Plenary Session I

### P1 THE MRC HIP TRIAL: A MULTICENTRE RANDOMISED TRIAL OF ULTRASOUND IMAGING IN INFANTS WITH CLINICAL HIP INSTABILITY DETECTED BY SCREENING

C. Dezateux1, D. Elbourne2, R. Arthur3, A. Quinn4, A. King5, G. Russell5, N. Clarke6 on behalf of the MRC/UK Collaborative Hip Trial Group. Epidemiology, Institute of Child Health, London; Medical Statistics, London School of Hygiene, London; \( X \)-Ray Dept, General Infirmary, Leeds; NPEU, Oxford; St Michael’s Hospital, Bristol; SGH, Southampton, UK

**Background:** Although ultrasound (US) imaging is increasingly used to guide the subsequent management of infants with screen-detected clinical hip instability, the potential benefits and harms of this policy have not been evaluated in relation to longer-term hip development.

**Objective:** To assess the clinical effectiveness of US imaging to guide the further management of infants with clinical hip instability.

**Methods:** Infants with clinical hip instability confirmed by a senior doctor were recruited from maternity wards and paediatric orthopaedic outpatient clinics in 28 UK centres and randomised to a standardised US examination of the hips at age 2–8 weeks [US group: n=314] or clinical assessment alone [no ultrasound (NU) group: n=315]. Primary outcomes: abduction splinting and/or operative treatment by 24 months; blinded assessment of hip X-rays at 24 months; walking age. Intention to treat analysis.

**Results:** US and NU infants were similar with respect to key prognostic factors. Protocol compliance was high (90% US; 92% NU). X-ray information was available for 91% at 14 months and 80% at 24 months. US infants were less likely to receive abduction splinting treatment (RR 0.79; 95% CI 0.66–0.95), particularly in the first 2 weeks of life (RR 0.43; 95% CI 0.31–0.60). Late operative treatment (12–24 months) was required by 20% US (3.2%) and 14% NU (4.3%) infants (RR 0.72; 95% CI 0.32–1.59). By 24 months, subluxation, dislocation or acetabular dysplasia were present on X-ray in 21 US and 21 NU children (RR 1.05; 95% CI 0.59–1.88). All 10 (4 US) children with severe hip dysplasia or displacement had commenced treatment by 8 weeks. One US and 4 NU children were not walking at 24 months (RR 0.25; exact 95% CI 0.03–2.25).

**Conclusion:** The use of US imaging in infants with screen-detected clinical hip instability allows abduction splinting rates to be reduced, and is not associated with an increase in abnormal hip development or higher rates of operative treatment by 2 years of age.

### P2 THE LONG-TERM EFFECTS OF BEING BORN PREMATURELY ON BLOOD PRESSURE AND GLUCOSE TOLERANCE IN EARLY CHILDHOOD

N.P. Wright1, A.T. Gibson2, S. Carney3, J.K.H. Wales1. Sheffield Children’s Hospital and Jessop Hospital for Women, Sheffield, UK

**Aims:** Much evidence has been presented linking small size at birth with subsequent hypertension, insulin resistance and dyslipidaemia. Individuals born prematurely are small at birth but they may be an appropriate weight for their gestation. The aims of the study were to investigate whether prematurity programs for hypertension and insulin resistance, and to examine whether it is being small for dates or absolute size that is important.

**Methods:** As part of a longitudinal study of growth and prematurity, a cohort of 260 children aged 5–6 years followed since birth were invited to attend for investigations which included measurement of blood pressure, a glucose tolerance test, cholesterol, triglycerides, cortisol and IGF-1.

**Abstract P2**

<table>
<thead>
<tr>
<th>Gestational age</th>
<th>Systolic BP in mmHg (SD)</th>
<th>Resting heart rate</th>
<th>Fasting insulin/ glucose ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;30 weeks (n=30)</td>
<td>101.9 (88.7)</td>
<td>101/mm</td>
<td>1.31 (20.8)</td>
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<tr>
<td>30–34 weeks (n=99)</td>
<td>99.6 (80.5)</td>
<td>98/min</td>
<td>1.25 (20.8)</td>
</tr>
<tr>
<td>34–37 weeks (n=34)</td>
<td>95.8 (77.8)</td>
<td>98/min</td>
<td>1.05 (20.7)</td>
</tr>
<tr>
<td>Term controls (n=41)</td>
<td>95.1 (77.0)</td>
<td>95/min</td>
<td>1.01 (20.5)</td>
</tr>
</tbody>
</table>

**Results:** Blood pressure (systolic & diastolic) and resting heart rate increased with decreasing gestational age (\( r^2 =0.07, p<0.001 \)). Being small for gestation was also inversely related (\( r^2 =0.04, p<0.01 \)) to blood pressure and heart rate, but the strongest association was with gestational age. Prematurity was also associated with elevated fasting insulin/glucose levels. Of the metabolic variables the most significant was IGF-1, mean 120 (SD46) IU/l, 34 weeks compared to 95 (SD52) IU/l in controls (p<0.05) (see table).

**Conclusions:** Children born prematurely have higher blood pressure, higher heart rates and evidence of insulin resistance. This suggests that they may be more likely to develop hypertension and diabetes in later life. Whilst being small for dates is also associated with blood pressure and insulin resistance it is the degree of prematurity that is most important. We would speculate that the GH-IGF-1 axis may mediate hypertension and insulin resistance.

### P3 ORGANISMS ISOLATED FROM URINARY TRACTS OF CHILDREN IN THE COMMUNITY AND THOSE WITH UNDERLYING RENAL ABNORMALITIES: A FIVE-YEAR PROSPECTIVE SURVEILLANCE STUDY

S. Ladhani, W. Grandsen1, Departments of Paediatrics and Microbiology, Guy’s Hospital, London Bridge SEI 9RT, UK

**Background:** Although urinary tract infections (UTI) are common in children, very little information is available on the organisms isolated from the urinary tract or their antimicrobial susceptibilities.

**Methods:** A five-year prospective surveillance programme was performed on all organisms isolated from the urinary tract of two groups of children: those in the community and those with underlying renal problems.

