

**Abstract P94 Table 1** Change in haematological and respiratory indices with hydroxyurea

	Before Median (Interquartile range)	On Hydroxyurea Median (Interquartile range)	*P value
Hb (g/L)	76 (69.5–86.5)	83 (72.7–87.7)	0.04
HbF (%)	6.1 (3.7–12.9)	8.8 (6–16)	<0.001
Average overnight SpO <sub>2</sub> (%)	93.5 (88–97)	95.2 (93–98)	0.01
Nadir overnight SpO <sub>2</sub> (%)	84 (77.4–89)	87 (83–91)	0.009
3% ODI overnight (events/hour)	3.0 (1.5–5.2)	2.8 (1.1–4.6)	0.08
Mean overnight PCO <sub>2</sub> (kPa)	5.7 (4.7–6.2)	5.5 (5.2–6.0)	0.3
Spot daytime SpO <sub>2</sub> (%)	93.5 (91–97)	96.3 (94–98)	0.001
% FEV <sub>1</sub>	70 (61.5–83.5)	73 (68–88)	0.6

\*P values based on Wilcoxon matched-pairs signed rank test.

**Conclusion** In children with SCD, the use of hydroxyurea was associated with a significant increase in awake and nocturnal baseline oxygen saturation, but no change in intermittent nocturnal desaturation indices or lung function. This preliminary data suggests that improving oxygen saturation may be an important outcome of hydroxyurea therapy with potential benefits in reducing not only vaso-occlusive crises but future respiratory morbidities. This hypothesis would need to be tested by a prospective multicenter trial.

## REFERENCE

- Charache S, Terrin ML, Moore RD, *et al.* Effect of hydroxyurea on the frequency of painful crises in sickle cell anemia. *Investigators of the Multicenter Study of Hydroxyurea in Sickle Cell Anemia. N Engl J Med* 1995;**332**:1317–1322

## P95 GROWTH AND NUTRITION IN ATAXIA TELANGIECTASIA

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10.1136/thoraxjnl-2015-207770.232

**Background** Ataxia telangiectasia (A-T) is a rare multisystem disease with high early mortality from lung disease and cancer. Nutritional failure adversely impacts outcomes in many respiratory diseases. Several factors influence nutrition in children with A-T including catabolism during recurrent infections and inadequate oral intake (fatigue, difficulties with chewing or swallowing, poor appetite, and nausea due to medications). We hypothesised that children with A-T have progressive growth failure.

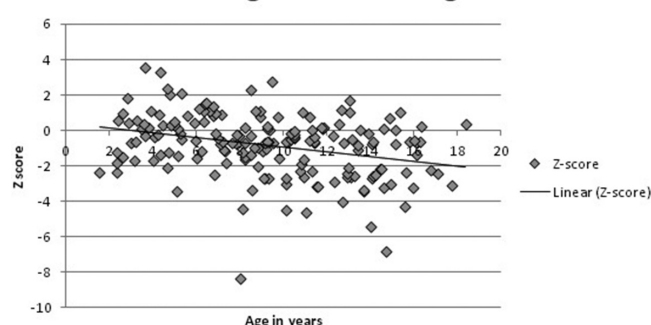
**Methods** Data was collected prospectively on weight, height and body mass index (BMI) at the national paediatric A-T specialist clinic in Nottingham. Adequacy and safety of oral intake was assessed. Nutritional advice was given at each multidisciplinary review.

**Results** 92 children (46 girls) (33 once, 37 twice, 20 thrice, 1 child four times and 1 child 5 times) had 176 measurements since 2009. Median (range) age was 9.2 (1.5 to 18.4) years. Weight, height and BMI Z-scores were respectively -0.84 (-8.34 to 3.58), -0.98 (-5.85 to 3.66) and -0.24 (-4.45 to 2.75). Weight, height and BMI Z-scores inexorably declined over time. 10

children had a gastrostomy, with longitudinal data available for 8. 87.5% of these children improved their BMI Z-score with time. 18.5% (17) children were considered wasted (BMI Z-score  $\leq -2$ ). All of these children were above 8 years old. Longitudinal data was available for 14 wasted children. 6 of these children had a gastrostomy inserted and 5 then improved their Z-score. Of the remaining 8 children without gastrostomy, 7 (87.5%) continued to decrease their BMI over time despite dietary advice to fortify food or add in supplements.

