There are some components of this condition, which if identified can be treated. It has been recognised that these patients are often subjected to aesthetic or plastic procedures prior to diagnosis. We describe female, twelve-year-old monozygotic twins diagnosed with Trichorhinophalangeal Syndrome Type 1 at a dermatology clinic and referred to our endocrinology clinic for short stature.

The estimated final height for each of these girls was below the 5th centile. GH treatment has been shown to be useful in other bony dysplasias. We postulated that growth hormone (GH) may accelerate growth velocity resulting in an increased final height. As both girls were in puberty, pubertal progress was halted with GNRH analogue and each was prescribed the dose of GH consistent with normal GH levels (as used in Turners Syndrome).

Over a two year period these girls have maintained a growth velocity between the 80th and 90th centiles, over and above the initial growth spurt expected in those beginning GH treatment.

It appears that increased growth velocity may be gained by commencing GH therapy in patients with Trichorhinophalangeal Syndrome Type 1. This can improve their final height outcome. In those children who have started puberty, benefit may be gained by stopping puberty first. This stresses the importance of identifying patients with bony dysplasias in the dermatology clinic where they are most commonly seen and diagnosed.

Allergy, Immunity, and Infection

G194 THE PRO- AND ANTI-INFLAMMATORY CYTOKINE PROFILE IN CHILDREN WITH MENINGOCOCCAL DISEASE

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Introduction: In meningococcal disease (MCD) there is early activation of both pro- and anti-inflammatory cytokines triggered by the release of endotoxin. Some studies of MCD have claimed that an anti-inflammatory cytokine profile is associated with a fatal outcome, so contra-indicating pro-inflammatory cytokine inhibition therapies. Other studies have demonstrated down-regulation of pro-inflammatory cytokines and up-regulation of anti-inflammatory cytokines and suggested this as a protective strategy in MCD.

Aims: To determine whether an anti-inflammatory cytokine profile in MCD was associated with an increased risk of severe disease or death.

Methods: A total of 112 children with MCD were prospectively studied. Plasma concentrations of interleukin-1 receptor antagonist (IL-1Ra), interleukin-6 (IL-6), and tumour necrosis factor-α (TNF-α) were assayed on admission. Severe disease was defined as a Glasgow Meningococcal Septicaemia Prognostic Score (GMSPS) of ⩾ 8.

Results: A high IL-1Ra:TNF-α ratio (>20) was associated with less severe disease (p=0.014). There was a trend in favour of an association between lower IL-1Ra:TNF-α ratios and death, but this was not significant (p=0.283). A lower proportion of children with a high IL-1Ra:TNF-α ratio developed septic shock (6%) than those with a low ratio (38%), p<0.0005. In children with a high IL-1Ra:TNF-α ratio the relative risk of severe disease was 0.63 (95%CI 0.42 –0.91), odds ratio 0.39 (95% CI 0.17–0.89). A high IL-1Ra:IL-6 ratio was not significantly associated with severity of disease or risk of death.

Conclusions: An anti-inflammatory profile with a high IL-1Ra:TNF-α ratio appears to be associated with a favourable prognosis and supports the concept that early IL-1Ra therapy with TNF-α inhibition might be beneficial.

G195 *Taq*I POLYMORPHISM IN THE 3' FLANKING REGION OF THE ALPHA-1 ANTITRYPSIN GENE IN CHILDREN WITH MENINGOCOCCAL SEPTICAEMIA

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Introduction: As part of the inflammatory response in patients with meningococcal septicaemia, large numbers of neutrophils are stimulated, releasing elastase, a proteolytic enzyme which causes vascular endothelial injury which is normally counteracted by the inhibitor α-1-antitrypsin (A1AT). It is hypothesized that a polymorphism in a *Taq*I restriction enzyme recognition site, 3' to the gene for A1AT, results in an inability to produce sufficient A1AT during the acute phase response, and therefore increases susceptibility to septic shock.

Method: Blood samples were collected from paediatric patients with meningococcal septicaemia (n=112) and a control group of paediatric patients (n=154). DNA was extracted and the *Taq*I recognition site was amplified using PCR and the fragments digested using *Taq*I restriction enzyme.

Results: Almost twice as many meningococcal patients had the *Taq*I polymorphism than in the control group (20.5% and 11.6% respectively, χ^2 =3.89, p<0.05).

Conclusions: The results provide further evidence of a link between α-1-antitrypsin and susceptibility to meningococcal septicaemia. Further investigations are needed to elucidate the exact effect of the *Taq*I polymorphism.

G196 CARDIAC TROPONIN T LEVELS PREDICT MORTALITY MENINGOCOCCAL DISEASE

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Background and aims: Cardiac Troponin T (cTnT) is a specific component of cardiac muscle that accurately confirms myocardial insults. We aimed to determine whether cTnT levels correlate with inotrope usage and if they predict severity and mortality in meningococcal disease (MCD).

