IMMUNOLOGY AND INFECTIOUS DISEASES

G180 | NEUTROPHILS OF STRESSED AND HEALTHY NEONATES ARE MORE SENSITIVE TO STIMULATION THAN ADULT NEUTROPHILS

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Introduction: Neonatal neutrophils are thought to be deficient compared to adult, especially at times of stress. To investigate sensitivity of respiratory burst to stimulation neutrophils from adults, healthy neonates (HN) and stressed neonates (SN) were stimulated with serially increasing concentrations of PMA. Changes in respiratory burst production and cell size were also recorded.

Method: A whole blood technique of flow cytometry was used to determine respiratory burst. Adult (n=10), HN (n=10) (median gestation age = 35wk (8d)) and SN (n=6) (median gestation age =27wk (19d)) samples were tested simultaneously. Changes in side scatter and forward scatter properties of the neutrophil populations were recorded as measures of granularity and cell size, respectively.

Results: Median fluorescence (milli-equivalents of fluorescence) following maximum stimulation were adult=16.4, HN=63 (p<0.01), SN=99.7 (p<0.01). Resting fluorescence (without stimulation) of each population were not significantly different. Regression coefficients (slope, b) of fluorescence for increasing and, but those that were sens (p<0.001), and SN=1.19 (p<0.001). Both neonatal lines of regression were significantly different from adult (P<0.01). Granule production and discharge, as judged by granularity and size of the cell populations, occurred at lower concentrations of stimulus for the adult cells.

Conclusion: By these measures neonatal neutrophils are more sensitive to stimulation with PMA than adult. This study’s findings are contrary to reports that neutrophils from stressed neonates are less efficient than healthy neonatal or adult neutrophils.

G181 | PROSPECTIVE STUDY OF THE PREVALENCE OF LATEX ALLERGY IN CHILDREN REFERRED TO A SUPRAREGIONAL SURGICAL CENTRE


Background: The prevalence of latex allergy is highest in children who have multiple operations, with rates of 60% reported in children with spina bifida and urogenital malformations. No prospective studies of the prevalence of latex sensitisation in children have been undertaken in Britain.

Method: We investigated the prevalence of latex allergy and sensitisation in children due for surgery at Great Ormond Street Hospital using a questionnaire based on the ISAAC questionnaire. Total IgE and latex-specific IgE were measured with the Unicap system.

Results: 255 subjects, 160 males. 127 (49.8%) gave a history of atopic disease. Median current age was 47 months and median number of operations was 4. Fifty subjects (20%) had >6 previous operations. Seventy-seven subjects had total IgE above normal for their age (35 with atopic history, 42 without). Two subjects gave a convincing positive history of reactions to latex. Both had raised latex-specific IgE, giving a prevalence of latex allergy in this paediatric surgical population of 0.8%. Four of the seven subjects had raised latex-specific IgE but had not reported clinical reactions to latex. The prevalence of asymptomatic latex sensitisation is 1.6%. The combined prevalence of latex allergy and latex sensitisation is 2.4%. Five of the six subjects with raised latex IgE had a clinical diagnosis at first presentation that would have predicted multiple surgical procedures. The prevalence of latex allergy or latex sensitisation in subjects with >5 previous operations is 5/50 (10%). Comparing the 6 latex allergic or sensitised subjects with the total group of 255, they were older (median age 12.75 years, p=0.007), and had more operations (median 16, p=0.022).

Conclusions: Latex allergy affects 0.8% of the highly selected population studied here. The prevalence of latex allergy or sensitisation is 2.4%. A policy to minimise latex sensitisation of children needs to be developed.

G182 | DEVELOPMENT OF IMMUNE TOLERANCE IN PEANUT ALLERGY

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Many children have been unnecessarily prescribed self-injectable adrenaline for peanut allergy previously considered to be life long. Little is known of the development of immune tolerance to peanut antigens. This study aimed to seek evidence of immune tolerance by direct challenge in peanut allergic children over 5 years of age. 13 children were selected, all had their first reaction at < 4yrs. All were carrying adrenaline although none had used it. None had had an anaphylactic reaction but symptoms varied from tingling of the tongue with swollen lips, to facial swelling and wheeze.

Under close in-patient medical supervision and with an I.V cannula in situ, a skin prick test was performed followed by a staged oral challenge with peanut butter.

5/13 children had no reaction on skin prick testing, 3/13 had a weal of < 6mm², 5/13 > 64mm². Of these, 12 were challenged orally, 7/12 had a negative result and were able to discontinue carrying adrenaline.

In this group of selected children with relatively mild reactions, no evidence of anaphylaxis and whose reactions had been at a relatively early age, 54% appeared to have developed immune tolerance. All children that had a succesful challenge, had a weal size of <6mm² These children were able to discontinue carrying their adrenaline. No child had a severe reaction during the oral challenge.

