Allergy, immunity, and infection, and respiratory joint session

G227 THE CLINICO-EPIDEMIOLOGICAL BURDEN OF INFLUENZA IN INFANTS AND YOUNG CHILDREN IN EAST LONDON, UK

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Objective: Epidemiological studies done in the US have demonstrated high hospitalisation and outpatient rates attributable to influenza in children between 6 and 23 months, rates being comparable to those seen in children with high risk conditions. Based on these results the Advisory Committee on Immunisation Practices has recommended that this age group be immunised against influenza. There are insufficient data on the overall health and economic impact of influenza in European children due to a paucity of epidemiological studies and consequently vaccination is not yet recommended.

Methods: This is a prospective study that recruited children <6 years in the hospital and GP presenting with acute influenza-like illnesses during two winter seasons, 2002/03 and 2003/04. A questionnaire was administered and nasopharyngeal aspirates were sent for viral immunofluorescence and PCR. Influenza incidence rates were stratified by age, clinical diagnoses, and inpatient outpatient status, and rates were also estimated from a predictive clinical diagnosis model.

Results: During the two seasons 977 children were recruited and the influenza A attack rate was 6%. The average influenza A hospitalisation incidence rate was $2.9/10^4$ person-months (95% CI 2.3 to 3.7) whereas the influenza A accident and emergency (A&E) outpatient rate was $30.0/10^4$ person-months (95% CI 27.8 to 32.4). The highest age specific influenza hospitalisation incidence rate was seen in the 12–23 months, $5.2/10^4$ person-months (95% CI 3.2 to 8.0) and the highest age specific influenza A&E outpatient incidence rate was in the 6 to 11 months, $68.0/10^4$ person-months (95% CI 50.9 to 80.7). The estimated influenza incidence in children <6 years presenting to the GP was $13.9/10^4$ person-months (95% CI 7.9 to 22.3). An influenza predictive model based was generated from the first season's data and consisted of five variables: upper respiratory tract infection (URTI), tonsillitis, pneumonia, and the incidence of otitis media and febrile illnesses. There was a relatively good fit of the model for the data collected in the second seasons PPV 19–40% and NPV 94–99%. The estimated influenza incidence rates were $25.8/10^4$ person-months (95% CI 23.1 to 28.8) and $26.2/10^4$ person-months (95% CI 23.1 to 29.6) in the 2002/03 and 2003/04 seasons, respectively. Influenza rates were highest in children presenting with pharyngotonsillitis, febrile seizures, otitis media, and URTI.

Conclusion: Influenza in children generates hospitalisations, AE and GP visits in the UK, and even during low intensity, transmission seasons. Children between 6–23 months had the highest influenza rates. The highest influenza positivity was in those with pharyngotonsillitis. The predictive model had a good fit for the 2003/04 season and can be used to estimate influenza rates in children as under reporting is inevitable. These findings can be used to inform influenza immunisation policy in the UK.

G228 VORICONAZOLE THERAPY IN CHILDREN WITH CYSTIC FIBROSIS

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Background: There is increasing evidence for the efficacy of the antifungal voriconazole, particularly in immunosuppressed adults and children. We have noted significant improvements in two children with cystic fibrosis and recurrent allergic bronchopulmonary aspergillosis (ABPA) in response to voriconazole monotherapy. We describe these cases in the context of our wider experience of voriconazole in children with cystic fibrosis with and without ABPA.

Methods: We performed a retrospective case note review of all children with cystic fibrosis treated with voriconazole in a single tertiary paediatric centre over an 18 month period.

Results: A total of 21 children aged 5 to 16 years (median 11.3) received voriconazole for between 1 and 50 (22) weeks. Voriconazole was used in two children with recurrent ABPA and a history of previous steroid treatment as monotherapy; significant, and sustained improvements in clinical and serological parameters for up to 13 months were observed, without recourse to further oral steroids. Voriconazole was used in combination with an immunomodulatory agent (oral corticosteroids in nine, methotrexate in one case, and intravenous immunoglobulin in another) in a further 11 children with ABPA, with significant improvement in pulmonary function and serology. Eight children who did not meet the criteria for ABPA but had recurrent *Aspergillus fumigatus* isolates and an increase in symptoms also received voriconazole; children in this group did not an improve with treatment. Adverse effects occurred in seven children (33%: photosensitivity reaction three, nausea two, rise in hepatic enzymes one, hair loss one).

