neutrophilic airway inflammation. Long-term, low dose macrolide antibiotics reduce neutrophilic airway inflammation in other inflammatory airway diseases. We tested the hypothesis that long-term low dose erythromycin reduces the induced sputum neutrophil count and 24 h cough frequency in patients with unexplained chronic cough.

Methods Thirty patients with an unexplained chronic cough lasting >8 weeks were randomised to take 250 mg of erythromycin once daily (n = 15) or placebo (n = 15) for 12 weeks in a double-blind parallel group study. 24 h ambulatory cough frequency, the concentration of inhaled capsacain required to cause two (C2) and five (C5) coughs, the induced sputum neutrophil count, the Leicester Cough Questionnaire (LCQ) and a 100 mm cough visual analogue score (VAS) were measured before and 6, 12 and 24 weeks after the start of treatment. The primary outcome measure was change in 24 h cough frequency at 12 weeks.

Results 24 h cough frequency at baseline and 12 weeks was 358 and 245 (mean fold difference 1.45, 95% CI 1.02 to 2.17) with erythromycin, and 356 and 390 (mean fold difference 1.57, 95% CI 1.15 to 1.64) with placebo. There was no significant difference in the change in cough frequency between the groups at 12 weeks (mean difference 0.84, 95% CI -0.80 to 2.48, p=0.358) or at other times. The induced sputum neutrophil count reduced significantly from 67.2% to 56.6% after 12 weeks treatment with erythromycin and there was a significant between-treatment difference in the change in percentage sputum neutrophils at 12 weeks (−10.2 vs +6.6; mean difference 18.8, 95% CI 11.6 to 32.1, p = 0.03) but not at other times. There was no difference in the change in LCQ, cough VAS, C2 and C5 between treatments.

Conclusions Treatment with low dose erythromycin for 3 months does not reduce cough frequency in patients with unexplained chronic cough despite significantly reducing neutrophilic airway inflammation.

Clinical problems in childhood

S28 CHILDHOOD ASTHMA IN NORTH EAST SCOTLAND: A 45-YEAR PERSPECTIVE

doi:10.1136/thx.2009.127068b

Introduction The Aberdeen Schools Asthma Surveys (ASAS) have described changing prevalences of childhood asthma from 1964. The ASASs were among the first to report a rise in asthma prevalence in the UK and westernised countries during the 1980s and 1990s. A history of asthma ever was reported in 7% of children in 1964, rising to 24% in 1999 and 28% in 2004, although the prevalence of wheeze in the last 3 years fell from 28% to 25% between 1999 and 2004. A history of wheezy bronchitis remained static at about 7% between 1964 and 2004. The present study tested the hypothesis that the prevalence of asthma fell between 2004 and 2009 and the prevalence of wheezy bronchitis remained unchanged.

Methods Schools within the 1964 boundaries of Aberdeen city were invited to participate. Children in primary years 3–7 were eligible (ages 7–12 years). The questionnaire used and validated in previous surveys was distributed to children by teaching staff, completed by parents at home, returned to the classroom and collected by researchers. Wheezy bronchitis was defined as the presence of wheeze only in association with an upper respiratory tract infection.

Results Thirty-one schools were invited to participate, of which 26 took part. There were 3709 eligible children and 2004 (54%) questionnaires returned. The mean age was 9.8 (SD 1.5) years and 958 (48%) were boys. A history of asthma ever was reported in 21% of children (381/1811), and wheeze in the last 3 years was reported in 22% (432/1975). A history of wheezy bronchitis was reported in 5% (107/1988) of the children.

Conclusions The proportion of children with a history of asthma ever, wheeze in the last 3 years and wheezy bronchitis fell in Aberdeen between 2004 and 2009. The reasons for the reduction in asthma symptoms are not understood and, while changes in diagnostic criteria may have played a part, the data are also consistent with a genuine fall in disease prevalence.