G183 | LIVER DISEASE IN CHILDREN WITH HYPER IGM SYNDROME

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Hyper IgM syndrome is an immunodeficiency caused in most cases by an X-linked deficiency of CD40 ligand (CD40L) expression. The patients have life-threatening infections in infancy, may become colonised with Cryptosporidium parvum (Cp) and develop scarring cholangitis (SC). To determine liver involvement and outcome of patients with hyper IgM syndrome, we reviewed retrospectively 20 children (all boys), from 16 families, referred to us between 1990-99. Seventeen had CD40L deficiency confirmed by genetic studies. Patients were assessed by liver function tests (LFTs) (20), ultrasound scan (US) (20), liver biopsy (19), ERCP (17) and Cp screening by microscopy and PCR in the stools (17) and bile (7). SC was diagnosed in 9 patients (45%) based on ERCP and histology (5), ERCP (3), and histology (1). Five children had severe, 1 mild and 2 minor radiological changes. US was abnormal in 6/9 (67%) patients with SC. Of the 13 (65%) with normal LFTs, 2 had minor and 2 mild cholangiopathy. All children with persistently abnormal LFTs (5) (median AST 117 IU/l, range: 77-142; GGT 182 IU/l, range: 128-299) had abnormal US, liver biopsy and ERCP. 17 bile and 5/17 stool specimens tested were C. positive. For C. positive patients have SC. Four patients had bone marrow transplant (BMT) [1 non-myeloablative (nm) and 1 combined liver transplant (LT) and nm-BMT, Two boys died of disseminated Cp, 1 after conventional BMT and urgent LT for liver failure, the other after re-LT. The boy, Cp negative, who had combined LT and nm-BMT has normal immune and liver function 1 year later. In conclusion, children with hyper IgM syndrome and persistently abnormal LFTs have established cholangiopathy. If colonised with C. their outcome after BMT and LT is uncertain. BMT should be considered before severe liver damage. Combined LT and nm-BMT should be attempted in advanced liver disease.

G184 | DETECTION OF LIVER KIDNEY MICROSOMAL TYPE 1 ANTIBODY USING MOLECULARLY BASED IMMUNOASSAYS

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Liver kidney microsomal antibody type 1 (LKM1), the hallmark of autoimmune hepatitis type 2 (AHI2) is often mistaken for anticholinergic antibody when it is detected by the conventional technique of immunofluorescence ([IFL] Gastroenterology 1992; 103: 1290). LKM1 is also found in up to 10% of patients with chronic HCV infection, where its presence may be associated with serious side effects during interferon treatment (Gut 1999; 45: 440-441). The molecular target of LKM1 has been identified as cytochrome P450 2D6 (CYP2D6) enabling development of immunoassays detecting anti-CYP2D6 antibodies. Using IFL as reference, we measured anti-CYP2D6 with an in-house ELISA (J Immunol Meth 1999; 223:227) and 2 new commercial immunoassays (Varelisa and MLB) in 31 patients with AHI2 - all positive at diagnosis for LKM1 - obtained at different stages of its disease. Controls were 29 patients with AIH1, 8 with >1 antithrysin deficiency, 8 with Apllela’s syndrome, and 10 healthy children. Twenty nine of the 31 sera from AIH2 were positive by IFL and by the in-house ELISA, 28 by Varelisa and by MLB. All 53 sera by IFL were negative by the in-house ELISA and Varelisa, while 11 marginally exceeded the upper limit of normal indicated by the manufacturers for the MLB assay, though their absorbance values were significantly lower than those of the positive. Kappa values for the in-house ELISA, the Varelisa and the MLB when compared with IFL were 0.95, 0.87 and 0.76, respectively, indicating a high degree of concordance. We concluded that the two available commercial immunoassays are reliable for the measure of LKM1. Their use should abolish one of the most frequent errors of the immunodiagnostic laboratory.
Adenose Deaminase (ADA) deficiency is an inherited disorder that results in abnormalities of the immune system leading to severe combined immunodeficiency (SCID). In severely affected patients, death occurs in the first year of life. Successful immunological correction is now available for ADA-SCID patients by bone marrow transplantation (BMT). However, immunological dysfunction remains even after BMT, notably psychological and behavioural abnormalities have been observed, though not previously investigated in a controlled manner.

Independent matched pairs were drawn from the outpatient population of Great Ormond Street Hospital. Eleven pairs of ADA-SCID patients and non-ADA-SCID transplanted patients were matched for gender, age, age at transplant and type of transplant. Psychological assessment and psychometric tests were administered to evaluate and document the behavioural, psychological and neuro-development functioning in ADA-SCID patients after BMT.

Results indicate the ADA-SCID group functioning in the abnormal/pathological range on all measured socio-behavioural domains; mean behavioural scores for the control group were all within normal limits. Paired T-tests indicated significant differences (p<0.05), with large effect sizes, in the domains of social behaviour and hyperactivity and large differences across other behavioural domains (involving cognitive ability (below average for both groups) and educational attainment were not different between the ADA-SCIDs and controls.

These findings suggest that ADA-SCID patients experience significant behavioural difficulties even after treatment and this may reflect the natural history of the condition now that survival is assured through BMT. Further assessment of other UK and European ADA deficient children is planned.

UK EXPERIENCE OF BONE MARROW TRANSPLANTATION FOR CD40 LIGAND DEFICIENCY

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CD40 Ligand deficiency (CD40LD) is an X linked disorder of primary immunodeficiency resulting in failure of immunoglobulin isotype switching as well as susceptibility to intracellular pathogens including Cryptosporidium parvum (CP) infection. European data shows only 20% survival of affected boys beyond the age of 25 years. Liver disease, including sclerosing cholangitis which may be CP associated, is a major determinant of mortality. Attempted cure by BMT was performed in 11 boys of median age 10 years (range 3-18) in two UK centres. Matched sibling donors were used in 4, fully matched donor in 3 and one antigen mismatched unrelated donor in 4. Conditioned regimens were Busulphan/Cyclophosphamide (7), total body irradiation / cyclophosphamide (1) or a non myeloablative regimen (Fludarabine / Melphalan) in 3. Six had sclerosing cholangitis including one with 2 chronic pancreatitis. 4 had known previous or current cryptosporidial infection. One patient underwent elective liver transplant prior to BMT.