Conclusions: Voriconazole may be a useful adjunctive therapy for ABPA in cystic fibrosis. Voriconazole monotherapy appears to be an alternative treatment strategy when oral corticosteroids may not be suitable.

G229 DIAGNOSIS OF SEROTYPE 1 PNEUMOCOCCAL EMPYEMA IN CHILDREN BY ANTIGEN DETECTION: IMPLICATIONS FOR PRIMARY PREVENTION

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Background: The number of children presenting locally with empyema increased from 10 to 31 per year from 2002–03 to 2003–04. No internal system, service delivery, or referral changes explained this increase.

Aim: To identify the pneumococcal serotypes responsible for cases of empyema in children and explore other explanatory factors.

Methods: For 12 months from September 2003, all empyema cases were prospectively ascertained in our secondary/tertiary paediatric centre. All cases were confirmed by CXR and ultrasound examination, and were attributable to community acquired infection in otherwise well children. Informed signed consent (as approved by L/MREC) was obtained to record clinical details and analyse empyema fluid/pus for evidence of pneumococcal infection. Parents were also interviewed to ascertain recent antibiotic use. Empyema fluid samples were subjected to pneumococcal capsular polysaccharide antigen ELISA (PCPE) for 13 common serotypes and C polysaccharide antigen ELISA (CPE) analysis.

Results: Thirty four children were recruited to the study, 28 transferred from their local hospitals for surgical review (median age 6.3 years, range 0.8–14.8, 12 girls). Of the 34 cases, 21 were culture negative (pleural fluid and blood), presumably reflecting the duration of antibiotic therapy prior to chest aspiration. Despite this, of 29 pleural fluid samples available, 27 were positive for pneumococcus on antigen testing, with serotypes being identified in 26. Serotype 1 predominated (18 cases), other identified serotypes being 7F, 3, 4, 9V, and 23F. Of the three PCPE-negative cases, one was CPE positive, suggesting pneumococcal infection with a serotype not in the PCPE ELISA panel and two had positive pleural fluid cultures for Gp A streptococcus. In five children where no pleural fluid was available for ELISA analysis, two had positive non-pneumococcal pleural fluid cultures, one Gram-positive cocci (culture negative) in pleural fluid and all investigations were negative in two. Eighteen of 34 children had received no antibiotics prior to hospital admission and the delay between onset of illness and antibiotic treatment ranged from 0 to 51 days (median 5 days). Time between commencing antibiotics and first pleural fluid sampling ranged from 0 to 14 days.

Conclusions: Pneumococcal antigen analysis of empyema fluid may provide a definitive diagnosis where routine testing has failed, even after significant antibiotic therapy. The relation between antibiotic prescribing and incidence on childhood empyema requires further investigation. Immunisation with a higher valency pneumococcal conjugate vaccine (which includes serotype 1), rather than the 7 valent, would be needed effectively to reduce the morbidity reported here.

G230 A RANDOMISED CONTROLLED EQUIVALENCE TRIAL TO COMPARE ORAL AND INTRAVENOUS TREATMENT AND THE DIRECT AND INDIRECT COSTS OF TREATING CHILDREN WITH COMMUNITY ACQUIRED PNEUMONIA: PIVOT TRIAL

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Background: Pneumonia affects 2.5 million children each year in Europe. At 1992/93 prices £440.7 million was spent treating 261 000 annual episodes of community acquired pneumonia (CAP) in the UK (adults and children). Currently, most UK children who require admission to hospital with community acquired pneumonia are treated with intravenous antibiotics. There have been no RCTs to compare oral and intravenous treatment.