Background Intrauterine environment and fetal growth are important for optimal lung growth and the maturation of the developing immune system. In epidemiological studies, both fetal overnutrition and undernutrition, as approximated by anthropometry at birth, have been proposed to increase the risk of allergic conditions and asthma. However, the findings remain confusing and contradictory. Furthermore, heterogeneity between study populations and methodology has made interstudy comparison difficult.

Objectives In this study, we explored the relationship of size at birth and asthma/atopy and respiratory function in prepubertal children.

Methods and Study population The Avon Longitudinal Study of Parents and Children (ALSPAC) is a longitudinal birth cohort study of children born between 1 January 1991 and 31 December 1992 in Avon, UK. Details on birth anthropometry of term newborns included birth weight, birth length, head circumference and ponderal index (birth weight/length³). All raw data were converted to their respective sex specific z-scores using the 1990 UK population reference data. The association of birth measures with parent-reported asthma (7.5 years), atopy based on skin prick tests (7.5 years), serum immunoglobulin E (IgE) (7.5 years) and lung function measured by spirometry (8.5 years) was estimated using logistic regression. Analyses were then adjusted for a range of possible confounding variables.

Results A total of 14 541 women were enrolled during pregnancy, resulting in 14 062 live births. Exposure data were ascertained in ~13 000 subjects, whereas outcome measures were available in 7000 subjects (~4000 for IgE). Univariable analyses showed that heavier boys (>4500 g) were more likely to have asthma (odds ratio (OR) 2.12 (95% CI 1.05 to 4.27)) and atopy (OR 2.26 (CI 1.05 to 4.87)). In contrast, low birth weight boys (<2500 g) were more likely to have a

Abstract S29 Table Asthma according to birth weight categories

<table>
<thead>
<tr>
<th>Boys</th>
<th>OR (95% CI)</th>
<th>OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;2500 g (n = 69 boys and 86 girls)</td>
<td>2.14 (1.31 to 3.49)</td>
<td>1.17 (0.68 to 1.99)</td>
</tr>
<tr>
<td>Unadjusted analysis</td>
<td>Adjusted analysis*</td>
<td>1.62 (0.79 to 3.32)</td>
</tr>
<tr>
<td>&gt;4500 g (n = 99 boys and 37 girls)</td>
<td>0.74 (0.45 to 1.24)</td>
<td>2.12 (1.05 to 4.27)</td>
</tr>
<tr>
<td>Unadjusted analysis</td>
<td>Adjusted analysis*</td>
<td>0.76 (0.41 to 1.43)</td>
</tr>
</tbody>
</table>

Atopy according to birth weight categories

<table>
<thead>
<tr>
<th>Boys</th>
<th>OR (95% CI)</th>
<th>OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt;4500 g (n = 87 boys and 31 girls)</td>
<td>1.02 (0.62 to 1.68)</td>
<td>2.26 (1.05 to 4.87)</td>
</tr>
<tr>
<td>Unadjusted analysis</td>
<td>Adjusted analysis*</td>
<td>1.13 (0.62 to 2.05)</td>
</tr>
</tbody>
</table>

*Adjusted for maternal/paternal history of asthma/eczema, maternal smoking in pregnancy, any environmental tobacco smoke at home, maternal age at delivery, child’s ethnicity, maternal parity/birth order, maternal social class, gross household income and current body mass index.
diagnosis of asthma (OR 2.14 (95% CI 1.31 to 3.5)). These associations were attenuated after adjustment. An increase in birth weight z-score was associated with reduced risk of asthma in boys (adjusted OR 0.90 (95% CI 0.81 to 0.99)). Lower birth weight categories were associated with small decrements in lung function at age 8 years. Serum IgE was not associated with birth anthropometric indices.

**Conclusion** In this study we found little evidence to support unconfounded associations between birth size and asthma/atopy or respiratory function in prepubertal children.