Methods: Admission (n=63) and sequential (n=24) serum samples were obtained from children with probable or possible MCD as well as from children with other febrile illness (control population, n=19). Severity in PICU patients was graded by the Paediatric Risk of Mortality score (PRISM). Cardiac TnT was measured by an automated Electro-Chemical-Luminescence ImmunoAssay (ECLIA) method (sensitivity of 0.01ng/ml).

Results: Levels of cTnT were undetectable in children with non-meningococcal febrile illnesses. Only two children with MCD (5%), not admitted to the PICU, had detectable cTnT levels (to < 0.02 ng/ml). 29% (n=7) of children admitted to the PICU had increased cTnT levels. Low cTnT levels were detectable at admission in only one PICU patients. Levels in survivors increased to a maximum at 24–36 hours (n=5, median 0.036ng/ml) and then fell. Cardiac TnT levels in those who died increased steadily (n=3, median 0.39ng/ml). Cardiac TnT levels at 12–48 hours correlated significantly with PRISM scores and peak and total adrenaline and noradrenaline doses, but not with dobutamine doses.

Conclusion: Cardiac TnT levels are significantly raised only in severe MCD. Levels correlated with degree of inotrope (adrenaline and noradrenaline) usage. Sequential measurements may allow us to predict mortality.

G197 SEASONAL INFLUENCE ON THYMIC SIZE IN RURAL GAMBIAN INFANTS

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In rural Gambia, birth during and shortly after the annual wet season (July—December) may predict increased infection-related mortality in early adulthood[1]. Thymic development is critical to competent and controlled immunity. To test whether thymic size is influenced by season, we studied 138 rural Gambian infants from birth, comprising 94% of singleton births in 5 villages over 14 consecutive months. A validated sonographic method[2] was used to derive a volume-related thymic index (TI) at 1, 8, 24 and 52 weeks of age. One observer (ACC) performed all scans, blind to obtained values. Growth, morbidity and feeding status were assessed at each visit. Multiple regression analysis included adjustment for sex and gestation, with $p < 0.01$ considered significant. Mean (range) birth weight and gestation were 2855g (2020–3900g) and 38.6 weeks (35.4–41.2 weeks). TI was associated with current weight ($p<0.0005$), but not independently with BW or birth-season. However, mean TI was smaller in July—December, most notably at 8-weeks. This season-of-measurement effect persisted after adjustment for birth-season, current size, and infectious morbidity ($p = 0.0074$ at 8-weeks, $p = 0.0019$ all ages combined). All infants but one were exclusively breast-fed at 8-weeks. The thymus may be larger in breast-fed than formula-fed infants[2], suggesting enhancement by breast-milk immune factors. Wet-season intake of most breast-milk immunoproteins is known to be depressed in this community. We have identified a seasonal effect on the infant thymus, which appears not to be explained by growth status or infection. A possible effect of breast-milk immune factors merits investigation.

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2. Hasselbalch H, et al. Decreased thymus size in formula-fed infants compared with breastfed infants. *Acta Paediatrica* 1996. **85**(9): p. 1029–32.

G198 HIGH EFFICIENCY TRANSFER OF SUICIDE GENES INTO T LYMPHOCYTES

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T lymphocytes, genetically modified to increase their susceptibility to specific pro-drugs, can be harnessed for their beneficial effects during bone marrow transplantation (enhanced engraftment, antiviral effects and anti-leukaemic potential). In the event of serious graft versus host disease they can be targeted for selective elimination by administration of the pro-drug. Pilot studies have demonstrated the benefit of this strategy in the treatment of leukaemic relapse following bone marrow transplantation. Aims:To improve T cell trandsuction efficiency and evaluate novel retroviral vectors carrying the Herpes Simplex Virus Thymidine Kinase (HSV-TK)/Ganciclovir suicide gene system. Methods:Hybrid retroviral constructs were cloned to carry either a marker protein (eGFP) or HSV-TK linked to a benign surface receptor (ΔLNGFR). Virus was packaged using the PG13 cell line and the supernatant was used to transduce leukaemic T cells or peripheral blood lymphocytes (PBLs). Cells were selected using a monoclonal antibody against ΔLNGFR and then exposed to ganciclovir. HSV-TK was compared against an enhanced mutant, HSV-TK39, using a spectrophotometric based assay of cell survival. Results:T cell transduction was optimised using dual protein marking. Over 80% of Jurkat T cells and 30–60% of PBLs were consistently transduced. Populations could be enriched to above 90% purity on the basis of ΔLNGFR expression using. HSV-TK39 increased susceptibility to ganciclovir when compared to HSV-TK. Conclusions:We have developed protocols for highly efficient transduction and rapid selection of T cells modified to carry HSV-TK and HSV-TK39. Such modified T cells may improve the safety of donor lymphocyte infusions in relapsed leukaemia, or could be used to enhance immune reconstitution following allogeneic BMT.