**Results:** 2815 and 1314 significant organisms were isolated from the urinary tracts of community and renal children respectively. Klebsiella spp., Staphylococcus aureus and other staphylococci, Pseudomonas spp., Enterobacter spp. and S. maltophilia were proportionally more common among renal isolates, while E. coli and proteus spp. were proportionally more common among community isolates (p<0.05). Almost all renal isolates were more resistant to most antibiotics compared to community isolates. The antimicrobial resistance for community E. coli isolates were (renal isolates): amoxycillin 51.1% (59.2%), cefadroxil 15.0% (6.7%), cefuroxime 9.0% (5.9%), co-amoxiclav 3.6% (10.6%), gentamicin 0.1% (1.5%), ciprofloxacin 0.6% (5.9%), nitrofurantoin 5.9% (16.7%) and trimethoprim 27.6% (50.4%). In particular, trimethoprim resistance has consistently increased from 24.1% in 1995 to 31.5% in 1999 among community isolates and from 37.4% in 1995 to 62.5% in 1999 among renal isolates. Vancomycin-resistant enterococci among renal patients has also increased from 0% in 1995 to 10.7% in 1999 (p<0.05).

**Conclusions:** Organisms isolated from urinary tracts of children are becoming increasingly resistant to commonly used antibiotics. In particular, up to a third of community E. coli isolates and over half the E. coli isolates from children with renal problems may be resistant to trimethoprim. This study suggests that renal isolates are consistently more resistant to most antibiotics than community isolates and this should be considered when empirically treating urinary tract infections in such children.

### P4 OUTBREAK OF MEASLES: DUBLIN 2000

J. McBrien1, J. Murphy1, W.W. Hall2, C. O’Donovan1, D. Gill1, M. Cafferkey1. ‘The Children’s Hospital, Temple Street, Dublin;’ Virus Reference Laboratory, Belfield, Dublin, Ireland

**Introduction:** In a climate of vaccination and possible eradication of the potentially serious illness, measles, an outbreak occurred in Dublin between December 1999 and July 2000. The majority of cases occurred in the catchment area of our hospital.

**Methods:** We present the epidemiological and clinical data of all the children who were admitted to The Children’s Hospital with a laboratory or clinical diagnosis of measles.

**Results:** 355 children presented to the Accident and Emergency department with measles and 111 were admitted. 47% were female, 53% male and 26% had underlying chronic disorders or serious acute illnesses. They ranged in age from five months to ten years, mean age 2 years. Two were less than six months of age, 53% from six to fifteen months and 45% over fifteen months. Of those over fifteen months only 38% had received the Measles/Mumps/Rubella vaccine (MMR), 62% were not vaccinated. The majority of patients were admitted with dehydration (8/111, 79%), tracheitis (3/311, 32%), and pneumonia.

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or pneumonitis (52/111, 47%). The spectrum of clinical presentation included a rash (106/111, 95%), pyrexia (105/111 95%), cough (93/111, 84%), conjunctivitis (60/111, 54%), vomiting (45/111, 40%), diarrhoea (43/111, 49%), otitis media (37/111, 33%), febrile seizure, (9/111, 8%), and aspiration or apnoea (4 cases). The clinical picture was atypical in 11 cases and two were treated for concurrent Kawasaki disease. Thirteen patients required admission to the intensive care unit (ICU), seven were ventilated and two children died. The inpatient stay ranged from 1 to 43 days, median 6 days and the ICU stay ranged from 1 to 28 days, median 5 days.

Conclusions: (1) Measles is not a benign illness and (2) it has not gone away. (3) It is vital that we explore reasons for the very poor vaccination rate and devise measures to improve it. (4) Measures taken to prevent further spread of the outbreak were successful. (5) The morbidity of this outbreak is not yet complete as sequelae such as subacute sclerosing panencephalitis may occur many years later.

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**Plenary Session II**

**P5 A RANDOMISED CONTROLLED TRIAL OF WEIGHT-BEARING STANDING PROGRAMME ON VERTEBRAL TRABECULAR BONE MINERAL DENSITY IN NON-AMBULANT CHILDREN WITH CEREBRAL PALSY**

M.Z. Mughal, J.M. Caulton, G. Dunn, C. Alisop, J.E. Adams. St Mary's Hospital, School of Physiotherapy, School of Epidemiology & Health Sciences, Department Of Radiology, University of Manchester, UK

Severely disabled children with cerebral palsy (CP) are prone to atraumatic fractures, which are associated with reduced bone mineral density. The aim of this pilot randomised controlled trial (RCT) was to determine whether participation in increased weight-bearing standing programme (vertical or prone standing) during a school year would lead to an increase in vertebral trabecular bone mineral density (vTBMD) of non-ambulant children with CP.

Twenty-six prepubertal children with CP, 14 boys and 12 girls, age 7.32 ± 1.8 years (4.33 -10.83) participated in this pilot RCT. Quantitative computer tomography in conjunction with a spiral 3-D software was used to measure vTBMD (g/cm³). Matched pairs of subjects were created using initial vTBMD standard deviation scores. Children within the pairs were randomly allocated to either control or intervention. The average standing period of the children in the intervention group was 60% higher than in the controls, over a 9-month period.

Analysis using the random effects model (allowing for the type of CP, initial standing duration, type of standing, and the average dietary calcium intake) produced an estimate of the effect intervention on vTBMD change of +8.91 g/cm³ (95% CI, 2.40 - 15.41; p=0.007). This represents a mean increase in vTBMD of 6.6 % in the intervention group. Based on the results of this pilot RCT, we conclude that longer period of vertical or prone standing in non-ambulant children with CP would result in increased bone strength and lower risk of vertebral fractures.

**P6 RESULT OF AN RCT INTO HOSPITAL AT HOME CARE FOR ACUTE ILLNESS IN CHILDHOOD**

P.J. Todd, M.J. Maxwell, S.A. Sartain, A.R. Haycox, P.E. Bundred. Arrowe Park Hospital, Wirral, UK

This is the first Randomised Controlled Trial (RCT) to compare hospital care (HC) with hospital at home care (HAH) for acutely ill children.