Hypotheses: Oral treatment is as effective as intravenous treatment for children 6 months to 16 years with community acquired pneumonia; and the cost of treating children with community acquired pneumonia with oral antibiotics will be less than treatment with intravenous antibiotics.

Method: A multicentre randomised but non-blinded equivalence trial of oral amoxicillin and intravenous benzylpenicillin. Inclusion criteria: respiratory symptoms or signs, temperature of 37.5 degrees or above, and a radiological diagnosis of pneumonia. The primary outcome measure was time from randomisation until the temperature had been <38 degrees for 24 continuous hours and oxygen requirement had ceased. The direct costs of treating a child with pneumonia included the cost of any health contacts in the week prior to admission, cost of inpatient stay, investigations and treatment, and cost of any further health contacts following discharge until the child made a full recovery. Indirect and parental costs included: time off work with loss of earnings, travel to and from hospital, and expenditure whilet in hospital. For an 80% powered study 196 children were needed in total.

Results: 252 children were randomised (126 to oral and 120 to intravenous). Median time for the temperature to be <38 degrees for 24 hours in the intravenous group and oral groups, respectively, was 1.31 and 1.34 days, (p 0.0013). Median length of stay in hospital was 2.1 and 1.77 days in the intravenous and oral groups, respectively ($p<0.001$). The mean total cost to the NHS of treating a child with pneumonia was £1394.56 in the intravenous group and £1014.95 in the oral group ($p<0.001$). The mean cost to the families was £176.86 and £136.87 in the intravenous and oral groups, respectively (p 0.221).

Conclusion: Oral amoxicillin and intravenous benzyl penicillin have been shown to be equivalent for treatment of community acquired pneumonia. The direct costs of treatment with oral antibiotics are significantly less than treatment with intravnous antibiotics. Costs to the parents were less in the oral group although this difference was not significant. In the future it is expected that the majority of children with pneumonia will be treated with oral antibiotics. It is anticipated that most children will spend a shorter period in hospital. There will be major cost savings to both the NHS and family.

G231 SERVICE PROVISION FOR CHILDHOOD TUBERCULOSIS OUTSIDE GREATER LONDON

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Aim: We aimed to determine the provision of services for children with tuberculosis (TB) living in the UK, outside of London. This follows a similar study carried out in London.

Method: We sent a postal questionnaire to the most appropriate paediatrician and adult physician in every acute hospital trust in the UK outside Greater London. If there was no reply after an appropriate delay, a further questionnaire was sent. We asked about inpatient and outpatient services for children with TB and for children in contact with TB.

Results: Responses were received from 268 individuals working in 173 of the 179 trusts approached. In 55% of trusts, responses were received from both physicians and paediatricians, in a further 35% from only paediatricians, and solely from physicians in 10% of trusts. The median number of children with TB seen per year at each trust was said to be 1.5 (range 0–30). All children with TB were admitted to paediatric wards (159 general wards) and in 138 trusts (79%) were looked after by paediatricians. In 47 trusts, care was shared between physicians and paediatricians. This was a formal arrangement in only 20 (43%) of these trusts. 112 (65%) trusts stated there was a named consultant for children with TB. Negative pressure isolation rooms were said to be available in 37 trusts (21%). As outpatients, children with TB were seen in paediatric clinics in 151 trusts (87%). In 20 trusts (12%) they were seen in both paediatric and adult clinics. Only seven trusts had designated family TB clinics. Children in contact with TB were managed by paediatricians in 65 trusts (38%) and by physicians in 59 trusts (34%). In a further 46 trusts, contacts were managed by both, while respondents from three trusts were not aware of arrangements for contact management.144 (83%) trusts had access to a TB nurse, to help with management of cases and contacts. Directly observed therapy could be provided by 94 (54%) trusts.

