### G117 FEASIBILITY OF INTERRUPTER RESISTANCE (Rint) MEASUREMENT IN ACUTE ASTHMA

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**Aims:** Feasibility of measuring interrupter resistance (Rint) in acute asthmatics presenting to the paediatric emergency department and assess its value in assisting clinical decision making.

**Methods:** Clinical parameters were recorded and Rint measurements attempted (Superspiro, Micromedical UK) prior to and 30 minutes after first nebulised bronchodilator (BD). 10 interruptions were performed at both time points. Pressure waveforms were visualised and technically unsatisfactory interruptions were rejected. Rint was expressed as the median of all satisfactory measurements. Decisions regarding admission were made independently by the clinical team, and Rint measurement of children admitted was subsequently compared with those allowed home.

**Results:** 27 children were assessed. Median (range) age was 4.3 years. Rint measurement was successful in 27/27 children pre-BD and 26/27 post-BD: only in 3 children were 10 acceptable interruptions achieved. Measurements were all completed within 2 minutes. The 10 children admitted had a higher (SD) post-bronchodilator Rint (7.8 ± 5.5) compared with 6.9 ± 5.1 for the 17 allowed home. Table shows mean (SD) parameters pre- and post-BD.

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<tr>
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<th>Pre-BD</th>
<th>Post-BD</th>
<th>Change</th>
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<tbody>
<tr>
<td>Resp rate (breaths/min)</td>
<td>42.1 (13.7)</td>
<td>38 (12.5)</td>
<td>4.1 (6.8)</td>
</tr>
<tr>
<td>Heart rate (beats/min)</td>
<td>131 (18.5)</td>
<td>137.6 (23.2)</td>
<td>6.5 (16.5)</td>
</tr>
<tr>
<td>SatO₂ %</td>
<td>94.0 (0.2)</td>
<td>95 (0.02)</td>
<td>12 (0.2)</td>
</tr>
<tr>
<td>Rint (kPa/L/s)</td>
<td>1.03 (0.5)</td>
<td>0.8 (0.4)</td>
<td>0.22 (0.3)</td>
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**Conclusion:** Rint measurement is feasible and rapidly performed in children with acute asthma, with a high rate of technically acceptable pressure waveforms. The technique may have the potential to assist in clinical decision making.

### G118 A CLINICAL ROLE FOR RESISTANCE BY INTERRUPTION (Rint) IN INFANTS?

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**Introduction:** Rint is relatively easy to apply in children, and reference values and bronchodilator response have been studied in that age group. Compared with other infant lung function tests, Rint is simple to perform and does not necessarily require sedation. Published reports of Rint in infants include a total of only 39 subjects. We have examined the feasibility and variability of Rint in sedated and unsedated infants.

**Methods:** 21 sedated wheezy babies (mean age 41 weeks), and 56 healthy unsedated babies were studied (mean age 9 weeks). Raw data were subject to strict quality control criteria before analysis: Rint was estimated using 3 methods, based on polynomial (Rint) and linear (Rint) back extrapolations of pressure, and end oscillation pressure (Rint). Variability was expressed as the within-subject coefficient of variation (CV). Rint was deemed successful if >4 technically acceptable measurements were obtained, and the percentage of the total interruptions deemed acceptable was calculated.

**Results:** Rint (mean [SD]) kPa/L s and CV in Sedated & Unsedated infants: see table. Rint was measured successfully in 85% of sedated infants, 60% of unsedated infants in the laboratory (50% in the home). Acceptability (data quality) was significantly greater in the older, sedated infants (55% v. 35%, unpaired t test p<0.01). There were no significant differences in variability between the two groups.

**Conclusion:** Despite increased success rates in sedated infants, measurements obtained in unsedated infants do not have greater variability. High variability will limit the value of Rint in infancy either to detect abnormality or change after a clinical intervention.