G199 SEQUENTIAL DETERMINATION OF TH1, TH2 AND TH3 CIRCULATING CYTOKINE LEVELS DEFINE DIFFERENT OUTCOMES TO INTERFERON-α TREATMENT IN CHRONIC HEPATITIS C VIRUS INFECTION

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The cytokine profile characterising the acquisition of protective immunity to hepatitis C virus (HCV) infection is controversial. The aim of the present study was to investigate longitudinally the circulating T helper 1 (Th1), Th2 and Th3 cytokine levels in children with chronic HCV infection undergoing interferon-α2b (IFN-α) treatment. Twenty-two consecutive anti-HCV and HCV RNA positive children (12 boys, median age 4.6yrs, range 2.1–11) were treated with IFN-α (5MU/m^2 three times/week for 1 year). Serum was obtained at baseline, 1, 2, 3 weeks and 2, 3, 4, 6, 9 and 12 months from commencement of IFN-α. Six patients achieved sustained virological and biochemical response (SR), 9 partial virological or biochemical response (PR), while 7 were non responders (NR). Using in-house established ELISAs, the following cytokines were measured: IFN-α [Th1], IL-4 and IL-10 [Th2] and TGF-β1 [Th3]. Three distinct patterns, all with elevated levels of IFN-α, were observed: *R) Responsive* = median levels of TGF-β1 and IL-10 0 pg/ml, and low median levels of IL-4 < 125 pg/ml; *I) Intermediate* = mostly undetectable levels of TGF-β1 and/or IL-10, median IL-4 levels between 300–900 pg/ml; *U) Unresponsive* = high levels of IL-10 (>900pg/ml) and/or TGF-β1 (>480pg/ml) and/or median IL-4 levels >900pg/ml. The 6 SR and 1 of the PR patient had pattern *R*, the other 8 PR patients had pattern *I*, while 5 of the 7 NR patients had pattern *U*. The remaining 2 NR patients had undetectable levels of TGF-β1 and of IL-10 on most of the ten sera tested, elevated levels of IL-4 (median > 300pg/ml), and undetectable IFN-α from the 6th month of treatment. These results suggest that an increase of the immunosuppressive cytokines (TGF-β1, IL-4 and IL-10) and/or the exhaustion of IFN-α production favour persistence of HCV in chronically infected patients undergoing IFN-α treatment.

G200 A STUDY OF NEONATAL BCG IMMUNISATION WITHIN THE SOUTH TEES ACUTE HOSPITALS NHS TRUST

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Background: Tuberculosis (TB) is a re-emerging problem in the United Kingdom. BCG immunisation administered in the neonatal period is protective. Standards are published locally to identify infants for whom BCG immunisation is recommended.

Aims: The study aimed to calculate the rate of identification of infants 'at risk' by parental ethnic group and / or family history of TB, to determine subsequent immunisation uptake, and to describe characteristics associated with missed BCG immunisation.

Methods: A retrospective audit was conducted. Demographic data was collected, from a computer database of antenatal booking data, for 2043 pregnancies delivering between 1st October 1998 and 30th April 1999. A cohort of infants 'at risk' was defined and infants referred for BCG immunisation were identified. A manual search of immunisation records determined immunisation uptake.

Results: A cohort of 247 (12% pregnancies) was 'at risk'. 55% of the cohort 'at risk' was correctly identified and 42% correctly identified and immunised. The largest subgroup of the cohort, 48%, was Caucasian with a positive family history of TB. Family history of TB was the most important risk factor, and was missed in 86% of cases.

Conclusions: Despite the local publication of established guidelines, 58% of infants 'at risk' failed to be immunised. Family history of TB was more important than parental ethnic group in predicting risk for the cohort, and was missed in the majority of cases. Appropriate guidelines alone do not guarantee good practice. Guidelines should be introduced in conjunction with regular audit to ensure effective implementation.

G201 CLINICAL AND COST IMPACT OF ROTAVIRUS DIARRHOEA IN OXFORDSHIRE NURSERIES AND PRIMARY CARE PATIENTS

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Aims: To document the severity and clinical and cost impact of community acquired rotavirus using conventional diagnostic techniques and reverse-transcription polymerase chain reaction (RT-PCR) methods.

Methods: Cohorts of children aged 6–24 months, attending Oxfordshire nurseries were followed over 2 seasons: Season 1 Nov 1998—May 1999, 105 children, 11 nurseries; Season 2 Dec 1999—May 2000, 82 children, 9 nurseries. Nurseries were visited twice weekly and specimens collected from study children with diarrhoea reported. For each diarrhoeal episode, parents were sent two questionnaires detailing the clinical course and impact upon the family and health services. A parallel study in Hertfordshire, Gloucestershire, Cambridgeshire and Birmingham general practices sought clinical and cost impact information by questionnaire from families presenting with diarrhoea (tested for rotavirus by conventional diagnostic techniques). Costs were calculated from direct health care and indirect parental time-off work costs.