Five patients with pre-existing liver disease died: three from progressive cryptosporidial infection and liver inflammation, one from GVHD and disseminated adenosivus infection and one from severe GVHD. Six patients are alive and well with normal immune function including 4 with no pre-existing liver disease and 2 with liver disease who received the non myeloablative regimen (follow up 5-30 months).

Younger, absence of cryptosporidial and normal liver histology was associated with better outcome. Non myeloablative conditioning regimen may be associated with a better outcome in the higher risk patients.

MANAGEMENT OF A HOSPITAL OUTBREAK OF INVASIVE ASPERGILLOSIS IN IMMUNOCOMPRIMED AND ICOE PATEINTS ASSOCIATED WITH INCREASED ENVIRONMENTAL EXPOSURE


Aspergillus is an ubiquitous environmental organism, only causing significant disease in immunocompromised or sick patients. Mortality from invasive aspergillosis (IA) ranges from 30% in AIDS patients to over 90% in neutropenic BMT patients. Increasing rates of increasing due to increases in transplantation programmes, aggressive chemotherapy regimens and HIV disease. A source of infection is often not identified, and many cases may result from activation of endogenous colonisation. Prevention of cases relies on identification of at-risk patients, adoption of prophylaxis in at-risk patients, adoption of prophylaxis in at-risk patients, adoption of prophylaxis in at-risk patients.

We report a cluster of 7 cases of proven and suspected IA, fatal in 37/43% (37/43%) where increased exposure to building dust from a large-scale on-site demolition project may have been a significant factor. The first patient was admitted with meningococcal septicaemia, development bowel perforation due to Aspergillus fumigatus and died. A second case of IA in an adult PBLT autograft patient was diagnosed 2 weeks later. A multi-disciplinary infection control team advised stopping demolition after identification of case of 2, further cases of definite and probable IA (1 PICU patient, 1 allogeneic BMT (died), 1 PBSC autograft patient and 2 oncology patients receiving chemotherapy) were subsequently diagnosed. Heiner aspergillus contamination was found in all ward areas and air conditioning systems sampled, except cubicles with HEPA filtration or laminar air flow. Additional measures to interrupt spine transmission included sealing windows and ducts, increased cleaning, partitioning of internal building work and removal of plants and flowers from clinical areas. Positive pressure HEPA filtration ventilation was installed in additional key areas. Surveillance using air sampling techniques demonstrated a reduction in IA cases after these actions. Evidence for an environmental source of aspergillus included historically low rates of IA (1 in the previous year), temporal clustering of cases and lack of further cases after demolition ceased. Further demolition is due to start after these measures are in place. Environmental and clinical monitoring will continue.

DETECTION OF CRYPTOSPORIDIUM BY POLYMERASE CHAIN REACTION (PCR) IN PATIENTS WITH PRIMARY IMMUNODEFICIENCIES

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Cryptosporidium parvum (CP) is associated with chronic infection of the biliary tree leading to sclerosing cholangitis in patients with immunodeficiency disorders. The conventional method of diagnosis involves microscopic detection of oocysts. It is possible that asymptomatic carriage of Cp occurs below the limits of detection of these tests. This study set out to assess the role of PCR in the detection of Cp gene sequences in patients with primary immunodeficiencies.

Samples (n=28) from 15 children with CD40 ligand deficiency (6); unspecified combined immunodeficiency (7); MHC Class II deficiency (1) and interferon-g receptor deficiency (1) were examined by light microscopy (following staining by modified Ziehl Neelsen and immunofluorescence) and by using three different PCR procedures: one for cryptosporidium outer wall protein gene (COOP) and two different 18S RNA sequences. Samples included: 14 stool, 8 bile, 5 liver tissue and 1 urine. Four samples only (from 2 patients) were collected during episodes of diarrhoea . The urine and all liver samples were negative by all tests. Cp was detected in 2/14 stools (both collected during diarrhoeal episodes) by both microscopy methods and by all three PCR procedures. All other samples were negative by microscopy, but one of the 18S RNA sequences was detected in one further stool and one bile sample. COOP gene sequences were detected in a further 5 stools (including the additional one positive by 18S RNA PCR) and in 2 bile samples.

Detection of Cp nucleic acid by PCR is more sensitive than microscopy when applied to asymptomatic children with primary immunodeficiencies. Detection of Cp fragments was the most sensitive method used here.

STUDIES ON THE VACCINE CANDIDATE OF INNER CORE LIPOLYSACCHARIDE (LPS) IN NEISSERIA MENINGITIS (NM) GROUP B

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Aims: To identify conserved, accessible and potentially cross-reactive Nm serogroup B LPS epitopes that may be potential vaccine candidates.

