random and fixed effect models. The robustness was explored by subgroup (ethnicity) and sensitivity (cut-point alteration) analysis.

Results Twenty-seven articles were included in the systematic review which comprised nine longitudinal, 15 cross-sectional, one case-control, and two review studies. Five studies featured longitudinal observations and were included in the meta-analysis (total

Abstract S84 Figure 1 Random effect meta-analysis of physical activity (PA) and new-onset childhood asthma.

participants n=12 889; total new-onset asthma n=912). Meta-analysis of these studies showed the following associations of high PA with new-onset asthma: Random effect model: OR (95% CI) 0.854 (0.713; 1.023) (Abstract S84 Figure 1) and fixed effect model: 0.909 (0.855; 0.967). I-squared=62.7% (both models).

Conclusion The results of this review did support some inverse association between high levels of PA and asthma development in children. However, a limited number of eligible studies were identified and considerable heterogeneity was present.

S85 THE EFFECTS OF EXPOSURE TO IL-9 ALONE OR IN COMBINATION WITH IL-13 ON THE MUCOCILIARY DIFFERENTIATION OF BRONCHIAL EPITHELIAL CELLS FROM NORMAL AND ASTHMATIC CHILDREN.

doi:10.1136/thx.2010.150938.36

¹J C Parker, ¹S T Thavagnanam, ²G Skibinski, ¹M D Shields, ¹L G Heaney. ¹Centre for Infection and Immunity, Queen's University Belfast, Belfast, UK; ²School of Medicine, Dentistry and Biomedical Sciences, Queen's University Belfast, Belfast, UK

Background IL-9 is a pleiotropic Th2 cytokine that has been implicated in the pathogenesis of asthma. IL-9 has been linked to goblet cell hyperplasia and decreased ciliogenesis in animal models and an epithelial injury model in adults. We tested the effects of IL-9 alone and in combination with IL-13, an important cytokine in allergic asthma, during differentiation of bronchial epithelial cells from both asthmatic and normal children.

Hypothesis We hypothesised that bronchial epithelial cells from normal children exposed to IL-9 would result in goblet cell hyperplasia and decreased ciliogenesis, with additional augmented response when treated with a combination of IL-9 and IL-13.

Methods We cultured bronchial epithelial cells from asthmatic and normal children at an air-liquid interface for 28 days. We enumerated the presence of goblet and ciliated cells at the end of the experimental period.

Results IL-9 stimulation alone did not alter goblet cell numbers in differentiating cultures from normal or asthmatic children. IL-9 stimulated PBECs from normal children had reduced ciliated cell numbers and increased MUC5AC secretion at the apical surface which was not seen in asthmatic cells. Combining IL-9 and IL-13 had no additional synergistic effect.

Conclusions We conclude that IL-9 alone or in combination with IL-13 did not stimulate goblet cell hyperplasia in bronchial epithelial cells cultures from normal children. We have shown that it does lower the number of ciliated cells during differentiation of PBECs

from normal children however this effect is not seen in cells from asthmatic children.

S86 EFFECTS OF EXPOSURE TO IL-13, IL-31 AND AN IL-13/31 COMBINATION ON MUCOCILIARY DIFFERENTIATION OF BRONCHIAL EPITHELIAL CELLS FROM NORMAL CHILDREN

doi:10.1136/thx.2010.150938.37

¹J C Parker, ¹S T Thavagnanam, ²G Skibinski, ¹L G Heaney, ¹M D Shields. ¹Centre for Infection and Immunity, Queen's University Belfast, Belfast, UK; ²School of Medicine, Dentistry and Biomedical Sciences, Queen's University Belfast, Belfast, UK

Background Asthma is characterised by airway remodelling which includes smooth muscle hypertrophy, goblet cell hyperplasia and subsequent mucus hyper-secretion. Th2 cytokines including IL-13 and more recently IL-31 have been implicated in the pathogenesis of asthma.

Objectives We aimed to examine the effects of IL-13 (20 ng/ml), IL-31 (20 ng/ml) and an IL-13/31 combination (20 ng/ml of both) on the in vitro mucociliary differentiation of paediatric bronchial epithelial cells (PBECs) from normal patients.

Hypothesis We hypothesised that cells from normal children exposed to IL-13, IL-31 or an IL-13/31 combination would alter their phenotype towards that of an asthmatic epithelium.

Methods Markers of differentiation, real time PCR for MUC5AC, MUC5AC ELISA and transepithelial electrical resistance (TEER) were assessed.

Results We found that well-differentiated paediatric bronchial epithelial cells highly expressed the IL-31 receptor (IL-31RA). Transepithelial electrical resistance (TEER) indicated good formation of tight junctions which was found to be similar across all treatment groups. We found that IL-13 stimulation reduced the number of ciliated cells compared with control (IL-13 stimulation: mean=4.8% (SD=2.5); Control: mean=18.1%, (SD=5.9)). We did not find that the combination of IL-13 and IL-31 had any additional effects to that of IL-13 alone (IL-13/31 combination stimulation: mean=5.1% (SD=4.6); Control: mean=18.1%, (SD=5.9)). Stimulation with IL-13, IL-31 and the IL-13/IL-31 combination did not result in any changes of goblet cell numbers.

Conclusions IL-31RA receptor is present in abundance in well-differentiated paediatric bronchial epithelial cells however IL-31 does not exhibit any detrimental effects on mucociliary differentiation or proliferation. In addition, IL-31 does not appear to have a synergistic effect when combined in culture with IL-13, in the differentiation process.

S87 RELATIONSHIP BETWEEN BRONCHIAL RETICULAR BASEMENT MEMBRANE THICKNESS (RBM) AND SMOOTH MUSCLE MASS IN CHILDHOOD SEVERE ASTHMA (SA)

doi:10.1136/thx.2010.150938.38

¹C J Bossley, ¹N Regamey, ¹L Fleming, ²T Oates, ²C Lloyd, ¹A Bush, ²S Saglani. ¹Royal Brompton Hospital, London, UK; ²Imperial College, London, UK

Background In asthma there is a direct relationship between tissue eosinophilic inflammation and RBM thickness. However, relationships between components of remodelling have not been explored, but may be important especially in determining disease severity. There are no reports of an association between smooth muscle mass and asthma severity in children. We hypothesised that increases in both RBM thickness and smooth muscle mass is present in children with SA, only increased RBM thickness is present in mild asthma and neither feature is present in controls.

Methods 75 children, mean age 11.8 (5.6–17.3) years, 53 with SA, 7 with mild/moderate asthma and 15 non-asthmatic controls