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**S30 TOWARDS A METABOLIC APPROACH TO RESPIRATORY DISEASE IN CHILDHOOD: FEASIBILITY AND ACCEPTABILITY OF A NOVEL BREATH SAMPLING PROCEDURE AND INITIAL BREATH ANALYSIS DATA**

1F Gahleitner, 2C Guallar-Hoyas, 2G Blackburn, 1CS Beardmore, 1CLP Thomas, 1H Pandya. 1Department of Infection, Immunity and Inflammation, Child Health Section, University of Leicester, Leicester, UK; 2Department of Chemistry, Loughborough University, Loughborough, UK

doi:10.1136/thx.2009.127068d

**Introduction and Objectives** Asthma diagnosis and treatment is based mainly on the presence of symptoms and response to treatment. This carries the risk of misdiagnosis and undertreatment or overtreatment. The focus in asthma management has shifted to the underlying chronic airway inflammation. We are developing a novel approach in which breath samples are analysed for volatile organic compounds (VOCs) that alone or in combination may be used as biomarkers for airway inflammation. The aims of the current study are (1) to determine the feasibility and acceptability of the sampling procedures for children aged 8–16 years, and (2) to collect preliminary data on potential candidate markers.

**Methods** Children were recruited from Asthma clinics, or in response to posters in the hospital (controls). Nitric oxide and spirometry measurements were carried out and clinical metadata recorded. Exhaled breath was collected onto an adsorbent VOC sampling tube using a face mask supplied with purified medical-air under computer control to enhance reproducibility. Breath samples were collected with the child in a relaxed state watching TV. No specific breathing manoeuvres were required. Three attempts to collect breath from each child were made (5–8 min per sample). The child completed a feedback form on the procedure, based on a Likert scale. Breath samples were analysed by thermal desorption–gas chromatography–mass spectrometry/differential mobility spectrometry.

**Results** At the time of abstract submission, seven children aged 9–14 (5 with asthma) had participated. All were able to provide three samples and feedback showed that they were all “willing to undertake this test again if asked to do so”. One participant reported slight discomfort while wearing the face mask. The gas chromatography–mass spectrometry data (fig 1) that allow the relative concentrations of the different volatile components of exhaled breath to be estimated were comparable with data previously obtained in adults.

**Conclusions** The sampling procedure is entirely acceptable to children. Larger numbers of children should reveal whether this new metabolomic approach to asthma, coupled with advanced statistical approaches, is likely to provide molecular biomarkers useful for non-invasive diagnosis and management.


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**S31 SAFETY AND TOLERABILITY OFomalizumab IN CHILDREN WITH INADEQUATELY CONTROLLED moderate-to-Severe allergic (IGE-MEDIATED) ASTHMA**

1H Milgrom, 2J Fink, 3A Fowler-Taylor, 3C Fernandez Vidaurre, 4M Blogg. 1National Jewish Health, Denver, USA; 2Medical College of Wisconsin, Milwaukee, USA; 3Novartis Pharmaceuticals Corporation, East Hanover, USA; 4Novartis Horsham Research Centre, Horsham, UK

doi:10.1136/thx.2009.127068e

**Background** Omalizumab is currently approved to treat adolescents and adults (>12 years) with inadequately controlled moderate-to-severe (US) or severe (EU) allergic (immunoglobulin E (IgE)-mediated) asthma. A large international phase III clinical study...
evaluated the safety and tolerability of omalizumab in children (6 to <12 years) with moderate-to-severe allergic (IgE-mediated) asthma.

**Methods** Omalizumab (75–375 mg subcutaneously, twice or four times a week) or placebo was given as add-on therapy to children receiving inhaled corticosteroids, with or without other controller medications, for 52 weeks. Safety assessments consisted of adverse events (AEs), serious AEs (SAEs), vital signs and laboratory evaluations.