**Method:** Patients admitted with three common acute problems (diarrhoea & vomiting, breathing difficulties and fever) were randomised to either HC or HAH. HAH care was protocol driven and provided by a round the clock nursing team. Re-admission rate within 3 months was recorded (proxy for improved parental coping strategies). A qualitative evaluation was made of parents and children's perceptions of the two types of care and an assessment was made of cost effectiveness.

**Results:** see table.

HAH was preferred by 36/40 parents and 7/11 children in the qualitative evaluation. Cost to parents of HAH was similar to HC. Cost per case economic analysis did not identify any significant difference between NHS costs for the 2 groups.

**Conclusions:** HAH is a clinically acceptable form of care for acute illness managed within a defined protocol. Parents and patients prefer it. There is no evidence that it increases parental coping strategies for further illness within the next 3 months. We will discuss the difficulties of comparing NHS costs within the constraints of a RCT and the role of an impact model in assessing the generalisability of the results throughout the NHS.

**Abstract P6**

<table>
<thead>
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<th>Type of care</th>
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<th>HC</th>
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<tr>
<td>Total patient numbers</td>
<td>210</td>
<td>189</td>
<td>399</td>
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<tr>
<td>Number of re-admission episodes</td>
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<td>17</td>
<td>39</td>
<td>0.619</td>
</tr>
<tr>
<td>% rate for readmission episodes</td>
<td>10%</td>
<td>9%</td>
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</table>
**P7** EFFECT OF MATERNAL NUTRIENT RESTRICTION IN EARLY TO MID GESTATION ON THE PROGRAMMING OF FETAL KIDNEY DEVELOPMENT

M.E. Symonds1, H. Budge1, K. Firth1, C. Whorwood1. ‘Academic Division of Child Health, University Hospital, Nottingham; Department of Biomedical Sciences, University of Southampton, UK

**Aims:** Fetal kidney growth is highly sensitive to maternal nutrition and fetal cortisol status. This effect may be mediated by changes in glucocorticoid receptor (GR) abundance and hydroxysteroid dehydrogenase-2 (11HSD) activity. We investigated the effects of maternal nutrient restriction (NR) between early and mid-gestation on kidney development near to term.

**Methods:** Fifty-one-singleton bearing Welsh Mountain ewes were individually housed from 28 days gestation, with 29 animals being NR. These consumed 3.2 MJ of metabolisable energy (ME) per day (± 50% of ME requirements for maintenance and growth of the conceptus) between 28 and 80 days gestation, with controls consuming 6.7 MJ/day. After 80 days gestation, until term (147 days) all animals were fed to requirements and consumed 6.8–7.5 MJ/day, with no difference in intake between groups. At 144–6 days gestation each lamb was delivered by Caesarean section and kidneys sampled, mRNA encoding GR and 11HSD was then analysed by Northern blot and relative levels quantified in relation to 18S rRNA.

**Results:** Lambs born to NR ewes had a heavier (20.8±1.4 vs 16.9±2.3 g (P<0.05)) but shorter kidney (32.5±1.0 mm vs. 33.7±1.5 mm (P<0.001)) compared to controls. Levels of GR mRNA expression were higher (1.0±0.1 vs. 0.7±0.2 (P<0.05)) but 11HSD lower (0.2±0.0 vs 0.3±0.04 (P<0.05)) in kidneys of NR lambs. There was no difference in birth weight between groups but NR lambs had a larger placenta (243±27 vs 169±25g (P<0.01)).

**Conclusion:** Increased kidney expression of GR in conjunction with a lower expression of 11HSD in response to a defined period of maternal NR during early- to mid-gestation, suggests that gene expression has been reprogrammed. These data suggest key mechanisms by which maternal nutrition prenatally programmes physiological pathways thereby contributing to cardio-vascular disease in later life.

**P8** BLOOD PRESSURE AND FASTING INSULIN LEVELS IN TWINS; CONTRIBUTIONS OF GENETIC FACTORS AND LOW BIRTHWEIGHT

N.P. Murphy, K. Ong, E. Moore, D. Danger. Department of Paediatrics, University of Oxford and Department of Paediatrics, University of Cambridge, UK

**Aims/methods:** Low birthweight is related to features of syndrome X, including hypertension and insulin resistance. In order to distinguish genetic and environmental determinants of these birthweight associations, we measured height, weight, arterial blood pressure (BP) and fasting insulin levels in 16 identical (MZ) and 19 non-identical (DZ) twin pairs (age range 7.2–9.3 years) and compared these values to their birthweights.

**Results:** Age and sex independent standard deviation scores for all variables were calculated and used in all analyses. Between-pair correlations were higher among identical than non-identical twins for birthweight (R for MZ vs DZ: 15% vs 9%), diastolic BP (57% vs 17%), systolic BP (23% vs 2%) and fasting insulin levels (47% vs 27%) indicating significant genetic contributions. Birthweight was inversely associated with diastolic BP (r=-0.26, p=0.03) and systolic BP (r=-0.26, p=0.01) and these relationships were stronger among MZ twins (diastolic BP: r=-0.34, p<0.05; systolic BP: r=-0.48, p=0.007) than among DZ twins (diastolic BP: r=-0.17, p=0.3; systolic BP: r=-0.24, p=0.16). The between-pair discordance in birthweight was also significantly related to discordance in diastolic BP; thus in each pair the twin with the lower birthweight had the higher diastolic BP (r=-0.57, p=0.007) and this effect was similar in MZ and DZ twin pairs. No relationship was seen between birthweight and fasting insulin levels in these twins.

**Conclusions:** In summary, these data indicate the presence of significant genetic contributions to birthweight, BP and fasting insulin levels in childhood, but also non-genetic co-determinants of lower birthweight and higher diastolic and systolic BP.

**P9** ROUTINE NEONATAL EXAMINATION—EFFECTIVENESS OF PAEDIATRICIAN COMPARED TO ADVANCED NEONATAL NURSE PRACTITIONER

T.W.R. Lee, R.E. Skelton, C. Skene. Department of Paediatrics, Hull and East Yorkshire Hospitals NHS Trust, Anlaby Road, Hull HU3 2YJ, UK

**Objective:** To compare the effectiveness of the routine neonatal examination performed by senior house officers (SHOs) and advanced neonatal nurse practitioners (ANNPs).