Results: In season 1, 65 episodes of diarrhoea in nurseries were reported. 19 positive for rotavirus by RT-PCR; in season 2, 28 of 55 episodes were positive. Conventional diagnostic tests (EM season 1 and latex agglutination season 2) only detected 24 of these episodes. At least one questionnaire for 40 episodes. 51% of children visited a GP, 32% of families had secondary cases. 25 questionnaires were returned for rotavirus positive diarrhoeal episodes in general practice (of total 81 questionnaires returned). The mean age of nursery children with diarrhoea was 14.5m (GP 18.6m) 78% of nursery children (92% of GP attendees) vomited, for median 1 day, range 0–3 days (GP not available). Median duration of diarrhoea was 2.5d range 1–8d, with 1.5 days off nursery, range 0–15d. Mean time required off work by parents or guardians was 2.0 days (SD 1.3d) per nursery case and 0.8 days per GP case (range 0–5d). The mean cost per rotavirus diarrhoea episode was £173 in nurseries and £167 in general practice.

Conclusions: Rotavirus diarrhoea incidence and cost burden is under estimated by conventional diagnostic techniques.

G202 PERTUSSIS IS UNDER-ESTIMATED IN INFANTS ADMITTED ACUTELY TO HOSPITALS IN LONDON

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Aims: To diagnose pertussis in infants too young to be fully vaccinated and in children under 15 years admitted to hospitals in London using culture, the polymerase chain reaction (PCR) and serology, and to determine the likely source of such infections.

Subjects: Infants under 5 months of age admitted to London paediatric intensive care units (PICU) between November 1998 and October 1999 and March and October 2000 with: Respiratory failure, apnoea and/or bradycardia, or near-miss Sudden Infant Death Syndrome, or children under 15 years admitted to paediatric wards between July and October 1999 with a pertussis-compatible diagnosis were eligible. Household contacts were also investigated.

Results: 34/141 (24.1%, 95% confidence interval 17.0% to 31.2%) children had pertussis confirmed by PCR (23 children) or serology (3 children) or were epidemiologically linked to confirmed cases (8 children). One infant died. Only 7/34 (20.6%) of the children would have been identified by B.pertussis culture. Infants admitted to PICU were similar to those with respiratory syncytial virus (RSV) infection except for duration of cough (14.1 days with pertussis versus 5.1 days with RSV $p<0.0005$) and lymphocyte count (mean 8.6 for pertussis versus 3.6 for RSV $p=0.002$). Both parents and siblings brought pertussis into households. Co-infection with RSV was frequent.

Conclusion: Pertussis is under-diagnosed in hospitalised children. PCR and serology considerably increase diagnostic sensitivity. These results are minimum estimates of the burden of pertussis because the study was carried out during the lowest incidence of pertussis on record in the UK.

G203 SCREENING HIGH RISK CHILDREN FOR HEPATITIS C IN A TERTIARY PAEDIATRIC REFERRAL CENTRE

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Hepatitis C has emerged as a major public health problem with an estimated seroprevalence of 0.5–1% in the general population. Patients with chronic HCV infection are at risk of developing chronic hepatitis, cirrhosis and hepatocellular carcinoma with advancing age. Since the introduction of blood donor screening in 1991, the risk of transfusion acquired HCV infection in the UK has declined. However, the true prevalence in children is unknown and targeted screening of high risk groups is not standard practice. In response to this, a surveillance programme was established to counsel and test patients transfused before September 1991 when screening of blood donations was first introduced. To determine the incidence of HCV in children treated at this centre, 353 patients transfused between 1971–1991 were counselled and tested over a 2 year period. Patients eligible for testing were identified using a combination of database and laboratory searches. The majority of the cohort were haem/onc patients (303; 86.1%). Blood samples were screened for the presence of HCV antibodies and/or HCV RNA by PCR. The prevalence of HCV antibodies was 2.26% [n=8]; 7 patients (1.98%) were positive for HCV RNA on PCR. 6/8 patients had a history of paediatric malignancies [4 ALL; 2 NHL] and 2 were chronic surgical patients. Six were male and the mean age at diagnosis was 14.6 years. The median duration of infection was 13 years [range: 10–18], whilst the mean number of transfused units was 22.25 [range: 1 to 102]. Of those patients with chronic HCV, serum ALT levels are normal in 4/7 patients, and up to 2x limit of normal in 3/7 patients. Liver biopsies obtained in 2/7 patients show only mild inflammatory changes. In conclusion, the incidence of chronic Hepatitis C in a high risk paediatric patient cohort is around 2 %. In view of the long term complications from this disease, and the availability of potentially effective antiviral agents, we feel that targeted screening in high risk groups is of value in this setting.

