Background Epidemiological phenotypes for childhood wheeze were first proposed by the Tucson Children’s Respiratory Study (TCRS), describing four distinct phenotypes. A new, six phenotype, characterisation has recently been proposed by the Avon Longitudinal Study of Parents And Children (ALSPAC). No previous cohort has included 1 year atopic sensitisation data with infant lung function in their analysis.

Objectives To classify infant and 6 year lung function and allergic sensitisation data at 1, 3 and 6 years from the Southampton Women’s Survey (SWS) cohort according to the ALSPAC 6 class phenotype model. To contrast this with TCRS phenotypes to assess clinical and epidemiological utility.

Methods At 6 years, 926 children had assessment of respiratory symptoms. Spirometry was measured in 791 children, with exhaled nitric oxide (n=589) and methacholine challenge (n=234). At 5–14 weeks of age 95 of these children had lung function measured. Symptom data on wheeze status obtained at 6m, 12m, 2y, 3y and 6y follow up classified children into groups proposed from analyses of ALSPAC (never, early, transient, intermediate-onset, late-onset and persistent wheeze).

Results Persistent and intermediate-onset wheeze were significantly associated with atopy at 1, 3 and 6 years, and exhaled nitric oxide at 6 years. Late-onset wheeze was not associated with atopic sensitisation until 3 years. Persistent wheezers had lower infant(V’maxFRC p<0.05) and 6 year lung function (FEV1, FEV1/FVCp<0.05), whilst late- and intermediate-onset-wheeze showed no lung function deficits. Transient wheezers were non-atopic but showed persistent lung function deficits (FEF25-75 p<0.05 and V’maxFRC, p<0.001), except for those who wheezed only in the first year of life (early phenotype).

Conclusion The SWS cohort data maps well into the ALSPAC phenotype classification, demonstrating useful subdivision of TCRS wheeze phenotypes. Lung function and atopy successfully differentiate persistent, late-onset and intermediate-onset wheeze, whilst the classical ‘transient early’ wheeze phenotype can be sub-classified into groups that reflect early lung function. This has potential significance for research into childhood wheeze and long term respiratory morbidity of children in these phenotypes.

Conclusion Despite the high proportion of respiratory symptoms reported, the number of children with LFTs falling outside the limits of normal was relatively small. Results suggest a pattern of restrictive lung disease in children with SCD. Of the outcomes assessed, baseline spirometry appears to be the most useful for routine assessment of lung disease in young children with SCD.

1 J Kirkby, R Bonner, P Bates, R Stunk, F Kirkham, J Stocks, S Sonnappa. 2 UCL Institute of Child Health, London, UK; 2 Washington University, Missouri, USA

Introduction Sickle Cell Disease (SCD) is one of the most prevalent genetic diseases with an incidence of ~1 in 200 Afro-Caribbean children in the UK (WHO; 2006). Since SCD can result in significant respiratory morbidity,[1] lung function tests (LFTs) could play an important role in the clinical management of children with SCD.

Aim To determine the extent to which LFTs identify differences in children with SCD when compared with healthy Black children.

Methods A respiratory health questionnaire was administered, and four commercially available LFTs (Impulse oscillometry (IOS), specific effective airways resistance (sReff), plethysmographic lung volumes, and spirometry) were undertaken in up to 214 healthy Black children and 85 children with SCD aged 4–12y.

Results Amongst children with SCD, 50% reported cough on most days, and 25% had been reviewed by a specialist respiratory consultant within 3 months prior to the assessments. When compared with healthy children, 20% had a reduced total lung capacity (TLC), with concurrent reductions in FEV1 and FVC. No differences in sReff were observed and IOS outcomes proved to be of limited value, due to poorly defined limits of normality and large between-subject variability. No significant group differences in bronchodilator responsiveness in SCD or healthy children were observed regardless of the outcome measured (Table 1).

Conclusion Despite the high proportion of respiratory symptoms reported, the number of children with LFTs falling outside the limits of normal was relatively small. Results suggest a pattern of restrictive lung disease in children with SCD. Of the outcomes assessed, baseline spirometry appears to be the most useful for routine assessment of lung disease in young children with SCD.

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Background Many factors have been related to the development of childhood asthma but there is inconsistency between studies.

Objective To understand how early life factors are linked to the development of the various asthma phenotypes at age 6 years in the Southampton Women’s Survey (SWS) children’s cohort.

Methods Data was collected from 940 children and their parents, primarily through questionnaires during pregnancy and at 6m, 1, 3 and 6 years. Prevalent asthma was defined by a doctor’s diagnosis and a wheezing episode in the last year. Data was analysed using STATA v9. A relative risk analysis using a univariate approach was undertaken, followed by a multivariate analysis.

Results Both maternal (RR=1.61, p=0.041) and paternal (RR=2.05, p=0.002) atopic disease increased the risk of asthma at age 6 years. The risk increased with atopy, defined as a positive skin prick test, at 3 years (RR=3.05, p<0.001) and with wheeze in the first 3 years (RR=8.79, p<0.001). Episodes of bronchiolitis and chest infections were associated, in a dose-dependent manner, with the risk of asthma (RR=1.50, p=0.022). Predictors in the multivariate model were wheeze in the first 3 years (RR=10.74, p<0.001), atopy (RR=2.87, p<0.001) and maternal atopy (RR=2.22, p=0.01). When asthma at age 6 years was split into atopic and non-atopic asthma, the predictors were very different. Atopic asthma was associated with paternal atopy (RR=4.13, p=0.002), male sex (RR=2.56, p=0.030), atopy at 3 years (RR=10.31, p<0.001) and wheeze in the first 3 years (RR=5.91, p=0.004). In the multivariate analysis, the following were predictive: wheeze in the first 3 years (RR=13.55, p=0.012), atopy (RR=10.13, <0.001), paternal atopy (RR=2.97, p=0.017) and a 12 month infant dietary pattern that follows current guidelines (RR=1.79, p=0.016). For non-atopic asthma, bronchiolitis or chest infections (RR=1.76, p=0.047), wheeze in the first 3 years (RR=20.69, p=0.003) and tobacco smoke exposure at 6 years (RR=2.16, p=0.035) increased the risk. Only wheeze in the first 3 years remained in the multivariate model.

Conclusions Different hereditary and early life factors modify the risk of atopic and non-atopic asthma at 6 years of age. This suggests that these two asthma phenotypes have different pathophysiologies.

Pathophysiology of pulmonary vascular remodelling

S36 P38 MAPK: AN IMPORTANT PATHWAY IN THE PATHOBIOLOGY OF PULMONARY HYPERTENSION AND PULMONARY VASCULAR REMODELLING
doi:10.1136/thoraxjnl-2012-202678.042

1AC Church, 2R Wadsworth, 3G Bryson, 4DJ Welsh, 5AJ Peacock. 1Scottish Pulmonary vascular Unit, Glasgow, UK; 2University of Strathclyde, Glasgow, UK; 3University of Glasgow, Glasgow, UK

The p38 MAPK pathway is increasingly recognised as important in inflammation leading to systemic vascular disease but its role in pulmonary vascular disease is unclear. Our group has previously identified the p38MAPKα isoform to be critical in hypoxic-induced proliferation of pulmonary artery fibroblasts, a key step in the pathogenesis of pulmonary vascular remodelling. This study sought to investigate the role of p38MAPK in animal models of pulmonary hypertension and in human disease.

Methods Sprague Dawley rats were exposed to chronic hypoxia for 14 days and received a selective p38 MAPKα inhibitor from day 1