Conclusions: Many areas outside London see few children with TB, thus gaining little experience of disease management. Yet only 65% had a named consultant for children with TB. Most children with TB outside London are admitted to general paediatric wards and looked after by general paediatricians. Few trusts have negative pressure rooms for children, with serious implications in the light of increasing multi-drug resistant TB. Few children are seen in family clinics and in one third of trusts, childhood TB contacts are managed by adult physicians. Our study has found even more widely disparate models of care for children with TB, than those in the initial survey in London. The development of clinical service networks for children with TB outside London may improve the care of these children.

G232 COMPARISON OF COUGH PLATES WITH COUGH SWABS FOR IDENTIFYING LOWER RESPIRATORY TRACT PATHOGENS IN CHILDREN WITH CYSTIC FIBROSIS

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Background: Accurate identification of lower respiratory pathogens is vital in cystic fibrosis as early aggressive treatment can delay progression of lung disease. Sputum is reliable but few children under10 years can expectorate. Broncho alveolar lavage is invasive and cannot be recommended for regular screening. Cough swabs are used routinely but a negative result does not rule out the presence of pathogens.

Aim: We evaluated the use of cough plates incorporating selective media as an alternative method for obtaining lower respiratory samples from cystic fibrosis patients.

Methods: A randomised prospective study of respiratory sample collection was undertaken in 111 children above 3 years of age. Four specimens were collected: a cough swab and three cough plates incorporating separate selective media-blood agar, Haem agar, and *B cepacia* specific agar. Cough swabs were subsequently plated on the same selective media.

Results: There were 22 positive isolations of organisms on cough plates compared with only seven on cough swabs. More importantly, cough plates identified *Pseudomonas aeruginosa* on 15/17 occasions whereas cough swabs did so only on 3/17 occasions (these three were identified by cough plates also) *B cepacia* and *H influenzae* were identified only on cepacia plate and haem plate, respectively, but were missed by cough swabs. Cough swabs identified two *S aureus* and one Aspergillus that were not identified by cough plates. The McNemar test showed significantly better sensitivities for cough plates over cough swabs in isolating microorganisms.

Conclusions: Our study shows that cough plates are superior to cough swabs in identifying lower respiratory tract pathogens in younger, non-sputum producing patients. Use of selective media in cough plates enhanced isolation rates of *P aeruginosa* and *B cepacia*. Most of our patients preferred cough plates over cough swabs for specimen collection.

1. **Maiya S**, Desai M, Baruah A, *et al. Arch Dis Child* **89**:577–9.
2. **Armstrong DS**, Grimwwod K, Carlin JB. *Paediatr Pulmonol* 1996;**21**:265–6.
3. **Rosenfeld M**, Emerson J. *Paediatr Pulmonol* 1999;**28**:321–8.

G233 COMPLICATIONS ASSOCIATED WITH THE BACILLE CALMETTE GUERIN VACCINATION IN IRELAND

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Background: Bacille Calmette Guerin (BCG), a live attenuated *Mycobacterium bovis* vaccination, has been provided in Ireland since

1937. It is currently recommended for all newborns except where specifically contraindicated.

Aim: We report the marked increase in the number of referrals of patients with localised complications to two Dublin paediatric hospitals. This report details complications incurred by children inoculated in the two years following the introduction of the new SSI strain of vaccine in July 2002.

Results: In the 2 year period 56 patients with regional BCG complications were identified; 29 with suppurative adenitis, 20 with inoculation site abscess, an additional three patients with both inoculation site abscess and suppurative adenitis, and four with non-suppurative adenopathy. Significantly, 26 infants required surgery; three of whom required more than one procedure. The remaining infants were managed conservatively and are well. *Mycobacterium tuberculosis* complex was isolated from 12 of 23 patients sampled. 4/11 isolates were resistant to INH. This report includes 32 cases of suppurative lymphadenitis giving an estimated rate of one case per 1687 vaccinees and an overall complication rate of 1/964.

Conclusion: This series highlights the importance both of strengthening the existing systems of adverse event reporting and it raises a serious question as to the suitability of this strain for use in a national immunisation programme in a country where the prevalence of tuberculous disease has declined to <10/100 000. Also very concerning is the presence of INH resistance, which would seriously limit therapeutic options for disseminated disease in susceptible infants.