G204 RECENT TRENDS IN NUMBERS OF CHILDREN AND WOMEN REQUIRING CARE FOR HIV INFECTION IN THE UK

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Aims: Government statements on future numbers of people requiring care for HIV infection have focused on the needs of adult patients. These analyses consider the service needs of children and their mothers.

Methods: Surveillance data come from obstetricians reporting cases of HIV infected women receiving care in pregnancy (RCOG Scheme), paediatricians providing care for HIV infected children (BPSU Scheme), and laboratories (CDR Reporting). Routine returns of numbers of adults receiving care are made from districts to CDSC (SOPHID Survey). All reporting is voluntary and confidential.

Results: Between January 1995 and April 2000 numbers of children receiving care in the UK because of HIV infection have increased by 73%, from 228 to 396. Over the period 1995 to 1999 the number of women receiving care for HIV increased by 84% in England and Wales from around 2100 to 3800. The majority (59%) of infected children are over five years and 17% are between 10 and 14. There have been particular increases in London and the South East. In the rest of the UK the overall total has changed little although as children infected through blood products have contributed less, the number of vertically infected children rose from 28 to 85. The numbers of women and children requiring HIV-related care rose particularly after 1998 with increased screening of women in pregnancy. There are indications that women are choosing pregnancy who would previously have avoided giving birth. Not only has the number of women diagnosed with HIV during pregnancy increased from 18 in 1995 to 85 in 1999, but also the number of diagnosed prior to conception from 43 to 116.

Conclusions: The need for medical care of HIV infected women and children is steadily increasing and should be included in funding plans.

G205 ANTIBODY RESPONSES TO *NEISSERIA MENINGITIDIS* GROUP C CONJUGATE VACCINE IN CHILDREN WITH HUMAN IMMUNODEFICIENCY VIRUS INFECTION

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Meningococcal C conjugate vaccines (Men C) have been licensed for use in the UK based on immunogenicity studies conducted in healthy children. Consideration needs to be given to children with immune deficiency as they may require different vaccination policies.

Aim: (1) to assess the immunogenicity of Men C in children with HIV, (2) to assess the effect of Men C on CD4 count and HIV viral load.

Methods: Written consent to participate in the study was obtained from the parents of children attending the Paediatric HIV clinic. Blood was obtained pre and post one dose of Men C at the same time as routine samples. Men C antibody was analysed at the MRU by standardised ELISA and bactericidal (SBA) assays.

Results: Results are available on 28 children with a median age of 7.7 years (range 2.5–15.4). Only 39% achieved a titre of ⩾ 1: 8 (SBA) (range <4 -512) taken a median of 2.5 months post vaccination (range 0.7–5.6). The median CD4 counts and viral loads pre and post vaccination were 731 and 785 and 8090 and 2473 respectively.

Conclusions: In this small study the majority of HIV-infected children did not achieve a "protective" titre of antibody post Men C vaccine. Further studies are required and are underway. There were no adverse effects on CD4 count and HIV viral load following 1 dose of Men C vaccine.

G206 SAFETY STUDY OF A NEW CONJUGATE MENINGOCOCCAL C VACCINE IN INFANTS

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Conjugate meningococcal C (Men C) vaccination was introduced into the immunisation schedule in the UK in November 1999. There has been extensive public interest in its safety and efficacy. We conducted a study to identify uncommon adverse events associated with a new Men C - CRM 197 vaccine (Chiron). 2796 healthy infants aged 2 months were recruited onto this study from areas in and around Sheffield and from Scotland. Enrolled infants received the Men C vaccine at 2, 3 and 4 months with DTP/Hib/OPV, and data regarding adverse events and their possible relationship to vaccination were collected up to one month after each dose.

Results: There were no deaths. A total of 1804 subjects (65%) reported adverse events, considered possibly related to vaccine in 49 subjects (2%). Serious adverse events were reported in 5% of subjects but were considered possibly related to the vaccine in only 4 infants (0.14%). These consisted of a hypotonic episode, screaming syndrome, maculopapular rash and agitation respectively. All subjects recovered completely. These data indicate a favourable safety profile. This vaccine was licensed for use in infants in the UK in October 2000.

G207 MENINGOCOCCAL DISEASE IN A HYPERENDEMIC REGION—DO SOCIODEMOGRAPHIC FACTORS INFLUENCE ITS OCCURRENCE, COURSE AND PROGNOSIS?

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Aims: I)To assess whether sociodemographic factors influence the prevalence of invasive meningococcal disease(IMD) in a defined hyperendemic region (rates of IMD 13.1–19.3/100,000). II)To assess the important symptoms noted by parents, the nature and speed of the medical response and to correlate this with outcome.