**Design:** A prospective study of all infants seen in specialist orthopaedic, ophthalmology, and cardiology clinics. A standardised pro-forma was used to record details of birthplace, type of neonatal check with any abnormalities discovered, source of the referral to the specialist clinic, and specialist findings.

**Setting:** Two maternity units, one staffed by paediatric SHOs, one by ANNPs, and 3 specialist clinics in a large district general hospital.

**Participants:** 537 infants were recruited, of whom 527 had undergone neonatal check in the study hospitals.

**Main outcome measures:** Sensitivity and positive predictive values in detecting abnormalities during the neonatal check performed by paediatric SHOs and ANNPs respectively.

**Results:** For hip abnormalities ANNPs displayed a greater sensitivity than SHOs (96% v. 74%; p<0.05). Similarly for eye abnormalities ANNPs were more sensitive (100% v. 33%; p<0.05). There were no significant differences between ANNPs and SHOs in terms of positive predictive values, or effectiveness of detecting cardiac abnormalities. There was no difference in the prevalence of abnormalities between the 2 hospitals.

**Conclusion:** ANNPs are significantly more effective in detecting abnormalities during the neonatal check. This has implications both for future workforce planning and current methods of medical training.

**P10** EVALUATION OF PHENOBARBITONE TREATMENT FOR NEONATAL SEIZURES

G. Boylan, J.M. Rennie, R. Pressler, G. Wilson, C.B. Binnie. Departments of Child Health and Neurophysiology, King's College Hospital, London, UK

**Aims:** To assess the electrographic and electroclinical seizure burden before and after initiation of phenobarbitone therapy in the newborn, because of accumulating evidence that this treatment is ineffective.

**Methods:** Babies who required phenobarbitone had continuous Video-EEG recording. Recordings made one hour before (T0), and hour after treatment (T1), two hours after treatment (T2) and a further hour within 12–24 hours of phenobarbitone (T24) were analysed. The number, duration and type of seizures per hour was calculated.

**Results:** Five out of thirteen babies were in status epilepticus prior to the commencement of therapy. There was no significant change in total seizure burden (electrographic and electroclinical) after therapy. A significant change in seizure type was seen following therapy i.e. clinical signs of seizure decreased (p<0.01) and subclinical or electrographic seizures increased (see fig).

**Conclusions:** Phenobarbitone is ineffective in neonates with seizures. Babies who respond to treatment are more likely to have a normal inter-ictal EEG and a small seizure burden. In babies with a high seizure burden, phenobarbitone causes a reduction in clinically apparent seizures while electrographic seizures often continue or increase.

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**Plenary Session III**

**P7** EFFECT OF MATERNAL NUTRIENT RESTRICTION IN EARLY TO MID GESTATION ON THE PROGRAMMING OF FETAL KIDNEY DEVELOPMENT

**Plenary Session III**

**P9** ROUTINE NEONATAL EXAMINATION—EFFECTIVENESS OF PAEDIATRICIAN COMPARED TO ADVANCED NEONATAL NURSE PRACTITIONER

**P8** BLOOD PRESSURE AND FASTING INSULIN LEVELS IN TWINS; CONTRIBUTIONS OF GENETIC FACTORS AND LOW BIRTHWEIGHT

**P10** EVALUATION OF PHENOBARBITONE TREATMENT FOR NEONATAL SEIZURES
**P11 EVALUATION OF ELEMENTAL DIET THERAPY AS A LONG-TERM STRATEGY FOR MANAGING CROHN’S DISEASE IN CHILDHOOD**

T. Randell, M.S. Murphy. Institute of Child Health, University of Birmingham & Department of Paediatric Gastroenterology, Birmingham Children’s Hospital, UK

**Background:** It is widely believed that elemental diet therapy (EDT) is preferable to corticosteroid treatment in paediatric Crohn’s disease. It avoids steroid toxicity, and short-term studies suggest that it promotes growth. Surprisingly, however, there are no long-term studies of efficacy.

**Aim:** To examine the success in implementing a strategy whereby disease relapses would be managed with EDT in order to avoid steroids.

**Methods:** The subjects consisted of 53 children (aged 3.7–16.9 years, median 11.8) who presented consecutively with active Crohn’s disease and who received a course of EDT as their initial treatment. In each of these cases, subsequent relapses and their management were documented. Follow-up ranged from 0.4–8.2 (median 3.1) years.

**Results:** The initial course of EDT induced a remission in 34/53 (64%). The duration of remission ranged from 2.7–305 (median 21.4) weeks. These 34 children subsequently suffered a combined total of 82 relapses; 21 (26%) of these relapses were successfully treated with EDT, but 60 (73%) were treated with steroids. Of the 19/53 (36%) who failed to enter remission with the initial course of EDT, only 3 ever received EDT again. Overall, only 9 (17%) of the 53 children completely avoided steroid treatment, and 7 of these had never experienced a relapse. The policy of using EDT as the preferred treatment postponed the use of steroids for a median period of only 18.9 weeks. The reasons for using steroids were examined: they included failure of EDT, early relapse following EDT and psychosocial difficulties.

**Conclusion:** The potential benefits of EDT are offset by the considerable difficulty of sustaining this treatment strategy over a prolonged period.