G234 A PILOT STUDY INVESTIGATING THE DEVELOPMENT OF MUCOSAL IMMUNE FUNCTION IN THE PRETERM INFANT

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Background: The very low birth weight infant (VLBW) has the capacity to synthesise immune factors necessary to mount an efficient response to infection, yet sepsis remains a major cause of morbidity and mortality. The gut mucosa is an important portal of entry for bacteria yet little is known of the function or development of the mucosal immune system in the preterm infant. The principle effector of the specific immunity against intraluminal bacteria is immunoglobulin A (IgA).

Aim: To measure the development of mucosal immune function in the VLBW infant by determination of total immunoglobulin A (IgA) and secretory immunoglobulin A (SIgA) in saliva and faeces.

Methods: Eleven VLBW infants (mean gestation 27 weeks) and 10 healthy new born controls (mean gestation 39 weeks) were studied. Saliva and faeces were obtained at 1, 3, 6, and 9 weeks of age in the VLBW infants and at 1 and 6 weeks in the term controls. SIgA and IgA were measured by radial immunodiffusion.

Results: SIgA and IgA can be detected in the saliva of only 9% of VLBW infants at one week of age compared with 70% of the term controls. Concentrations of SIgA and IgA in saliva are strongly correlated with age and rise over the first few weeks of life. At six weeks of age SIgA is detected in 81% and IgA in 73% of the VLBW infants at concentrations comparable with those of the term infant. No significant difference exists between the concentrations of faecal SIgA and IgA in the term and preterm infants; however, problems with sample collection and storage existed.

Conclusion: Salivary SIgA and IgA can be detected in only 9% of VLBW infants at one week of age, the levels rise to become comparable with the healthy term infant by six weeks of age. It may be possible to use salivary SIgA and IgA as a measure of mucosal immune function in the VLBW infant and thereby evaluate future therapeutic options.

G235 CHANGES IN ANTIBIOTIC PRESCRIBING IN GENERAL PRACTICE AND HOSPITAL ADMISSIONS FOR QUINSY, MASTOIDITIS, AND RHEUMATIC FEVER IN CHILDREN

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Aim: To estimate whether the change in antibiotic prescribing to children in the UK we have previously reported has led to change in the incidence of complications from bacterial infection of the upper respiratory tract.

Design: Observational comparison of time trends 1993–2002/3.

Method: Data on antibiotic prescribing to children by general practitioners were obtained from the Prescription Pricing Authority, England and the IMS Disease Analyzer - Mediplus UK database. Data on hospital admissions of children for quinsy, rheumatic fever, mastoiditis, and simple mastoidectomy were obtained from Hospital Episode Statistics (HES) data for England. Data on general practice consultations for mastoiditis and hospital referrals involving mastoiditis or mastoidectomy were purchased from the Medicines and Healthcare products Regulatory Authority (MHRA) General Practice Research Database.

Main Results: Between 1993 and 2003 general practice prescribing of antibiotics to children fell by 37% while the number of prescriptions taken by parents to pharmacists fell by 47%. As previously noted, most of the fall in prescribing by general practitioners (34%) occurred between 1996 and 1999. There has been little change in hospital admission rates for quinsy or rheumatic fever but a sharp rise in hospital admissions for mastoiditis or simple mastoidectomy (from 6.9/100 000 children aged 0–14 in 1993 to 8.2/100 000 in 2002) coincident with the fall in prescribing. This increase is restricted to children age 0–4 years and is not reflected in the general practice morbidity data.

Conclusion: Antibiotic use by children has halved in the past decade due initially to a sharp reduction in prescribing by general practitioners and latterly to a reduction in the proportion of prescriptions taken by parents to a pharmacist, consistent with ''delayed prescribing''. This reduction has been associated with an increase of about 120 additional admissions for mastoiditis or simple mastoidectomy in England annually. The possibility that this association is causal must be set beside the estimate that between 2500 and 5000 children would need to be treated with antibiotics to prevent each case.