Methods: All patients with confirmed Polymerase Chain Reaction (PCR) positive IMD were prospectively studied over a 3 year period (1997–2000). Parents were requested to answer a meningococcal questionnaire during hospitalization highlighting who noted the first symptoms, the response of the family doctor and the sequence of events prior to and post-hospitalization. Details of the Glasgow Meningococcal Prognostic Score (GMSPS) and all medical management including time to doctor assesment, admission and treatment were tabulated and entered onto an Epi-info 6 database. Neurological status at discharge and Paediatric Overall Performance Scale were used to assess overall outcome.

Results: Of 70 PCR-proven IMD patients(70% group b, 20% c), 57% were male. Median age (+/-S.D) was 17 (+/- 32) months. Parental smoking 70%(regional rate 30%) and paternal unemployment 54% (regional rate <10%) were overrepresented ($p<0.005$*). In 80% (n=56) a rash (invariably the trunk, buttocks or limbs) was present before admission. In 90%, the mother was the first to notice symptoms. Of 34 patients presenting to their family doctor, 11(32%) received parenteral penicillin. The mean time from first symptoms to hospitalization was 15.4(+/-12) hours and was not influenced by sociodemographic factors. Mean time to doctor review in hospital was 17(+/- 25) minutes with a mean time to intravenous antibiotics of 60 (+/- 90) minutes.The mean admission GMSPS was 4.5(+/-3.2). Only 12% (n=8) had a GMSPS > 10, accounting for a low mortality rate of 2.9% (n=2) and overall excellent outcome.

Conclusions: Passive smoking and paternal unemployment appear to represent risk factors for IMD. High index of suspicion (both parental and medical) appears to be associated with speedy recognition, lower GMSPS scores and improved overall outcome independent of social factors.

G208 SEROLOGICAL EVIDENCE FOR HEPATITIS B INFECTION IN THE SOMALI POPULATION OF LIVERPOOL

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Objective: To describe the prevalence of Hepatitis B core antibody (HbcAb) and surface antigen (HbsAg) in the Somali population in Liverpool and identify at risk groups who may benefit from vaccination.

Methods: A cross sectional study of Somali households. Open sessions were held at local health centres consisting of an interview in Somali and blood sampling.

Results: 439 subjects from 151 households, aged between 10 months and 80 years, were screened for HbcAb and HbsAg. 194 (43.3%) were children aged less than 15 years. 309 (69%) were born in Somalia and 122 (27.2%) were born in the UK. 5.7% were seropositive carriers for HbsAg (9.4% in adults aged 20—44 years). History of a surgical procedure in Somalia was a significant risk factor for HbsAg. Prevalence of HbcAb was 27.5%, increasing with age over four decades. 7/75 (9.3%) children born in the UK aged under 6 had evidence of exposure to Hepatitis B, of whom only one had a close family member who was a carrier.

Conclusions: HbsAg carriage and HbcAb from previous infection are common in this population. Horizontal transmission may be continuing at an early age, suggesting a population of at risk individuals who would benefit from vaccination.

G209 SELECTIVE USE OF VANCOMYCIN FOR EMPIRICAL TREATMENT OF NEONATAL SEPSIS: EFFECTS ON CLINICAL OUTCOME AND GLYCOPEPTIDE USAGE

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Background: Coagulase-negative Staphylococci (CONS) are the foremost cause of nosocomial neonatal sepsis. Glycopeptides are widely used in treatment, reflecting *in vitro* sensitivities. There is mounting evidence for the successful treatment of CONS sepsis with β-lactam antibiotics despite apparent *in vitro* resistance.

Aim: To determine the effect of highly selective Vancomycin use on clinical outcomes and the rates of Glycopeptide prescription.

Methods: A policy of highly selective Vancomycin use was adopted in this unit for the empirical treatment of nosocomial sepsis. Beyond 48 hours of age, infants receive Flucloxacillin and Netilmicin pending culture results. Vancomycin is reserved for infants failing to respond to treatment or having received a full course of Flucloxacillin within 2 weeks. This retrospective review compared clinical outcomes and Vancomycin usage before and after adopting this policy.

Results: 31 infants in the 9 months before and 45 in the 9 months after the change in policy received empirical antibiotic treatment after 48 hours of age. Positive blood cultures were obtained from 31 (69%) cases during the former period (60% CONS) and from 21 (34%) cases in the latter period (30% CONS). Five infants with blood cultures growing CONS received Vancomycin after failing to respond to Flucloxacillin - all recovered fully. There were 4 deaths in the former period and 1 death in the latter period. Vancomycin use fell from 42 of 45 (93%) to 17 of 61 (28%) among cases of suspected nosocomial sepsis.

Conclusions: Selective use of Vancomycin dramatically reduces Glycopeptide usage without adversely affecting clinical outcomes.

G210 EVALUATION OF SERIAL MATERNAL URINE PCR FOR DETECTION OF PRIMARY ACQUISITION OF CYTOMEGALOVIRUS (CMV) DURING PREGNANCY

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Background: Congenital CMV occurs in 0.5—1.5% of births, and is a major cause of deafness, and handicap. There is currently no antenatal screening programme. Primary maternal infections are usually asymptomatic. Improved diagnosis of maternal infection could lead to perinatal CMV antiviral therapy.