**P12 ABSENCE OF LEUKAEMIC FUSION GENE TRANSCRIPTS IN LEUKOCYTES FROM PRE-TERM BABIES EXPOSED TO DIAGNOSTIC X-RAYS**

P.F. Ravetto, R. Agarwal, M. Chiswick, S. D’Souza, O.B. Eden, G.M. Taylor. Immunogenetics Laboratory, St Mary’s Hospital, Manchester, UK

Exposure of the fetus to diagnostic X-rays is known to increase the risk of childhood leukaemia. Recent advances in neonatal medicine have seen an increase in X-ray exposure to pre-term babies. Our aim was to develop a sensitive molecular technique capable of detecting novel “fusion-gene” transcripts characteristic of childhood leukaemia, and to assess whether fusion-genes occurred in pre-term babies as a result of exposure to X-rays. We collected blood samples prior to, and after, X-ray exposure from pre-term babies (N = 41) born at 24–30 weeks. For comparison, we collected cord blood samples from normal full-term babies (N = 100). Total RNA was extracted from the blood samples and subjected to a “nested” reverse transcription-polymerase chain reaction (RT-PCR) method to amplify TEL-AML1 or MLL-AF4 fusion-gene transcripts that occur in common acute lymphoblastic leukaemia (ALL) and pro-B ALL, respectively. Using oligonucleotide probes, we were able to detect these novel leukaemia-associated genes at a frequency of 1 in a million. Despite mean oligonucleotide probes, we were able to detect these novel leukaemia-associated genes at a frequency of 1 in a million. Despite mean

**P13 DOUBLE BLIND COMPARISON OF 2 DOSES OF BOTULINUM TOXIN A INJECTED INTO THE CALF MUSCLES IN CHILDREN WITH HEMIPLEGIC CEREBRAL PALSY**

R.E. Morton1, F. Polak1, A. Wallace1, F. Doderlein1, A. Molton1, C. Ward1, 1Derbyshire Children’s Hospital; 2Ronnie MacKeith Child Development Centre; 1Gast Lab, Derbyshire Royal Infirmary; 2Queen’s Medical Centre, Nottingham; 3Heidelberg University Clinic, Heidelberg; 4Kings Mill Hospital; 5Academic Dept of Rehabilitation Research, Derby City General Hospital, UK

Intra-muscular injections of Botulinum are increasingly used to reduce spasticity in cerebral palsy and it is important to determine optimal dosage for different muscles. We compared low (8 units per kg) with high (24 units per kg) of Botulinum A (Dysport) injected into the soleus and gastrocnemius muscle in children with hemiplegic cerebral palsy in order to determine the most effective dose without significant adverse effects.

**Method:** Forty Eight children were recruited for the study (ages 4 - 15) in 4 sites (Derby, Mansfield, Nottingham and Heidelberg). They were randomised to 8 units per kg Dysport Botulinum or 24 units Dysport Botulinum per kg injected into gastrocnemius and soleus on a standard protocol. Only the injecting Physician was unblinded to the dosage. Gait analysis was performed prior to the injection and at 4, 12 and 24 weeks afterwards. Parents were asked to fill in an adverse events questionnaire at these times.

**Results:** Calf power did not decrease in any child. Compared with baseline, the mean increase in dynamic gastrocnemius length at 4 weeks in the low dose group (N = 23) was 0.79% (% < 0.01) and for the high dose group (N = 23) was 1.1% (% < 0.01). However there was no significant difference between the 2 groups (P = 0.29). At 4 weeks, ankle dorsiflexion in stance and swing was significantly higher compared to baseline in the higher dose group only (P < 0.001 and P < 0.005 respectively). At 12 weeks the maximum dynamic length of gastrocnemius muscle remained significantly above baseline in the high dose group only (P < 0.001 and P < 0.005 respectively).

**Conclusion:** There was some evidence that the higher dose per kilogram of Botulinum was more effective and lasted longer. The optimal absolute dose range of Botulinum A (Dysport) to the soleus and gastrocnemius muscle in children with hemiplegia was found to be 200 - 500 units given in a concentration 100 units per ml.

**P14 RELATIONSHIP OF BRAIN ALKALINE INTRACELLULAR pH MEASURED BY PHOSPHORUS MAGNETIC RESONANCE SPECTROSCOPY AND ADVERSE NEURODEVELOPMENTAL OUTCOME AFTER NEONATAL ENCEPHALOPATHY**

N.J. Robertson1, F.M. Cowan1, I.J. Cox2, A.D. Edwards1. 1Departments of Paediatrics and Imaging, KSUM, Hammersmith Campus, London, UK

**Aim:** Intracellular pH (pHi) is maintained at 7.03 in normal neonatal brain. We studied the relationship of brain pH, and neurodevelopmental outcome for one year after neonatal encephalopathy (NE).

**Methods:** Repeated brain phosphorus magnetic resonance spectra were obtained in 78 infants during the first year after NE. pH was calculated from the relative chemical shift of inorganic phosphate (Pi) from phosphocreatine. The relationship of pH to Griffiths developmental quotients (DQ) and Optimality Scores (OS) at one year was assessed using appropriate analysis of variance.

**Abstract P14**

<table>
<thead>
<tr>
<th>Griffiths DQ</th>
<th>Mean (sd) pH, ≤ 14 days</th>
<th>Mean (sd) pH, up to 1 year</th>
</tr>
</thead>
<tbody>
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<td>≥85</td>
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<td>7.09 (0.08) (n=45)</td>
</tr>
<tr>
<td>50–84</td>
<td>7.16 (0.09) (n=15)</td>
<td>7.11 (0.08) (n=35)</td>
</tr>
<tr>
<td>&lt;50 or dead</td>
<td>7.27 (0.16) (n=27)</td>
<td>7.16 (0.14) (n=70)</td>
</tr>
</tbody>
</table>

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Results: At ≤14 days there was a significant difference between those with Griffiths DQ >85 and ≤50 or dead (p=0.003) (see table).

Age-corrected pH measured before 20 weeks was inversely related with Griffiths DQ and OS (p<0.05, p<0.001). 33 infants showed a persistent doublet structure of the Pi peak.

Conclusion: Infants with a bad outcome had a prolonged intracellular brain alkalosis. The doublet Pi peak may reflect heterogenous pH in different cells or subcellular compartments. In experimental models exaggerated Na+/H+ transport and cell death can be associated with intracellular alkalosis.

**P15** EFFECTS OF VERY LOW BIRTH WEIGHT (VLBW) ON LUNG FUNCTION IN ADOLESCENCE

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**Aims:** To determine if very low birth weight is associated with reduced lung function in adolescence and if so, whether it is associated with prematurity or intra-uterine growth retardation.