Methods: Previously we described an inner core LPS epitope that was accessible and conserved in 70% of a global collection of 100 Nm strains representative of all major groups [Plessed et al., 1999 IAI 67. 5417-5426]. The conserved epitope recognised by monoconal antibody (mab) B5 was identified in all Nm lipopolysaccharides with phosphothreonamine (PEth) in the 3-position of β-chain heptose (Hepl) of inner core LPS. Murine mabs to immunotype L4 (PEth in 6/7 position) obtained using formalin-fixed Nm L4 gaiE whole cells were screened by ELISA against purified LPS from Nm mutant and wild-type strains. Conservation and accessibility was assessed by: (1) dot blots of whole-cell lysates of Nm; (2) immunofluorescence microscopy.

Results: One of the mabs, A4 (IgG2a), demonstrated specificity for both L4 gaiE and L2 gaiE LPS and recognised all except 3 Nm mab B5- strains. Together mabs B5 and A4 recognised 37/100 Nm strains. Mab A4 accesses the inner core epitope in the L4 gaiE mutant in the presence of capsule.

Conclusion: Inner core glycoforms have been identified with PeN in either (i) 3- position of Hepl (mab B5), (ii) 6/-7 position of Hepl (mab A4) or (iii) absent. These studies of epitope that strains of Nm may possess at least 3 inner core epitopes, findings that support the feasibility that inner core LPS may have potential as a Nm Group B vaccine.

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G190 | OPTIMISING INVESTIGATIONS IN MENINGOCOCCAL DISEASE—A HOSPITAL BASED RETROSPECTIVE ANALYSIS

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Enhanced surveillance of meningococcal disease was started in 1998 for future evaluation of impact of vaccination. Recommended investigations include blood culture, PCR, throat swab, serology, CSF culture and PCR, and skin scraping if appropriate. An audit at North Staffordshire hospital in 1997 and a similar study in Birmingham showed laboratory confirmation of meningococcal disease was less than 60% and 42% respectively. We therefore implemented recommended guidelines to optimise investigations and improve laboratory confirmation.

Aims: To determine the proportion of cases of clinically diagnosed meningococcal disease that are investigated appropriately after implementation of guidelines and the proportion of cases that are confirmed by various laboratory methods.

Methods: Retrospective case notes review of all children aged 0-16 years admitted between January-December 1998 with clinically diagnosed meningococcal disease. All investigations performed during admission and subsequent follow-up were analysed.

Results: 40 children were admitted with meningococcal disease; 32 (80%) were investigated according to recommended guidelines. 30/40 (75%) cases had diagnosis confirmed by laboratory methods. Laboratory confirmation was 94% (30/32) in the group who had all investigations performed according to recommended guidelines.

Conclusion: The proportion of laboratory confirmed cases improved after implementation of guidelines and was significantly higher when all recommended investigations were performed to optimise laboratory confirmation. There needs to be an increased awareness of recommended guidelines for investigation of clinically suspected meningococcal disease.

G191 | THE ROLE OF RANTES IN MENINGOCOCCAL DISEASE

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Introduction: The chemokine RANTES (Regulated on Activation Normal T Cell Expressed and Secreted) is a potent regulator of leucocyte trafficking. RANTES has been shown to play an important role in directing the migration of monocytes, memory T lymphocytes, eosinophils, basophils and natural killer cells. It preferentially attracts mature CD4 cells as well as macrophages and eosinophils, but not neutrophils. Its role has not previously been described in meningococcal disease (MCD)

Aims: This study aimed to determine the role of RANTES in the pathophysiology of MCD

Methods: 165 children with MCD were prospectively studied. Plasma RANTES, IL-8, IL-6, IL-1Ra and TNF-α were measured by an enzyme amplified sensitivity immunoassay (EASIA) on admission. Severity of disease was stratified by the Glasgow Meningococcal Septicaemia Prognostic Score (GMSPS).

Results: RANTES levels correlated significantly with IL-8 levels (r = 0.36, p < 0.0005), GMSPS (r = 0.36, p < 0.0005), admission lactate levels (r = 0.26, p = 0.0001), platelets, prothrombin time (r = 0.32, p = 0.001), and APPT (r = 0.26, p = 0.006). RANTES levels were lower in those with severe disease (GMSPS >8) than those without (GMSPS <8), p = 0.001, in those with septic shock than in those without, p = 0.0005, and in non-survivors than in survivors, p = 0.048, Mann Whitney. There was no significant difference in RANTES levels between disease types: meningitis (MM), mixed meningitis/septicaemia (MMSM) and septicaemia (MS).

Conclusions: RANTES is a potential mediator in the pathophysiology of MCD. Its chemotactic properties for T cells and monocytes appear to be beneficial in modulating the effects of pro-inflammatory cytokines such as TNF-α.

G192 | INTERLEUKIN-6 GENE POLYMORPHISMS IN MENINGOCOCCAL DISEASE

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Introduction: Interleukin-6 (IL-6) is an important mediator in the pathophysiology of meningococcal disease (MCD). High levels of this cytokine are associated with more severe disease. Genetic factors are known to play an important role both in susceptibility to MCD and risk of severe disease. The aim of this study was to determine if polymorphisms in the IL-6 gene are associated with increased susceptibility to disease or increased risk of severe disease or death.