### G119 APOPTOSIS OF LYMPHOCYTES IN RSV BRONCHIOLITIS CAUSES LYMPHOPAENIA


**Respiratory syncytial virus (RSV) bronchiolitis may alter T cell memory responses to other environmental antigens and has recently been shown to cause lymphopenia in acute infection. We hypothesized that during RSV bronchiolitis programmed cell death (apoptosis) of circulating lymphocytes is mediated through the Fas/Fas ligand or TRAIL pathways. Apoptosis involves intracellular proteolytic enzymes, including caspase-1. Caspase-1 also activates IL-18, which up-regulates Fas ligand and has been linked to allergic diseases.**

**Aim:** To examine the evidence for, and mechanism of, lymphocyte apoptosis in acute RSV infection.

**Methods:** Blood was taken from infants during RSV bronchiolitis and at follow up. Lymphocyte Fas and TRAIL receptor were analysed by flow cytometry and plasma Caspase-1 and IL-18 by ELISA. The absolute lymphocyte count and clinical characteristics were recorded.

**Results:** Fas (p<0.001) and TRAIL receptor (p<0.001) cell surface expression was highly up-regulated in acute illness compared with convalescence. Lymphocyte counts were acutely depressed (p=0.01) but recovered. Caspase-1 levels were increased during bronchiolitis (p=0.037) but IL-18 levels remained unchanged.

**Conclusions:** During RSV-induced lymphopenia, circulating lymphocytes are primed for apoptosis. This may be a mechanism through which T cell memory is altered.

**Funded:** 2002 HC Roscoe Fellowship, BMA.

### G120 HOW COMMON IS A THROMBOPHILIC STATE IN CHILDREN WITH CYSTIC FIBROSIS?

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**Aims:** There are some children with CF in whom percutaneous long lines seem to block sooner than expected (due to thrombophlebitis or thrombosis). Also, many CF children have a totally implantable venous access device (TIVAD) and a known complication is thrombosis. This complication is more likely if the child has an underlying thrombotic tendency and this tendency may be present in the presence of inflammatory lung disease. There are no reports of an identified association of heritable thrombophilia with CF, although individual cases have been recognised. The aim was to determine the incidence of thrombophilia in children with CF.

**Methods:** In a tertiary paediatric CF centre, in addition to routine annual review blood testing, blood was screened for thrombophilia in all patients.

**Results:** A thrombotic abnormality was found in 40/198 (20%) patients. These included: activated protein C resistance/factor V Leiden [10/198, 5%], antithrombin deficiency [2/198, 1%], protein C deficiency [8/198, 4%), protein S deficiency [11/198, 6%] and lupus anticoagulant LA [18/198, 9%]. There were no differences found between those with thrombophilia in the following parameters: age, gender, genotyping, lung function (FEV₁), presence of Pseudomonas aeruginosa, prothrombin time, serum IgE, aspergillosis RAST, liver function (AST, γ-GT), blood inflammatory markers (IgG, ESR). 15 children had TIVADs, 4 of whom had evidence of thrombophilia.

**Conclusions:** A significant proportion of patients had a thrombotic abnormality, which was more than the known incidence in the normal population (7% for inherited abnormalities and 1-5% for acquired LA).

We recommend thrombophilia screening is performed prior to insertion of a TIVAD in children with CF. Some centres may prefer to screen their whole CF Clinic population, as there are implications for management of future long lines & any surgery.