**Results** 628 children who received ≥1 dose of study drug (omalizumab, n = 421; placebo, n = 207) and with ≥1 postbaseline assessment were included. The overall incidence of AEs was similar in both groups. The most frequently reported AEs were nasopharyngitis (27.5%) and upper respiratory tract infection (18.3%). Two omalizumab patients (serious bronchitis (n = 1); non-serious head-ache suspected treatment related (n = 1)) and 1 placebo patient (serious medulloblastoma (n = 1)) withdrew from the study due to side effects. AEs in omalizumab patients and 8.7% of placebo patients. No malignancy was reported in any of omalizumab patients and 8.7% of placebo patients. No malignancy or thrombocytopenia was reported in the omalizumab group; 1 malignancy was reported in the placebo group (this was the same placebo patient that withdrew from the study due to an AE). One patient in each group reported an anaphylactic reaction, but neither was suspected to be study drug-related (omalizumab: related to meperidine use; placebo: related to ingestion of nuts). Both rash and urticaria were reported in <3% of omalizumab patients and 4.3% of placebo patients. No serum sickness was reported. There were no between-group differences in laboratory evaluations or vital signs.

**Conclusion** Omalizumab was generally well tolerated in children aged 6 to <12 years, with a safety profile similar to that in previous studies in adolescents and adults.

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**S32**

**PAEDIATRIC EMPYEMA MANAGEMENT IN THE UK**

1M Thomas, 1D Cliff, 2S Beaton, 3SP Rushton, 1J Paton, 1DA Spencer. 1School of Biology, IRES, Newcastle University, Newcastle-Upon-Tyne, UK; 2University of Glasgow, Glasgow, UK; 3Department of Respiratory Paediatrics, Royal Victoria Infirmary, Newcastle-Upon-Tyne, UK
doi:10.1136/thx.2009.127068f

**Introduction and Objectives** Since the publication of the BTS Guidelines on the management of pleural infection in children1 in 2005, there has been no review of paediatric empyema management in the UK. We report data from the first year of prospective UK national surveillance of paediatric empyema which began in August 2008.

**Methods** Data were collected from children with a diagnosis of parapneumonic effusion or empyema managed in 22 collaborating tertiary paediatric centres. Anonymised clinical data were extracted from case records and entered into a web-based database.

**Results** 76 children were entered between 1 August 2008 and 21 July 2009 (median age 4 years; 68% male). 19 cases (24%) had some missing data. Median stay in the tertiary centre was 8 days (range: 2–58 days) and total hospital stay was 12 days (range: 4–46 days). Paediatric intensive care unit admission occurred in 15 (25% of 60 documented cases) but there were no deaths. 97% of children had chest ultrasound. 27% also had chest CT, although routine use of CT is not currently recommended.1 Chest drains were inserted in 62 (97%) cases. 40 (65%) received intrapleural fibrinolytics. 21 children (33%) had thoracic surgery (12 (21%) video-assisted thoracoscopic surgery (VATS)); 11 (19%) underwent thoracotomy). Two (3%) patients underwent both procedures due to presumed failure of VATS. Analysis was performed using the Cox proportional hazard model. The use of fibrinolytics did not have a significant effect on length of stay (coefficient 0.08, p = 0.8, 95% CI 1.0 to 1.1). VATS did appear to reduce length of stay when compared directly with thoracotomy (−0.7, p = 0.07 (95% CI 0.2 to 1.1) vs 0.1, p = 0.9 (95% CI 0.2 to 1.1)); however, this effect did not achieve significance. There was variation in median length of stay between centres (range: 7–15 days). When addressed in a subanalysis, no evidence of a centre-specific effect achieving significance was found, possibly as a consequence of the small sample size.

**Conclusions** Although there is evidence of variations in management of empyema in children, at present these do not appear to impact on length of stay nor, at present, is there evidence of a difference in length of stay between centres within the UK.