Methods: 127 children with meningococcal disease were prospectively studied. Severity of disease was stratified using the Glasgow Meningococcal Septicaemia Prognostic Score (GMSPS). Genomic DNA was extracted and a 200bp region of the IL-6 gene was amplified by polymerase chain reaction (PCR). After restriction digestion, a G/C restriction fragment length polymorphism (RFLP) was identified at position -174 of the IL-6 gene. 99 healthy adult blood donors were used as controls.

Findings: Three genotypes were identified: G/G, G/C and C/C. The frequency of the C allele was 0.307 (95% CI 0.283-0.332) in patients, compared to 0.445 (95% CI 0.38-0.51) in healthy adult controls. A higher proportion of those with the G/G genotype had MCD compared to the control population, $x^2=11.011, p<0.001$. Possession of the C allele was not associated with more severe disease (GMSPS >8) or death.

Conclusion: The lower frequency of the C allele in patients with MCD suggests that possession of this allele may confer protection against the development of disease. It does not appear to determine disease severity or risk of death.

G194 | SEQUENCING ANTIRETROVIRAL THERAPY (ART) IN THE SOUTH LONDON PAEDIATRIC HIV COHORT

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Background: Following the introduction of combination ART in 1997, 13 drugs are now available. No audit data is available on the paediatric use of ART outside clinical trials demonstrating their impact on standard outcome measures.

Objectives: To audit paediatric ART use in south London.

Design: Retrospective notes review.


Measurements: demographic variables, ART use, VL (start/nadir/end), CD4 count (start/peak/end).

Results: 84 children (83%) (47M; 54F median 6.4yrs) commenced combination ART, and have received 160 regimens. Following failure of first line ART regimen, children sequence onto second and third line regimens. The mean duration of completed regimens was 1st line—356 days, 2nd line 288 days, 3rd line—281 days. The mean VL reduction was 1st line—1.53 log_{10}, 2nd line—0.85 log_{10}, and 3rd line—0.83 log_{10}. 33% of the cohort reached an undetectable VL during first line regimens compared to 22% during third line therapy. Mean CD4 count increase was 1st line 287, 3rd line 200. Regimens were changed due to clinical—6%, immunological—6%, toxicity 19%, virological—60%, or adherence 25% failure.

Conclusion: Children with HIV rapidly sequencing through ART regimens. The duration and impact of each regimen decreases with each change. It is unclear whether new drug development will keep pace with current drug use. A more cautious approach to drug sequencing following virological failure may be appropriate.

WITHDRAWN
**G195**

**ONE YEAR EXPERIENCE OF NELFANVIR IN UK**

**PAEDIATRIC HIV-1 COHORT**

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**Objective:** To audit the long-term clinical experience of nelfinavir (NFV) in children with HIV-1 infection in the UK

**Method:** Retrospective multi-centre observational analysis of CD4 and viral load (VL) measurements in HIV-infected children enrolled into the NFV named patient programme.

**Results:** Fifty-five HIV-infected children (age 6 to 16 yrs: median 6 years), who had completed at least 12 month follow-up were analysed. 35 (66%) were CDC clinical category C, 76% were antiretroviral treated but only 7% PT performed. NFV was the first line agent used with NFV were d4T/3TC (53%), AZT/ddI (16%) and d4T/ddI (13%). In 18 (33%) NFV was added to existing NRTI regime. Mean dose of NFV was 70.8 mg/Kg/day (range: 41 to 98.7). Median CD4 counts were 164 cells/mm³ (baseline), 388(3m), 61(6m) and 648 (12m), showing an average 2.8-fold rise from baseline to 12 months. Median V1 was 5.04 log10 (baseline), 3.54 log10 (6m), 3.6 log10 (6m) and 3.9 log10 (12m). The proportion of children with undetectable VL (defined as <400 copies/ml) at 3.6 and 12 months was 33, 31 and 24% respectively. In a multiple regression analysis, younger age (p=0.003), higher NFV dose (p=0.03) and change of NRTI at commencement of NFV were associated with better CD4 response.

There was also a trend for higher doses of NFV to produce greater V1 reductions. 43/55 (78%) of children remained on full dose NFV at 12 months. Of the 12 who withdrew, 6 were due to treatment failure, 2 refused to take NFV and 1 child stopped due to side effects, 1 died and 2 left the UK.

**Conclusion:** Analysis of this cohort demonstrates that NFV remains well tolerated, with continued CD4 improvement, but a significant rise in V1 from nadir. Despite virological failure most of the children in the UK have not changed therapy.

**G196**

**THE SIGNIFICANCE OF FEVER IN CHILDREN**

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Fever is a common presenting symptom in childhood. Differentiating the seriously ill is difficult; previous studies have suggested that symptoms, signs and simple investigations may be helpful.

**Aims:** To assess causes of fever and identify clinical and laboratory features suggesting serious illness in children presenting with temperatures over 38°C; then to establish clinical guidelines.

**Methods:** For 3 months (August to October 1999) all children with a temperature of >38°C seen in two hospitals were assessed.

**Results:** 142 children were seen, 64% male, 51% aged 3 months - 2 years. 80% had temperatures between 38°C - 39°C. 95% were GP referrals and 5% were tertiary referrals. Serious infection was present in 24% (34) - 17% (24) microbiologically or radiologically proven; meningitis (7), sepsis (5), brain abscess (2), toxic shock (1), pneumonia (9), 20% (27/135) of GP referrals had serious infection. 42% (5/12) of GP referrals had serious infection. 42% (5/12) of microbiologically proven meningitis and sepsis and 36% (8/22) of all meningitis and sepsis were meningococcal. 77% had no serious infections: appendicitis (2), AOM (4), tonsillitis (12), gastroenteritis (8), febrile convulsion (16), UTI (5), abscess (1), stomatitis (1), lymphangitis (2), cellulitis (3), illitable hip (1).