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**Abstract G117**

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<tr>
<td>Sedated infants</td>
<td>3.2 (1.9)</td>
<td>2.8 (1.8)</td>
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<tr>
<td>95%CI for Mean CV (%)</td>
<td>11.4-24.1</td>
<td>13.1-27.9</td>
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<td>3.6 (2.3)</td>
<td>3.1 (2.1)</td>
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<td>95%CI for Mean CV (%)</td>
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THE EFFECTS OF INTRAVENOUS TOBRAMYCIN ON PREVALENCE OF SUBNORMAL ADRENAL FUNCTION IN CYSTIC FIBROSIS

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Introduction: Tobramycin is used to treat respiratory exacerbations in cystic fibrosis. It is also a renal tubular toxin. Tubular dysfunction leads to increased urinary levels of the proximal tubal lysosomal enzyme, N-acetyl-beta-D-glucosaminidase (NAG) and the proximal tubular protein, retinol-binding protein (RBP). Hypermagnesaemia and resulting hypomagnesaemia are indicative of more severe tubular damage occasionally seen following repeated courses of IV tobramycin. Using these biochemical markers we studied the effect of a 2-week course of this agent on tubular function.

Methods: 22 children, 11 boys and 11 girls, were studied, median age = 10.9 years, range 3.1–16.4 years. All had a normal predicted glomerular filtration rate (pGFR). They received tobramycin 3mg/kg/dose tds. Urinary NAG, RBP, creatinine and plasma magnesium and creatinine were assayed: a) immediately before commencing tobramycin, b) immediately following the course, and c) 4 weeks after the end of the course.

Results: See table. Using paired t tests the difference in urinary RBP from a) to b) was highly significant, p=0.003, but from a) to c) was not significant, p=0.9. For urinary NAG both results were highly significant, a) to b) p=0.001, a) to c) p=0.005. For all patients plasma magnesium and pGFR remained within normal limits.

Conclusions: Intravenous tobramycin produces acute tubular injury, which shows evidence of partial recovery after 4 weeks. Urinary NAG is a more sensitive marker of tubular dysfunction than urinary RBP. The insult to the tubules was not sufficient to produce hypomagnesaemia in our study group. To assess cumulative tubular damage it would be necessary to repeat this study after further courses of tobramycin.

PREVALENCE OF SUBNORMAL ADRENAL RESPONSES TO LOW DOSE SYNTHETIC ACTH (SYNACTHEN) IN CHILDREN RECEIVING ≥ 500 MCG DAILY OF THE INHALED STEROID FLUTICASONE PROPIONATE (FP)


Background: Inhaled fluticasone propionate (FP) is highly effective for the treatment of chronic asthma. Side-effects of clinical adrenal insufficiency have been reported with doses > 400 mcg daily licensed for the treatment of chronic asthma. Side-effects of clinical adrenal insufficiency can occur with doses of ≥ 500mcg daily. We determined adrenal function in children receiving high dose FP.

Methods: Children attending the Respiratory Clinic and recorded as prescribed FP ≥ 500 mcg daily were identified and invited to attend for detailed assessment including a detailed asthma drug history and a low dose synacthen test (500 gcg/1.73m² intravenously). Adrenal function was assessed as severely impaired, impaired, and normal according to a peak cortisol response of <250, 250 – 499, and ≥ 500 nmol/l.

Results: Of 286 patients recalled, 164 attended for assessment. Full biochemical and clinical data were available in 145 children aged 3-19 years. See table.

No relationship between age, FP dose and peak cortisol level could be identified. One child who developed encephalopathic symptoms during an intercurrent illness had a peak cortisol of 290 nmol/l. Of 9 children actually receiving FP in doses of <400mcg, 4 had peak cortisol levels of 417– 468 nmol/l.

Conclusion: 3% of the children studied had evidence of severe adrenal suppression with impairment in 43%. As no clear relationship could be demonstrated between dose of FP and age all patients receiving doses above the licensed amount should be considered at risk, and appropriate steps taken both to assess the children and to counsel families and GPs about potential adverse effects due to adrenal insufficiency.

THE BURDEN OF PNEUMONIA IN THE UK

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Aims: Little is known of the incidence and cost of childhood pneumonia in the UK. Data are essential to be able to access the burden to children and health service and the impact of new vaccines. This survey aims to establish number, presentation, investigation and treatment of pneumonia in the North East of England [child population; 500 000].