**Methods:** A cohort of 128 VLBW infants and age, sex and school matched normal birth weight controls born in 1980/81 in Merseyside comprise the study population. The index cohort and controls were examined at 15 years of age. For the index cases, birth weight ratio (Observed birth weight / expected birth weight for the gestation) was determined to assess the degree of growth retardation. Vital capacity (VC), Forced vital capacity (FVC), Peak expiratory flow (PEF), Forced expiratory flow in 1 second (FEV1) and Forced expiratory flow when 25%-75% (FEF 25-75) of FVC is expired were measured using a portable spirometer, were adjusted for height and weight.

**Results:** The mean differences between cases and control for VC and FVC were not statistically significant but for FEV1, PEF and FEF 25-75, the difference was highly significant (see table).

**Abstract P15**

<table>
<thead>
<tr>
<th>Lung function (Units)</th>
<th>Difference between means (95% Confidence interval; p Value)</th>
</tr>
</thead>
<tbody>
<tr>
<td>FEV1 (L)</td>
<td>0.23 (0.09-0.37; p&lt;0.001)</td>
</tr>
<tr>
<td>PEF (ml)</td>
<td>37.8 (18.3-57.3; p&lt;0.0001)</td>
</tr>
<tr>
<td>FEF 25-75% (L)</td>
<td>0.55 (0.33-0.77; p&lt;0.0001)</td>
</tr>
</tbody>
</table>

No correlation was found between the birth weight ratio and the lung function among the cases.

**Conclusion:** Very low birth weight is associated with reduction in the lung function in adolescence. The reduction is associated with prematurity rather than intra-uterine growth retardation.

**P16** PRELIMINARY VALIDATION OF A BEHAVIOUR RATING SCALE TO ASSESS PAIN IN CHILDREN WITH SEVERE NEUROLOGICAL IMPAIRMENT

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Children with severe neurological impairment have limited capacity to communicate pain and depend upon others to interpret their pain cues.

**Aims:** To evaluate validity and reliability of a 20-item behaviour rating scale specifically designed to assess pain in this population.

**Methods:** Children with severe neurological impairment (n=29) were filmed at home to provide three-minute episodes of each of five everyday activities. Saliva samples were collected concurrently for cortisol estimation. Three investigators independently rated 145 episodes of film using the assessment scale. 30 episodes re-rated by same investigator.

**Results:** “Known group” validity - Behaviour rating scale score (BRSS) differentiated between a “high” and “low” pain group (Independent samples T-Test, P= 0.009 to .023). Concurrent validity - BRSS correlated with global pain ratings of 1) raters (Pearson’s r .762 to .831 P<.001) and 2) investigators and parents at time of video-recording (Pearson’s r .382 to .765, P= .045 to <.001). Criterion validity - BRSS correlated with salivary cortisol concentration (Pearson's r = .393 to .749, P= .052 to .015). Mean inter-rater agreement (Intra-class correlation (ICC)) was moderate at 0.45 ± 0.16 (range 0.21 to 0.71). Mean intra-rater agreement (ICC) was substantial at 0.73 ± 0.19 (range 0.21 to 0.88). The reliability of the scale overall was .694 (ANOVA P<.001). Two-way ANOVA demonstrated “child” (P<.001) and “activity” (P=0.021) to be significant factors in BRSS but not “rater” (P=.789).

**Conclusion:** The scale has potential as a pain assessment tool for this population. Further validation of the tool is proceeding in clinical settings.

**P17** BEHAVIOURAL AND EMOTIONAL ADJUSTMENT OF TEENAGERS IN MAINSTREAM SCHOOL WHO WERE BORN BEFORE 29 WEEKS GESTATION


**Aims:** Babies born very pre-term are at increased risk of behavioural problems but have not previously been followed beyond middle childhood. We aimed to investigate at age 15–16 behavioural and emotional adjustment of teenagers born before 29 weeks.

**Methods:** We combined three cohorts of babies born before 29 weeks in 1983–4 in Scotland, Northern Region and Oxford. At age 15–16, 80% of survivors from the birth cohorts were traced, and those in mainstream school assessed by parents (n = 143), teachers (n = 120) and teenagers’ self-report (n = 143), using validated, standardised measures of psychological adjustment, compared with classroom controls (n = 107). Scales included Strengths and Difficulties Questionnaire (SDQ), Rosenberg’s self-esteem and Achenbach’s delinquency.

**Results:** Parents rated more index teenagers than controls in the ‘abnormal’ range on SDQ hyperactivity (8.4 vs. 1.0 %; difference 7.4%, 95% CI 2.4 - 12.3), peer relationship problems (18.9 vs. 5.1%; difference 13.8%, 95% CI 6.1 - 21.6) and emotional (18.2 vs. 7.1%; difference 11.1%, 95% CI 3.0 - 19.2), but not conduct problems (10.5 vs. 5.1%; difference 5.4%, 95% CI -1.2 - 12.1). Teachers reported the same pattern, but there were no differences between index and control groups in teenagers’ reports of these problems. Index teenagers reported similar scores on self-esteem as controls but lower delinquency scores.

**Conclusions:** Despite higher levels of parent and teacher-reported emotional, attentional and peer problems than controls, index teenagers do not show more serious conduct disorders or delinquency. Neither do they view themselves as having more problems than their mainstream classmates.
Plenary Session V

**P18** THE EFFICACY OF PEAK FLOW-BASED SELF-MANAGEMENT IN SCHOOL CHILDREN WITH ASThma

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It has not been established whether the addition of peak expiratory flow (PEF) measurement to symptom-based guided self-management for childhood asthma is worthwhile. We set out to answer this question, by means of a randomised controlled trial.

Ninety children, aged 7-14 years in receipt of regular preventer therapy (at least step 2 of the BTS guidelines) were recruited. After a 4 week run up period they were randomised to receive PEF and symptom-based management or symptom-based management alone. Children performed twice daily symptom (all values except PEF for the relevant group were hidden) and completed a symptom diary every morning. They were visited at 4 weekly intervals, for twelve weeks. At each visit quality of life and use of health services was recorded.