In cases of proven serious infection the temperature was 38°C - 38.5°C in 42%, 38.6°C - 39°C in 46%, 39.1°C - 39.5°C in 5% and 39.6°C - 40°C in 4%. 22% had received antibiotics, 22% had a rash. 42% of the non-serious group and 10% of the serious group had a history of poor feeding, history of vomiting was in 30% and 9% respectively. FBC was taken in 48% of patients; in 4% of serious and 10% non serious infections WBC was <5000, and it was between 5000 - 15000 in 52% and 54% respectively.

**Conclusions:** 1/5 of children referred with fever had serious infections. Clinical signs and laboratory investigations did not distinguish serious from non-serious infections. Guidelines will not replace clinical assessment of the child with a temperature.

**G197**

**ACYCloVIR THERAPY FOR VENTILATED CHILDREN WITH SUSPECTED HSE—WHO? WHEN? HOW LONG?**

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**Aims:** To review the presentation and investigations of ventilated patients, started on acyclovir for suspected Herpes Simplex Virus (HSV). To propose an algorithm for management of this subset of patients.

**Methods:** We reviewed patients, ventilated for neurorespiratory failure over a period of 36 months, in whom acyclovir was started on clinical suspicion of HSV prior to PICU admission. Each patient was investigated for HSV, following an algorithm which consisted of: a) EEG, b) Herpes simplex virus (HSV) serology, c) CSF examination (including PCR for HSV DNA and d) neuroimaging. Acyclovir was discontinued if bedside neurology was normal after extuba-

**Conclusion:** Ventilated children with cerebral presentations and sedation of seizure; with no abnormality on any of the above investigations. The rest were continued on acyclovir for up to 21 days. Acyclovir was stopped earlier (around week of treatment) if repeat investigations (a to d) and neurology were normal or if an alternative diagnosis was confirmed.

**Results:** 80 cases (age 2 weeks to 14 years), with encephalopathy, ventilated on PICU, received acyclovir. The commonest presentation was febrile encephalopathy with generalised seizures (n=40) followed by isolated febrile encephalopathy (n=25), poor feeding, irritability and apnoea (n=10, infants), focal seizures (n=5) and cranial nerve palsies (n=1). CSF PCR for HSV DNA was positive in 2 of the 59 cases tested. Commonest EEG abnormality (n=14) was generalised slowing. 31 patients completed acyclovir therapy.

**Conclusion:** Antiviral therapy for suspected HSE is initiated on clinical suspicion. However, in sedated, ventilated children bedside neurology is unreliable and lumbar puncture may be contraindicated in the acute phase. Our algo-

**G198**

**THE MANTOUX TUBERCULIN TEST AND ITS RELATIONSHIP TO THE HEAT TEST, BCG, AND TUBERCULOSIS**

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**Introduction:** The Mantoux test is one of the oldest diagnostic tests still in use, but its correlation with the Heat test, interpretation after previous BCG and use in detecting tuberculin is in inner city children today is unknown.

**Aims:** To correlate size of Mantoux with the above.

**Methods:** 254 school children seen in children found to be Heat positive at school pre BCG screening and in those screened as contacts of tuberculosis between 1997 and 1999 (27 months), and children with tuberculosis from 1991-99.

**Results:** 275 school children seen. Of 222 without prior BCG, 195/222 had Heat of 48% gave a Mantoux < 5mm, 26% 5-14mm, 25% ≤15mm. 27/222 had Heat ≥15 mm; 89% ≥ 15 mm, 33% ≥20 mm. Of 53 with BCG, 11/53 had Heat of 15 mm, of whom none gave a Mantoux < 5mm, 46% ≥15mm, 54% ≥ 15mm. 42/53 had Heat ≥15 mm; 95% ≥15mm, 71% ≥20mm. 111 contacts were seen, 59 without prior BCG, in whom Mantoux was Omm in 58 (88%). Of 52 with BCG 24/52 (46%) had a Mantoux of 0mm, 19% 5-9mm and 35% ≥ 10mm. In children with tuberculosis, 20% (7/35) were Mantoux negative at 0mm, 41% (15) of whom had meningitis), 3% 6-9mm, 74% >10mm, 43% ≥ 15mm and 31% ≥ 20mm.

**Conclusions:** 48% of Heat of 15 mm were Mantoux negative, 25% significant. Increasing Heat grade correlates with increasing Mantoux size. BCG does not change Mantoux size in 50%, but in 50% increases size between 5 and 10mm. Mantoux can be negative in tuberculosis in about 20%, although in most responses are ≥10mm.

**G199**

**DO WE REALLY NEED TO SEND STOOL SPECIMENS IN CHILDREN WITH GASTRO-ENTERITIS?**

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**Introduction:** Gastro-intestinal infection is one of the leading causes of morbidity and mortality worldwide and is caused by a wide variety of enter-pathogens. We were asked to limit our cost-benefit analysis to those with limited low diagnostic yield and very few need antimicrobial therapy. **Aim:** Our aim was to ascertain whether stool samples should be sent for examination in all cases of gastro-enteritis.