Methods: 1 year prospective survey. 13 hospitals recorded clinical details for all children seen by a paediatrician with signs, symptoms and CXR changes suggestive of infection over 1 year. Clinical bronchiolitis, RSV positive excluded.

Results: 721 children, 57% male, 53% ≤2 yrs, 74% ≤5 yrs. 29% took preadmission antibiotics. At presentation 54% were tachypnoeic, 52% temp>38°C, 19% Sa02 <90. 87% received antibiotics, 70% initially broad spectrum. 84% had at least one investigation, 75% CBC, 50% CXR, 47% blood culture. 87% received antibiotics, 70% initially intravenously, for 2-43 days (mean 3.4). 78% were given oral antibiotics for 1-90 days (mean 7). 11% had >2 l v antibiotics, <2 oral. Most frequent were iv cefuroxime in 42%, oral macrolide in 27%. Oxygen given to 39% for 1-28 days (mean 4), iv fluid to 20% for 1-28 days (mean 3). Peri hilar infiltrates. 84% received antibiotics, 70% initially intravenously, for 2-43 days (mean 3.4). 78% were given oral antibiotics for 1-90 days (mean 7). Average hospital stay was 4 days (median 3, 1-57). A pathogen was found in 25%; 44% bacterial, 11% mixed. Of these 25% RSV, 17% S pneumoniae (S), 15% mycoplasma, 12% Gp A Streptococcus, 10% adenovirus, 8% Influenza A, 6% associated with VZV. 33% with mycoplasma were ≤3 years, 61% S 2≤2 years and 25% RSV >2 years.

Conclusions: This is the largest survey of childhood pneumonia in the UK. Pneumonia has significant morbidity and cost in terms of treatment and hospital stay with 89% presenting to hospital being admitted. Antibiotic use was widely varied.

INCREASED RECOGNITION OF NON-CF BRONCHIECTASIS IN CHILDREN

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Background: Bronchiectasis unrelated to cystic fibrosis (CF) is often perceived to be rare and progressive in children in Western societies.

Aim: To describe the characteristics of 93 children diagnosed with non-CF bronchiectasis, presenting to a Tertiary Paediatric Referral Centre since 1996, and to investigate the diagnostic value of plain chest radiograph (CXR).

Methods: A retrospective case note review was performed. Radiological diagnosis was by high resolution computed tomography (HRCT) scan.
Results: The male : female ratio was 2 : 1. The median ages at diagnosis and symptom onset were 7.2 years (1.6-18.8) and 1.1 years (0-16) respectively. The commonest referral diagnosis was asthma (55%). This was subsequently refuted in 78% of cases. 17 had an immunodeficiency (13 humoral immune deficiencies, 4 chronic granulomatous disease) and 6 were immunosuppressed (5 post heart transplant, 1 acute lymphoblastic leukaemia). Specific antibody responses were measured in 73. 55 had low titres: 89% pneumococcus, 42% *Haemophilus influenzae* and 36% tetanus. 83% had a good response to booster vaccination. *Haemophilus influenzae* was the commonest pathogen (43%), followed by *Streptococcus pneumoniae* (19%). Associations were a previous pneumonic illness (31%), immunocompromise (22%), obliterative bronchiolitis (9%), congenital lung abnormality (4%), chronic aspiration (3%), eosinophilic oesophagitis (2%), familial syndrome (2%), primary ciliary dyskinesia (1%) and right middle lobe syndrome (1%). 8% had more than one associated diagnosis. CXR report agreed exactly with HRCT scan report, for diagnosis and lobe affected, in only 5%. 13% were reported as normal. Resolution of HRCT changes occurred in 4 children following treatment.

Conclusions: Non-CF bronchiectasis may not be as rare as previously thought. CXR is of little diagnostic value. Radiological resolution is possible with appropriate management. The diagnosis is associated most commonly with a previous pneumonic illness. Pneumococcal antibody titres are low in the majority, and there is a good response to booster vaccination. This has implications for childhood immunisation strategies.