There were no differences in mean daily symptom score, lung function, quality of life score or use of health services between the groups over time. During acute episodes, children responded appropriately to changes in symptoms, irrespective of the randomisation group, so that peak flow did not contribute to self-management decisions. The chosen criteria of 70% and 50% (of best PEF) were less sensitive than symptoms.

Knowledge of peak flow did not add significantly to the management of asthma in these children, even during acute exacerbations.

**P19** A RANDOMISED CONTROLLED TRIAL OF INHALED CORTICOSTEROID IN PRE-SCHOOL WHEEZERS—WHO BENEFITS?

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**Introduction:** UK family doctors prescribe inhaled corticosteroids (ICS) to almost 60% of pre-school asthmatics. Do they benefit?

**Aims:** To determine the effect of fluticasone propionate (FP) on airway resistance (R_{aw}) and symptoms in pre-school children with intermittent wheeze and the relationship of response to atopic status.

**Methods:** Children 2-5 years (n=62) with recurrent wheeze completed a randomised double-blind placebo-controlled 6 week crossover trial of FP 100µg bd. Changes in R_{aw}, bronchodilator responsiveness (BDR) and symptoms were outcome measures. Atopy was assessed by serum IgE and skin prick testing (SPT). A 10 week parallel extension was offered.

**Results:** (1) At 6 weeks measurements on FP compared to placebo improved: R_{aw} by 7.6% (95% confidence interval (CI) 3.4%-11.5%, p=0.0007); BDR by 5.6% (95% CI 0.55%-10.4%, p=0.03). (2) Symptom scores were unchanged (% change=0; p=0.75). (3) Response was unrelated to IgE, SPT positivity or initial symptoms. (4) There was no significant difference between 6 and 16 weeks FP (mean difference -1.7% 95% CI -11.6%-9.4%, p=0.75). (5) After stopping FP for 16 weeks, age corrected R_{aw} increased 5.3% (95% CI -2.7%-14.1%, p=0.004) (FP=26 placebo=18 completed).

**Conclusions:** In these children, FP produced a significant improvement of 7.6% in R_{aw} at 6 weeks that was sustained at 16 weeks. Symptoms were unchanged. On stopping treatment R_{aw} increased significantly. Atopic status did not predict response. ICS cause a modest improvement in lung function and may prevent deterioration in children with intermittent wheeze. (Funding: NHS R&D and National Asthma Campaign.)


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**P20** A COMPARATIVE STUDY OF HYPERTONIC SALINE, ALTERNATE DAY AND DAILY rhDNase IN CHILDREN WITH CYSTIC FIBROSIS


Daily recombinant human deoxyribonuclease (rhDNase) is an established, but expensive treatment in cystic fibrosis (CF). There have been no studies of alternate day rhDNase, which if equally effective would reduce the drug cost. Another potential alternative therapy is hypertonic saline (HS) which has improved lung function in short-term studies. We compared the effectiveness of daily rhDNase with HS and alternate day rhDNase in children with CF.

In a randomised, cross-over trial, 48 CF children were allocated consecutively to 12 weeks of daily 2.5mg rhDNase, alternate day 2.5mg rhDNase and twice-daily 5mls of 7% HS. The primary outcome was forced expiratory volume in one second (FEV1). Secondary outcomes were forced vital capacity, number of pulmonary exacerbations, weight gain, quality of life, exercise tolerance, total healthcare cost and sputum inflammatory marker activity.

Mean FEV1, increased by 16% (SD 25%), 14% (SD 22%) and 3% (SD 21%) with daily rhDNase, alternate day rhDNase and HS, respectively. There was no significant difference between daily rhDNase and alternate day rhDNase (p=0.55). However, daily rhDNase showed a greater increase in FEV1, compared with HS (p=0.01). The average difference in 12-week cost between daily and alternate day rhDNase was £493 and between daily rhDNase and HS was £1409. None of the secondary clinical outcomes, including inflammatory marker activity, showed significant differences between the treatments.

Alternate day rhDNase appears as effective as daily rhDNase, with the potential for considerable cost savings. HS is not as effective as daily rhDNase, although there is variation in individual response.
Aims: To use the mechanism of the British Paediatric Surveillance Unit (BPSU) to identify all cases of progressive intellectual and neurological deterioration (PIND) in children, particularly those with features suggestive of variant Creutzfeldt-Jakob Disease (vCJD).

Method: Prospective active surveillance using the BPSU report card commenced in May 1997. Paediatricians are asked to report any child who fulfils the surveillance case definition for PIND. Information is obtained via telephone interview or site visit. All cases are discussed by an Expert Neurological Advisory Group and allocated to a study category.

Results: After three and a half years of surveillance, 1015 children with suspected PIND have been reported. Among them were three fatal cases of vCJD who were all reported in 1999. One girl was aged 12 years at onset - the youngest ever case of vCJD. 696 cases have been discussed by the Expert Group. Of these, 389 have a confirmed underlying cause for their PIND, being categorised into 88 known neurodegenerative diseases. 145 are under investigation. 37 are idiopathic PIND with no further information (eg, died) but have no features of vCJD. 329 are not included (reporting errors, not meeting PIND criteria).

Conclusions: In view of the public health importance of vCJD, it is reassuring that this surveillance has found few children with suspected vCJD. However, three and a half years is a short time in which to draw conclusions, and surveillance continues. Since one probable and two definite cases of vCJD were reported in 1999 there is concern that more childhood cases may appear. The surveillance team is extremely grateful to paediatricians for their support.

Aims: Cardiovascular disease is a major cause of mortality amongst patients with chronic renal failure (CRF). This project was designed to investigate the mechanisms of premature atherosclerosis and a treatment strategy, when the process may be reversible. Homocysteine is associated with accelerated atherogenesis and folate is known to reduce levels in CRF. The clinical benefit of this has not been proven.

Methods: We conducted a double-blind placebo controlled randomised crossover trial of folic acid in 25 normotensive children aged 12±3 (7–17) years with CRF (GFR 26.8±13.2 ml/min/1.73 m²) in whom endothelial dysfunction had previously been demonstrated. We examined the effect of folic acid on the level of total homocysteine and its subsequent effect on endothelial function using an non-invasive ultrasound technique, flow mediated dilatation (FMD). The subjects underwent two treatment periods of 8 weeks separated by a rest period of 8 weeks.