**Method:** We collated data from the Microbiology Department on all children under 16 from whom stool cultures were sent over a four year period (January, 1996 to November,1999) and from those patients with positive bacterial infection and cryptosporidiosis.

**Results:** The total number of specimens sent = 20,173,3 (2048 for rotavirus, 2,300 for ova, cysts, parasites and 14,589 for culture and sensitivity, 16% were positive for rotavirus (523 out of 3,284), 2% for giardia (48 out of 2,300) and 1% for other organisms (81 salmonella, 75 campylobacter, 16 shigella, 11 crypto-

**Conclusion:** Stool specimens should only be sent of patients with bloody or prolonged diarrhoea, immuno-compromised patients, travellers from endemic areas, those with a family history of diarrhoea, farm visitors, toxic patients and during outbreak of diarrhoea.
G200  EARLY NEONATAL BONE MARROW TRANSPLANT IN SEVERE COMBINED IMMUNODEFICIENCY
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In utero BMT has been proposed as best treatment for SCID as only 50% mismatched BMT are successful. However in utero BMT is feasible only when positive family history leads to antenatal diagnosis. We reviewed 13 cases of SCID, diagnosed at birth, and referred to our unit for BMT between 1989 and 1997 (7 T-B-SCID, 3 T- B- and 3 adenosine deaminase (ADA) deficiency). Sixteen BMT’s were performed, one patient having 2 BMT’s and one 3 BMT’s. These BMT’s consisted of 8 T cell depleted (TCD) haplo-identical, parental, 3 TCD unrelated donor and 5 whole marrow (2 matched maternal, 2 sibling and 1 sibling cord). Seven patients were conditioned for TCD BMT: all had high-dose cyclophosphamide (200mg/kg) and busulphan (5 with highdose and 2 with 16mg/kg). Follow up post-BMT ranges from 67 days to 10 years (median 3 years 9 months). All are alive and well. Six suffered transient acute graft versus host disease (GvHD), grades 1 to 2, and two had chronic GvHD (cGvHD), now resolved. One patient has been transplanted 3 times for poor T and B cell function and are off intravenous immunoglobulin (IVig): six remain on IVig, for three insufficient B cell function and three are less than 1 year post BMT. Eight of eleven evaluable child have normal neurodevelopment (1 has behavioural problems, 1 has slow motor development, 1 with cGvHD related problems).

Conclusion: Early postnatal BMT for SCID before infection occurs has an excellent outcome with full survival and very high levels of T and B cell function. In our practice the utero-BMT will have to demonstrate no risk of hidden GvHD and good B cell function, as well 100% engraftment, to be preferential to early postnatal BMT.

G201  KAWASAKI DISEASE: DO WE NEED FULL AHA CRITERIA FOR DIAGNOSIS?
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Aim: To determine whether American Heart Association (AHA) criteria for diagnosis of Kawasaki disease (KD) are being met. To determine the prognostic factors from the clinical and laboratory data.

Method: 80 patients with KD admitted to our hospital between Jan 1995 and Nov 1999 were identified from a hospital database. Case notes were examined to obtain the clinical and laboratory data. 12 patients who came for a cardiology opinion from other hospitals were excluded from the study. Complete information was obtained on 45 patients.

Results: All the 45 patients received immunoglobulins (lg). 44% of them did not meet AHA criteria at diagnosis and start of treatment. Duration of illness before Ig therapy was 9.3 days in those who met the AHA criteria and 7.6 days in those who did not meet the criteria. In infants, 87% (7 out of 8) had irritability and 63% (5 out of 8) had cardiac involvement. In the remaining children, 72% had irritability and 27% had cardiac involvement. All infants and 90% of children between 1 and 8 years of age with cardiac involvement showed irritability at presentation. 51% of infants with complete AHA criteria had cardiac involvement, only 20% in the 1-8 year age group with incomplete criteria had cardiac involvement.

Conclusion: Nearly 50% of patients are being diagnosed with KD without meeting the full AHA criteria. Infants with cardiac involvement tend to present with incomplete AHA criteria. Irritability which is not among the AHA criteria should be considered as an important criterion for diagnosis in infants.

G202  USEFULNESS OF SCREENING AND CONTACT TRACING IN CHILDBIRTH TUBERCULOSIS
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De novo cases of tuberculosis (TB) make up 60% of our workload. Screening close contacts of adults with tuberculosis is also effective in identifying new cases. Referrals also come from the schools BCG service after positive Heaf tests. To date we have screened (i) all children in contact with TB, (ii) children in contact with Mantoux positive children without evidence of disease, (iii) those given BCG before (previous BCG) and (iv) Heaf IV (with BCG).

Aims: To find the proportion of children with old or active TB in each group.

Methods: Referrals from all groups were entered into a TB database. From these contacts GP’s and children between 1990-31/3/99 and children who were contacts of children either with TB or who were Mantoux positive were found, as was the number seen from schools between 1997-31/3/99 and the number between 1991 and 1996 estimated.