Aim: To evaluate serial urine CMV PCR for detection of primary CMV infection during pregnancy, and assess the associated anxiety.

Methods: All women who booked at St. George's in 1999 were screened for CMV IgG. The study group were women who were CMV IgG negative, aged <30 years, and/or having pre-school child. Women were invited to send monthly urine samples by post in the provided containers and prepaid envelopes. Cord bloods were CMV IgG tested where possible to detect seroconversion. A validated anxiety questionnaire was sent to all study participants.

Results: 3644 women booked in 1999; 2095(57.5%) CMV IgG positive, 1549 (42.5%) CMV IgG negative. 609 women participated in the study. PCR was performed on 2263 urine samples (mean of 3.7/pregnancy). Only 1 woman was detected as having a primary CMV infection by positive urine PCR in the third trimester (baby CMV negative). Cord bloods were available in 288/609. Only 1 woman seroconverted, and had been detected by the PCR. 254/609 women (41.7%) replied to the questionnaire. 214 (84.3%) had little or no anxiety, and 220 (86.6%) felt reassured by their study participation.

Conclusion: Although this a small pilot study, serial maternal urine PCR is a feasible but expensive method of detecting primary CMV infection during pregnancy.

G211 BACTERIAL LOAD IN MENINGOCOCCAL DISEASE CORRELATES WITH DISEASE SEVERITY AND DEATH

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Background: Disease severity in meningococcal disease (MCD) is related to endotoxin and pro-inflammatory cytokine levels. Routine blood culture techniques suggest maximum bacterial load is 10 colony-forming units/ml. The Taqman polymerase chain reaction (PCR) method allows meningococcal bacterial DNA load to be quantified.

Aims: To quantitate bacterial load at presentation in patients with MCD and determine how this relates to disease severity.

Methods: EDTA samples were obtained from 33 patients with septicaemia due to MCD. Bacterial DNA was extracted from whole blood specimens and analysed using Taqman PCR. Disease severity was stratified by the Glasgow Meningococcal Septicaemia Prognostic Score (GMSPS); severe disease defined as GMSPS ⩾8.

Results: Median bacterial load at admission was $2.3x10^6$ DNA copies/ml of blood (range $2.5x104–1.6x10^8$). Bacterial load is independent of the length of time a patient had clinical symptoms. Bacterial loads in patients with GMSPS D8 are significantly higher than for GMSPS ⩾8 (Mann Whitney p=0.007). This association is continuous across all GMSPS values (Spearman's coefficient 0.538, p=0.001). Bacterial load is significantly higher in patients who died (n=2) compared to survivors (n=31) (p=0.042).

Conclusions: Bacterial load is higher than previously demonstrated by culture techniques. Admission bacterial load is significantly higher in more severely affected patients and those who died. Measurement of admission bacterial loads may aid medical management of MCD.

G212 THE IMMUNE RESPONSE OF PREMATURE INFANTS TO DTAP-HIB AND MEN C VACCINES

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Aims: The UK was the first to introduce meningococcal group C conjugate vaccine (MenC) to its schedule. Licensure was based on antibody data alone with no data from premature infants. Combined diphtheria/tetanus/acellular pertussis—Haemophilus influenzae b vaccines (DTaP-Hib) reduce Hib response in term infants but induce memory. We aimed to determine premature infants' immune response to MenC and a combined three-component DTaP-Hib vaccine.

Methods: Infants were recruited from five neonatal units. Geometric mean (GM) IgG antibody concentrations (GMC) to Hib and GM serum bactericidal antibody (SBA) titres (GMT) to MenC were measured in blood samples taken before the first and one month after the third dose. Results were compared with those obtained in term infants given the same vaccines.

Results: 63 infants form the study group with a mean gestational age at birth of 29 weeks (range: 25–32) and a mean birth weight of 1282 g (range 490–2114). GMC to Hib was 0.21 mcg/l (95% CI 0.14–0.30) with 21% achieving > 1.0mcg/l, compared to 1.23 mcg/l (0.98–1.58) and 57% in term infants (p<0.01 and <0.001 respectively). SBA GMT to MenC was 330 (95% CI 211–516) with 89% achieving a 4-fold rise in SBA titre, compared to 1011 (702–1455) and 96% in term infants (p<0.01 and 0.22 respectively). There was no correlation between antibody response and gestational age, or weight, at birth.

Conclusion: When combined with DTaP, the anti-Hib GMC of premature infants is extremely low. The SBA GMT to MenC is also reduced when compared to that achieved by term infants. The antibody response, including avidity maturation, following a booster dose of Hib or MenC conjugate vaccine is now being studied.