**Conclusions** There is a remorseless decline in growth over time. There is an urgent need for new strategies, including an understanding of why growth falters. Undernutrition adversely affects acute and chronic lung health. Outcomes for late gastrostomy insertion in AT are poor (*Lefton Greif OJRD* 2011;210). We suggest early proactive consideration of gastrostomy from age 8 years upwards in order to prevent respiratory deterioration.

## Weight Z-score vs age



**Abstract P95 Figure 1**

## P96 INTERSTITIAL LUNG DISEASE CAUSED BY STING-ASSOCIATED VASCULOPATHY WITH ONSET IN INFANCY (SAVI)

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10.1136/thoraxjnl-2015-207770.233

**Introduction** An increasing number of monogenic auto-inflammatory conditions known as primary type I interferonopathies are being recognised. We present a case of the newly described condition, stimulator of interferon gene (STING) associated vasculopathy with onset in infancy (SAVI), with significant respiratory involvement.

**Presentation** A male infant, born to healthy non-consanguineous parents, presented to his local hospital with tachypnoea, intermittent fever and failure to thrive from 5 weeks of age. Over the following months, episodes of increased respiratory effort, cough and fever were attributed to infection. He subsequently developed a papular rash in discrete clusters over his back. At presentation to our centre at 7 months of age, he was tachypnoeic but not hypoxaemic. A chest radiograph showed extensive airspace shadowing with chest computed tomography demonstrating interstitial changes. Bronchoalveolar lavage was negative for infection. Laboratory tests revealed microcytic anaemia, raised inflammatory markers, positive anti-nuclear antibody, raised IgA and IgG and abnormal lymphocyte proliferation. A lung biopsy showed a mixed pattern of inflammation, with type 2 pneumocyte hyperplasia and endothelial tuboreticular

inclusions on electron microscopy. Given the combination of interstitial lung disease, skin rash and likely vasculopathy, SAVI was suspected. This was confirmed on genetic testing with a heterozygous somatic mutation (c.463G >A, p. V155M) in exon 5 of the *TMEM173*, the gene encoding STING.

**Treatment** Treatment with pulsed methylprednisolone was commenced without improvement. He gained weight with supplemental feeding but had persistent tachycardia, subsequently becoming hypoxaemic requiring low flow oxygen therapy. He commenced on a trial of monthly intravenous immunoglobulin (IVIg) with evidence of clinical efficacy awaited. We are considering the use of the Janus kinase inhibitor, baricitinib, as a specific targeted therapy to block interferon signalling.

**Conclusion** SAVI is a recently described interferonopathy in which lung involvement is a major clinical feature with consequent significant morbidity and mortality. Twelve patients have been reported so far in the literature, with overall poor response to glucocorticoids and disease modifying anti-rheumatic drugs. In the context of failure to thrive, fevers, rash and interstitial lung disease in early life, we urge clinicians to consider SAVI as a differential diagnosis and to seek testing for *TMEM173* mutations.

**P97 UPTAKE OF THE EMERGENCY SALBUTAMOL INHALER IN NORTH EAST ENGLAND SECONDARY SCHOOLS FOLLOWING AMENDMENT OF THE HUMAN MEDICINES REGULATIONS**

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10.1136/thoraxjnl-2015-207770.234

**Introduction and objectives** As a result of amendments to The Human Medicines Regulations 2012, schools have been permitted since 1<sup>st</sup> October 2014 to purchase salbutamol inhalers to be used by children diagnosed with asthma and prescribed an inhaler, where parents have given written permission for the emergency inhaler to be used. This regulatory change may represent a useful step in facilitating access to emergency asthma treatment in schools.

This study provides the first published data on the number of schools that have availed of this new power, through an assessment of uptake of the emergency salbutamol inhaler in secondary schools in North East England.