Results: (i) 0.3% (4/1161) of adults and 9% (1/117) of children screened as contacts of child had TB. (ii) 0.3% (4/1161) of adults and 9% (0/225) of children screened as contacts of children who were Mantoux positive without evidence of disease, had TB. (iii) Between 1991-9 1%-1.3% (8/6127-95) of school Heaf II children had evidence of TB (mostly old) and from 1997-9 0.8% (2/255) had TB (old). (iv) Between 1991-9 3.2-4% (71/711-219) school Heaf III/IV children had TB, mostly active, and 4.3% (3/69) went on to develop TB, mostly active. Importantly 5/8 of the school Heaf II positive children with TB had risk features e.g family history of TB, ethnicity, high incidence TB area.

Conclusion: In our population screening and contact tracing of children with TB is highly worthwhile, whereas screening contacts of children who are Mantoux positive without disease is not. Screening those with Heaf III/IV responses at school is also rewarding; screening Heaf II responses at school is of borderline value giving 1% mostly old TB, but appears more effective when only those from selected high risk populations are examined.

G203  TEENAGE LIFESTYLE AND RISK OF MEGACOLONIC DISEASE
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Background: The incidence of invasive megacolic disease (MD) has increased in the UK. Adolescents are at particular risk and have a high mortality. Previous studies have included insufficient numbers of teenagers to clearly identify their risk factors. In particular, data on active smoking is scanty.

Aim: To elucidate social, biological and psychological risk factors for the development of MD in 15 to 19 year olds.

Methods: A prospective case-control study was performed across six regions of England. Subjects with a clinical diagnosis of MD were matched to control identified controls of similar age and sex. A total of 130 case and 139 control questionnaires were completed about social behaviours in the two weeks prior to disease onset (cases) or interview (controls). Provisional results on 51 case control pairs are shown.

Results: N = 51 case control pairs. Mean age 17 years, 51% male, 96% white caucasian.

G204  HOSPITALIZATION FOR COMMUNITY-ACQUIRED ROTAVIRUS-ASSOCIATED DIARRHEA (RAD): A PROSPECTIVE LONGITUDINAL POPULATION-BASED STUDY
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Aims: To assess the need for rotavirus vaccine, contemporary population-based information on the burden of rotavirus illness, including hospitalization rate, is required. A prospective cohort study was conducted to determine the age specific hospitalization rate for RAD during the seasonal outbreak in an Ontario, Canada pediatric population.


Results: Of 224,160 children <5 y, in the region, the diarrhoea hospitalization rate was 4.81000 (9=1068) during the seasonal epidemic. Based on testing of 65% of these admissions , the RAD hospitalization rates was 1.3 1000:the cumulative incidence to age 5yr. was 1.66. Hospitalization most commonly occurred in previously healthy children age 6 to 36 mo. The mean duration of rotavirus hospitalization based on hospital records and parental questionnaires was respectively 2.4 +/- 1.7 and 3.6 +/- 1.6 days. Hospitalization was significantly less common in previously healthy children age 6 to 36 mo. Diarrhoea occurred concurrently in 74% of household contacts <3yr, 38% age 3-yr, and 29% age >3 yr.

Conclusions: Based on testing of 65% of children with diarrheoa, rotavirus resulted in hospitalization in a minimum of 1/160 children by age 5 yr. during the 9 month rotavirus outbreak. Had 100% of young children with diarrheoa been tested, the extrapolated cumulative incidence of rotavirus-associated diarrhoea by age 5 yr. may have been 1/106 during the 8 month period.

G205  IMMUNISATION OF HOUSEHOLD CONTACTS OF WOMEN IDENTIFIED WITH HIV POSITIVE BY ANTENatal SCREENING
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Arch Dis Child: first published as 10.1136/adc.82.suppl_1.A48 on 1 April 2000. Downloaded from http://adc.bmj.com/ on September 23, 2023 by guest. Protected by copyright.
Introduction: Universal antenatal screening for hepatitis B is now recommended in the United Kingdom, but there are concerns about adequacy of follow up. Children born to hepatitis B carrier women are at risk of both vertical and horizontal transmission of hepatitis B.

Aim: To assess the hepatitis B status and immunisation coverage of household contacts of women diagnosed to hepatitis B carriers on antenatal screening.

Methods: All hepatitis B carriers detected antenatally over a three year period were identified from laboratory records and sent a questionnaire to obtain details of household contacts and their hepatitis B immunisation status. Non-responders were contacted through the health visitor.

Results: Responses were received from 23/29 (79%) women. Only 7/19 (37%) current sexual partners and 5/11 (45%) other adult household members had been fully immunised against hepatitis B. 4/12 unimmunised sexual partners had known hepatitis B status one was a hepatitis B carrier, one was naturally immune and two remained susceptible. Of 57 child contacts, 31 (54%) were fully immunised, 13 (23%) were partly immunised, 8 (14%) were unimmunised and in five, immunisation status was unknown. Serum antibody tests had not been done in 28/57 (49%) children and five (9%) were reported to be hepatitis B carriers. Two children (4%) had chronic liver disease.

Conclusions: Our study shows poor follow up and immunisation coverage in this high risk group. Unless proper follow up of hepatitis B carriers diagnosed by antenatal testing is achieved, the current United Kingdom policy of selective hepatitis B immunisation is unlikely to succeed in eliminating hepatitis B. Extra resources and health professionals with a defined responsibility are necessary to improve both immunisation coverage to this high risk group and awareness of the implications of hepatitis B carriage in these families.