Results: (Mean±SD) After oral folic acid, serum folate levels rose from 11.7±4.2 to 63±51 ng/ml (p=0.001), red cell folate levels rose from 364±195 to 2891±2623 µg/l (p<0.001), total homocysteine fell from 10.28±4.16 to 8.62±2.32 µmol/l (p=0.03) and an improvement in FMD was noted 7.21±2.8 to 8.47±3.01 % (p=0.036). Lag times for LDL oxidation were prolonged during the treatment phase 59.4±18.7 to 68.1±25.9 mins (p=0.01).

Conclusion: Homocysteine levels in children with CRF were within the normal range but were reduced with supra-normal folate levels without side-effects. This produced an improvement in endothelial function as measured by FMD. The mechanism for this may be reduction in antioxidant stress as indicated by the increased resistance of LDL to oxidation during the treatment period.
Aims: To determine whether APPLES, a Primary school based health promotion programme can reduce risk factors for obesity.

Methods: 10 schools in Leeds were paired and randomly allocated to receive APPLES for one year. The programme, underpinned by the Health Promoting Schools philosophy was evaluated in Classes 4 and 5 (634 children aged 7–9 years). It involved teacher training, and the development of individualised School Action Plans aimed at improving diet and physical activity. The process and impact of the programme were evaluated, and individual outcomes in terms of growth, diet, physical activity, and psychological state were analysed taking the cluster effect into account.

Results:

Process and impact—86% of action points in the School Action Plans were achieved, along with positive changes in school meal quality. There was a high level of support from staff and parents. Teachers reported satisfaction with the training, resources and support. Focus groups in intervention schools scored higher for knowledge, attitudes and self-reported behaviour change.

Outcomes—By 24 hour recall, vegetable intake was higher in intervention children (weighted mean difference 0.3 portions/child/day (95% CI 0.2, 0.4)) giving a 50% increase over baseline. No changes were seen in the consumption of fruit, foods high in fat and high in sugar, nor any difference in physical activity levels. No significant difference in BMI scores was observed, and no change in psychological or eating behaviour scores other than an increase in global self-worth for obese children 0.3 (CI 95% 0.3, 0.6).

Conclusions: In this first UK RCT for obesity prevention, APPLES was successful in its implementation, and in producing changes at school level. However, behavioural changes at the individual level were disappointing. In the face of an “epidemic” of obesity, stronger and longer interventions evaluated in larger trials are required.
ANTENATAL HIV TESTING—MAKING A DIFFERENCE

P.A. Tookey1, S. Cliffe2, on behalf of the HIV surveillance teams.1Institute of Child Health, London;1PHLS Communicable Disease Surveillance Centre;2Scottish Centre for Infection and Environmental Health, UK

Aims: The 1998 Intercollegiate Guidelines, recommending a universal offer of antenatal HIV testing, were followed in 1999 by the introduction of national targets for antenatal HIV testing uptake, detection of maternal infection and reductions in vertical transmission (VT). Progress towards these targets is described.

Methods: Confidential obstetric surveillance reports to the National Study of HIV in Pregnancy and Childhood are aligned with data from unlinked anonymous HIV monitoring programmes to estimate antenatal HIV detection rates. Paediatric surveillance of infants exposed to maternal infection monitors VT, and progression to AIDS.

Results: A universal offer of antenatal HIV testing was implemented in London earlier than elsewhere in the UK, and this is reflected in geographical differences in HIV detection rates over time. In London in 1997, maternal infection was diagnosed before delivery in an estimated 35% of 200 births to HIV infected women, rising to 64% of 262 births in 1999; elsewhere in England and Wales 16% and 25% respectively were diagnosed (17% and 30% in the UK as a whole, excluding London). The number of infected women conceiving while on anti-retroviral therapy (ART) is increasing, over 95% of diagnosed pregnant women accept prophylactic ART, and elective caesarean section rates are high. Infection in infants born to diagnosed women is rare and in almost all cases occurs in the absence of ART, or after diagnosis of maternal infection close to delivery. Consequently the number of annual AIDS diagnoses in under-5s has begun to decline in the UK, as occurred earlier in France, Italy, Spain and the USA.

Conclusions: The routine offer of antenatal HIV testing has led to improvements in antenatal diagnosis and reductions in VT in higher prevalence areas. These must be extended across the country if the national targets are to be met.

NRAMP1 POLYMORPHISMS AND SUSCEPTIBILITY TO INTRACELLULAR INFECTION IN THE MALTESE POPULATION


Background: There is convincing evidence that host genetic background is an important parameter in infectious disease susceptibility. In the mouse, resistance or susceptibility to infection with intracellular pathogens is controlled by the Natural Resistance Associated Macrophage Protein (Nramp1) gene which influences the rate of intracellular replication of these parasites in macrophages. Recent genetic studies have shown that allelic variants at the human NRAMP1 locus are associated with susceptibility to leprosy and tuberculosis (TB) and that a functional polymorphism in the promoter region of NRAMP1 drives different levels of gene expression and influences the strength of the inflammatory response.

Aim: to investigate the association of NRAMP1 polymorphisms with susceptibility to intracellular infection in a population from Malta.

Methods: DNA was collected from 174 patients with a past history of intracellular infection (leprosy N = 44, leishmaniasis N = 27, brucellosis N = 65 and TB N = 36) and from 225 healthy, new-born controls. Five polymorphic genetic markers were used to investigate an association of the NRAMP1 gene locus with disease susceptibility.

Results: Significant association was measured between the 2 polymorphisms 5’(GT)n, 1465–86 G/A and brucellosis (p< 0.001, p = 0.03), leprosy (p = 0.03, p = 0.03) and TB (p = 0.01, p <0.001). Additionally, combining results for all four intracellular infections showed that allele 2 of the 5’(GT)n in microsatellite was strongly associated with infection, X² = 20 (p< 0.001).

Conclusion: These results suggest that polymorphisms which regulate expression of a functional protein involved in macrophage activation determine infectious disease susceptibility.