**Methods** We compiled a list of all free-to attend schools within the 12 local authorities in North East England using listings on local authority websites. We limited our study to schools which served 16 year old mainstream pupils in order to aid interpretation of our results. Postal letters were sent to invite the included schools to complete a brief online or postal questionnaire asking if the school had an emergency salbutamol inhaler for use by pupils in an asthma emergency. Data was collected between November 2014 and May 2015.

**Results** Of 153 schools included in the study, 103 questionnaire responses were received. We excluded the response of 1 school due to lack of clarity. Of the remaining 102 responses, 45 (44%) indicated that the school had an emergency salbutamol inhaler available, while 57 (56%) indicated that the school did not have such an inhaler. The proportion of schools in which emergency salbutamol inhalers were available varied by local authority from 0% to 71%.

**Conclusions** Despite the change in legislation, 56% of schools included in this study did not possess an emergency salbutamol

inhaler. More needs to be done to increase the level of uptake of the emergency salbutamol inhaler to enable schools to better respond to asthma emergencies.

**P98 THE RELATIONSHIP BETWEEN INVASIVE AND NON-INVASIVE MEASURES OF INFLAMMATION IN CHILDREN WITH SEVERE THERAPY-RESISTANT ASTHMA**

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10.1136/thoraxjnl-2015-207770.235

**Background** Children with severe therapy-resistant asthma (STRA) are refractory to treatment despite optimal management. Assessment of airway inflammation to phenotype these patients can enable targeted therapy. Samples obtained at bronchoscopy provide the most direct measure of lower airway inflammation; however, non-invasive measures (induced sputum and exhaled nitric oxide (FeNO)) are of greater clinical utility. We have previously demonstrated a poor relationship between blood and bronchoalveolar lavage (BAL) eosinophilic phenotype using clinical cut-offs for children (blood eosinophils  $1.0 \times 10^9/L$ ).<sup>1</sup> Recent studies of the anti-IL-5 antibody mepolizumab have used a lower cut point ( $0.3 \times 10^9/L$ ) for blood eosinophils.<sup>2</sup> The aim of this study was to assess the concordance between BAL and non-invasive measures of inflammation.

**Methods** 113 children (aged 4–17 years) with STRA underwent bronchoscopy at the Royal Brompton Hospital. They had all previously been assessed and potentially modifiable factors such as poor adherence had been addressed. Inflammation was measured invasively using BAL cytology and non-invasively by blood eosinophils, induced sputum cytology, and FeNO. The eosinophilic phenotype was defined as BAL eosinophils  $>1.19\%$ ; blood eosinophils  $\geq 0.3 \times 10^9/L$ ; sputum eosinophils  $\geq 2.5\%$ ; and FeNO  $>35$ ppb. The relationship between measures was assessed using Spearman rank correlation and Receiver Operator Characteristic (ROC) curves were constructed to determine which cut points best determined BAL eosinophilia and positive and negative predictive values (PPV and NPV) calculated.

**Results** The predominant phenotype in all samples was eosinophilic. There was 75.6–77.8% concordance between the eosinophilic phenotype in BAL and each of the non-invasive measures.

**Abstract P98 Table 1** The predictive value of peripheral blood eosinophils, sputum eosinophils and FeNO for BAL eosinophilia

	Predicting BAL eosinophilia $>1.19\%$			
	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
<b>Blood eosinophils (<math>\times 10^9/L</math>)</b>				
$>0.15$	89.8	60	84.1	71.4
$\geq 0.3$	80	68	85.2	56.7
$>0.45$	59.3	84	89.7	46.7
<b>Sputum eosinophils, %</b>				
$>0$	90.9	38.5	78.9	62.5
$\geq 2.5$	78.8	61.5	83.9	53.3
$>5$	63.6	69.2	84	42.9
<b>FeNO (ppb)</b>				
$>23$	84.9	62.5	83.3	65.2
$>35$	79.2	75	87.5	62.1

PPV = positive predictive value, NPV = negative predictive value.