G213 EFFICACY OF THE MENINGOCOCCAL C VACCINE

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Background: 37% of invasive meningococcal disease (MD) in England and Wales is Group C, with 13% of cases occurring in 15–19 year olds. A conjugate Meningococcal Group C vaccine was introduced in the UK in November, 1999.

Aim: To estimate the efficacy of the Men C conjugate vaccine.

Methods: A prospective case control study was conducted across 6 regions of England. Subjects confirmed to have Group C MD were matched 1–3 controls for age, sex and GP. Vaccine status was ascertained.

Results: The total 15–17 year old population in these regions is 1,094,000. Of these 58.7% are in fulltime education, and the remainder in employment. Uptake of Men-C vaccine is higher in those in

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	Case	*Control*
Vaccinated	1	13
Unvaccinated	22	25

education (67% v 30%). The average vaccine uptake for this age group is 52%. The results are shown in the table for the period November 1999-November 2000. The odds ratio for MD of 0.09 was estimated from the table.

The vaccine efficacy of the MD vaccine was estimated at 91% (95%CI 48%, 98%) using the formula VE=(1-OR) x 100.

Correcting for vaccine failure leads an estimate of 87% vaccine efficacy, using the formula for screening method.

Conclusions: We estimate a protective efficacy of 87–91% for the Meningococcal C conjugate vaccine.

G214 CLINICAL RISK FACTORS FOR ADVERSE OUTCOMES OF MENINGOCOCCAL DISEASE

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Aims: To compare clinical risk factors, which may predict mortality and long-term morbidity following meningococcal disease (MCD).

Methods: Between 1988 and 1990, 152 cases of MCD were prospectively recruited: 139 survived. Between 1998 and 1999, 115 (83%) of the survivors were studied. Standard measures of neurological function, coordination, cognition, behaviour and hearing were used to assess neurodevelopmental status. Adverse outcomes were defined as: death (n =13); or significant neuro-developmental impairment (n=22).

Results: Demographic features such as age, sex, family size and referral hospital did not predict mortality or impairment. There were no deaths from pure meningitis. 6 (14%) cases of pure septicaemia died compared to 7 (8%) of mixed disease (p=0.35). Patients with a Glasgow Meningococcal Septicaemia Prognostic Score (GMSPS) [|] 8 on admission had significantly higher mortality (OR=37, 95% CI=5–295). On multivariate analysis of each part of the GMSPS hypotension was the only independent risk factor (OR= 17, 95% CI=5–66). By contrast, patients with moderate and severe impairments were evenly distributed within the diagnostic groups. Cases of meningitis were at greater risk of minor impairment (OR=4.4, 95% CI=1.4–13.6). GMSPS was not found to predict neurodevelopmental outcome.

Conclusion: Although accurate diagnosis and clinical severity predicted mortality from MCD they did not accurately predict neurodevelopmental morbidity. Clinicians should be aware that survivors of even mild disease may be at risk of subtle sequelae.

G215 A DESCRIPTION OF MENINGOCOCCAL DISEASE DEATHS—CAN WE SAVE THE UNSAVABLE? NATIONAL CONFIDENTIAL STUDY OF MENINGOCOCCAL DISEASE IN CHILDREN IN ENGLAND, WALES AND NORTHERN IRELAND

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Background: Meningococcal disease (MD) continues to be the leading cause of childhood death by infectious disease in the UK. Current practice of aggressive resuscitation and early intensive care is only of benefit if there is *early recognition* of the disease. This study reveals a significant number of deaths, 'potentially savable', with improvements in recognition of shock, raised ICP, and speed of treatment.

Aim: To describe a 15-month sample of deaths from MD in terms of i) proportion of meningitis:septicaemia cases ii) 'potentially savable' cases iii) appropriateness of hospital treatment.

Methods: All medical notes/intensive care charts were requested for deaths from MD over a 15-month period. Disease course, interventions and results were presented to an 'expert panel' who noted when complications were present and when interventions should optimally begin.

Preliminary results: 189 deaths occurred in the study period: 23(12%) meningitis, 155(82%) septicaemia and 11(6%) unknown. *Pre-hospital deaths:* 5(22%) meningitis and 22(14%) septicaemia. *Deaths within 3 hours of admission:* 3(13%) meningitis and 23(15%) septicaemia. *Inadequate triage:* 6(40%) meningitis, only 9(60%) had a pulse plus CNS recorded; 55(57%) septicaemia, only 43(44%) had a pulse plus blood pressure recorded. *Complications and severity of illness not recognised*: approximately 10(67%) of 'potentially savable' meningitis, 4(27%) having inappropriate lumbar puncture or CT scans; 34(35%) of 'potentially savable' septicaemia, 27(28%) receiving too little fluid and 40(41%) too little or inadequate inotropes.

Conclusion: 68%(112/165) of this sample were 'potentially savable' on admission to hospital. Septicaemia has greater morbidity than pure meningitis alone. The results of this study have implications not only for provision of care but also for clinical teaching.