**Acknowledgements** Thanks to all the staff at collaborating centres who have contributed to the project.


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**S33**

**MILD TO MODERATE PULMONARY HYPERTENSION IN CHILDREN WITH SICKLE CELL DISEASE IS DUE TO INCREASED PULMONARY BLOOD FLOW SECONDARY TO ANAEMIA RATHER THAN ELEVATED PULMONARY VASCULAR RESISTANCE**

1RA Chaudry, 2M Cikes, 3T Karu, 3C Hutchinson, 3S Ball, 3G Sutherland, 1M Rosenthal, 1A Bush, 2S Crowley. 1Royal Brompton Hospital, London, London, UK; 3St Georges Hospital, London, UK
doi:10.1136/thx.2009.127068g

**Introduction and Objectives** Pulmonary hypertension is a common and serious complication in adults with sickle cell disease (SCD), with a mortality rate of 40% within 40 months of diagnosis. However, death is rare in children with SCD who have PHT for reasons which are unclear. We hypothesised that PHT in paediatric patients with SCD may be secondary to anaemia-induced high cardiac output.

**Methods** 30 patients with SCD, median age 14.0 years (range 10–18) and 50 healthy matched controls were recruited. Two independent techniques, previously validated using cardiac catheterisation, were used to estimate pulmonary vascular resistance (PVR). First, tricuspid regurgitant jet velocity (TRV) and right ventricular outflow tract time–velocity integral (RVOT Vti) were measured using Doppler echocardiography; PVR was calculated from their ratio. Secondly, subjects performed inert gas rebreathing (acetylene) using respiratory mass spectrometry to measure effective pulmonary blood flow (Qeff in litres/min). Qeff was divided by heart rate and corrected for body surface area to calculate the stroke index (SI in ml/m2).

**Results** 52% (16/30) of patients and 8% (4/50) of control subjects had echocardiographic evidence of PHT (TRV ≥2.5 m/s). Children with higher TRV had lower calculated PVR and haemoglobin (Hb) but higher right ventricular stroke volume (RVSV) (p<0.05). Patients (n = 45) had a significantly higher mean (SD) SI at rest compared with controls (n = 45): 49.55(12.8) ml/m2 vs 40.01(11.59) ml/m2, p<0.001. There was a significant inverse relationship between SI and Hb (p<0.05) (fig 1). Repeat echocardiography in those with TRV ≥2.5 after a median of 20 months (range 16–27.5) showed no change in pulmonary artery pressure derived using the Bernoulli equation.

**Conclusions** PHT diagnosed using echocardiography is common in children with SCD. However, the inverse relationship between SI and Hb suggests that PHT in children with SCD is due to an anaemia-related increase in cardiac output and not raised PVR. This finding may explain the better prognosis in children with SCD compared with adults. We suggest that PHT due to raised cardiac output should be excluded before trials of specific therapies such as phosphodiesterase type-5 inhibitors are undertaken.
AN EARLY EXERCISE INTERVENTION PREVENTS QUADRICEPS WEAKNESS AFTER THORACOTOMY FOR NON-SMALL CELL LUNG CANCER: RANDOMISED CONTROLLED TRIAL

G Arbane, D Jackson, D Tropman, R Garrod. St George’s University of London, London, UK; St George’s Healthcare NHS Trust, London, UK; King’s College Hospital NHS Foundation Trust, London, UK

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Deterioration in exercise tolerance and impairment in quality of life (QoL) are common consequences of lung resection. This study evaluates additional exercise and strength training after lung resection on QoL, exercise tolerance and muscle strength.

53 (28 male) patients attending thoracotomy for lung cancer, mean age 64 years (range 32–82); mean pack years (SD) 31.9 (26.8); body mass index 25.6 (4.2); forced expiratory volume in 1 s (FEV₁) 2.0 (0.7) litres, were randomised to control (usual care) or intervention (twice daily training plus usual care). After discharge the intervention group received monthly home visits and weekly telephone calls; the control group received monthly telephone calls up to 12 weeks. Assessment preoperatively, 5 days and 12 weeks postoperatively consisted of quadriceps strength using magnetic stimulation, 6 minute walking distance (6MWD) and QoL-EORTC-QLC-C3.

QoL was unchanged over 12 weeks; 6MWD showed significant deterioration at 5 days postoperatively compared with...