manner. This demonstrates the potential for IL-1 signaling to impact on viral infection. In this study, we explored the ability of MyD88 to regulate responses to the natural viral pathogen, RV serotype 1B (RV-1B).

Methods MyD88 was stably knocked down in the immortalised bronchial epithelial cell line, BEAS-2B, using a lentiviral transduction system containing shRNA targeted to MyD88. Wildtype or MyD88^{KD} cells were stimulated, in the presence or absence of human monocytes, with TNF α and IL-1 β , poly(I:C), LPS and gardiquimod (TLR3, TLR4 and TLR7/8 agonists, respectively), or infected with RV-1B. Selected experiments were carried out in the presence of IL-1ra. Changes in cytokine release were measured by ELISA. Rates of viral replication were measured using quantitative PCR.

Results Costimulation of BEAS-2B cells with IL-1 and RV-1B caused a dramatic increase in proinflammatory (CXCL8), but not CCL5 production. MyD88^{KD} cells with ~70% reduction in MyD88 mRNA levels showed no impairment to TNF α or poly(I:C) stimulation, but significantly reduced responses to IL-1 β . MyD88^{KD} cells also had significantly impaired responses to RV-1B as assessed by production of CXCL8 and CCL5. Inhibition of RV-induced CXCL8 production could also be achieved by pre-treatment with the IL-1 antagonist, IL-1ra. IL-1 β was not produced from RV-infected cells, implicating other members of the IL-1 family in the response of epithelial cells to viral infection. Viral replication was more marked in MyD88^{KD} cells.

Conclusion A reduction in MyD88 signalling modulates specific epithelial cell responses to rhinovirus, and thus may be an important target to control acute inflammation induced by human viral pathogens.

Abstract S80 Figure 1

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S81

PRIMARY TYPE II ALVEOLAR EPITHELIAL CELLS RESPOND DIFFERENTIALLY TO BACTERIAL VIRULENCE FACTORS

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Introduction and objectives The pathogens most commonly implicated in ventilator-associated pneumonia (VAP) are *Pseudomonas aeruginosa* and *Staphylococcus aureus*. Although a florid inflammatory response characteristically occurs in the alveolar space in VAP, the underlying mechanisms remain unclear, partly owing to a lack of adequate models of alveolar injury. We therefore sought to characterise the response of primary human type II alveolar epithelial (ATII) cells to virulence factors from these pathogens.

Methods Primary ATII cells were derived from seven patients undergoing surgical resection for lung cancer. Lung tissue was refrigerated overnight; flushed with saline; incubated with trypsin; diced; incubated with DNase I; and strained/filtered. Macrophages and fibroblasts were removed by adherence. The resulting cell population was centrifuged, washed, resuspended and plated onto tissue culture plates pre-coated with type I bovine collagen at 2×10^6 cells/ml. When cells achieved confluence medium was replenished and the following were added for 24 h: 100 ng/ml *P. aeruginosa* lipopolysaccharide (LPS); 10 ug/ml *S. aureus* lipoteichoic acid (LTA); 10 ug/ml *S. aureus* peptidoglycan (PGN); 10 ng/ml human recombinant tumour necrosis factor alpha (TNF α); or control medium. Supernatant was aspirated at 24 h and cytokines were measured by cytometric bead array.

Results Interleukin (IL)-1 β , IL-6, IL-8 IL-10, IL-12p70 and TNF α were all detectable in control medium at 24 h. None of the measured cytokines were significantly altered by application of LPS or LTA. In contrast, PGN induced a significant rise in concentrations of IL-1 β , IL-6, IL-8 IL-10 and TNF α . Addition of TNF α induced a significant increase in IL-6, IL-8 and IL-10. The only cytokine to be uniformly uninfluenced by stimulation was IL-12p70.

Conclusions In our hands primary ATII cells appeared to be unresponsive to *P. aeruginosa* LPS or to *S. aureus* LTA. By contrast, *S. aureus* PGN provoked a brisk and significant inflammatory response simultaneously affecting a range of cytokines. These data suggest that ATII cells have strikingly different responses to individual bacterial virulence factors. They further suggest that PGN (but not LTA) contributes, at least in part, to the florid inflammatory response seen in Staphylococcal pneumonia.

S82

SURVIVAL OF HIV-INFECTED PATIENTS ADMITTED TO THE INTENSIVE CARE UNIT

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Background Several studies from USA and Europe have suggested the outcome for HIV-infected patients admitted to the intensive care unit (ICU) has improved, concurrent with both the introduction of highly active antiretroviral therapy (HAART) and

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

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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

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

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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