

**Methods:** A contingent model was developed that includes three stages across the first and early second trimesters, using serum markers and NT measurement. NT is only offered if the first trimester serum test result is not reassuring.

**Results:** A total of 1561 women entered into the 12-month screening programme. There was a total 10 cases of Down's syndrome in the screened population, and all (100%) were identified as high risk. The false positive rate was 26/1542 or 1.7% for normal karyotypes, with an additional four cases with other aneuploidies detected. Invasive procedures for maternal age were reduced from 34 per annum before the pilot to a total of five during the 12-month study period. The proportion of women in the screened population in each stage of the screening pathway were as predicted by modelling. Only 22% of women required an NT scan and 94% of women received their results in the first trimester.

**Conclusions:** The pilot suggests that three-stage contingency screening is effective, safe and acceptable for mothers and professionals and implementation is feasible. It performs at least as well as predicted by modelling and will be able to meet the NSC target, while staying within currently available ultrasound resources.

#### 4.5 DNA MICROARRAYS IN THE INVESTIGATION OF ABNORMAL ANTENATAL ULTRASOUND: A PROSPECTIVE PILOT STUDY

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The presence of fetal abnormalities on antenatal ultrasound assessment increases the risk of poor outcome, with an underlying chromosomal abnormality detected in up to 15% of cases. When fetal karyotype is normal, the risk of poor outcome persists; with a nuchal translucency of greater than 4.5 mm the likelihood of having a healthy baby is only 50%.

We hypothesise that a proportion of fetal ultrasound abnormality is caused by an underlying chromosomal imbalance currently undetectable by conventional methods. The limitations of antenatal karyotype are well documented and array comparative genomic hybridisation combines the advantages of a genome-wide screen with the increased resolution of molecular testing.

We have recruited 24 women with abnormal fetal ultrasound. Inclusion criteria are increased nuchal translucency (greater than 3 mm), major structural abnormality or multiple (more than two) soft markers. Routine karyotyping is performed as standard; however, surplus fetal tissue from either chorionic villus sampling or amniocentesis is cultured further for DNA extraction. DNA is further analyzed using a 500 kb resolution BAC-clone DNA microarray (BlueGnome Cytochip). Parental DNA is banked for later confirmation of fetal chromosomal imbalances.

Results from eight microarray experiments have been obtained. Three of eight fetuses had an aneuploidy identified on routine karyotyping. Of the five normally karyotyped fetuses, three had submicroscopic areas of chromosomal gain or loss. Poor quality DNA from cultured placental and amniotic cells increases the background noise in DNA microarray experiments, affecting the interpretation of results. Enhanced DNA extraction techniques and the use of direct fetal tissue improves quality control metrics and aids interpretation.

#### 4.6 GASTROSCHISIS IN THE UNITED KINGDOM: A PROSPECTIVE NATIONAL STUDY OF PREVALENCE, MANAGEMENT AND OUTCOMES USING OBSTETRIC, PAEDIATRIC SURGICAL AND CONGENITAL ANOMALY REPORTING SYSTEMS

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**Background:** The birth prevalence of gastroschisis has increased worldwide; however, incomplete geographical coverage by regional

congenital anomaly registers makes this difficult to study on a national basis in the United Kingdom. The aims of this study were to document the prevalence of gastroschisis nationally and to describe management and outcomes.

**Methods:** Parallel national descriptive studies were conducted using the UK Obstetric Surveillance System (UKOSS) and the British Association of Paediatric Surgeons Congenital Anomalies Surveillance System (BAPS-CASS), commencing in October 2006. Cases were compared with cases reported to the British Isles Network of Congenital Anomalies Registers (BINOCAR).

**Results:** There were 288 cases of gastroschisis identified through UKOSS and BAPS-CASS in an estimated 726 517 total births. Seven further cases were identified through BINOCAR, representing an estimated total prevalence of 4.1 cases/10 000 births (95% CI 3.6 to 4.6/10 000). 284 cases (99%) were diagnosed antenatally; 17 (6%) had additional non-bowel anomalies. The median age of mothers was 21 years (range 16–45). 5% admitted recreational drug use in early pregnancy. 35% had suspected intrauterine growth retardation antenatally, 20% had oligohydramnios and 3% had polyhydramnios. Outcomes are known for 260 pregnancies. Eight were terminated (five fetuses with additional anomalies); one miscarried; there were eight intrauterine deaths (32/1000 births) and seven infant deaths (28/1000 births).

**Discussion:** The national prevalence of gastroschisis estimated from this study is almost double the most recent figure from the National Congenital Anomaly System (NCAS), corroborating reports of under-ascertainment through NCAS. This study suggests the national prevalence of gastroschisis is increasing in line with estimates from BINOCAR.

### Session 4B BAPM/NNS: Brain

#### 4.7 NEONATAL RESUSCITATION AND CHILDHOOD COGNITIVE OUTCOMES

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**Background:** Neonatal encephalopathy has been considered an essential marker for perinatal cerebral injury. However, milder insults may cause subtle defects in functioning. The evidence for the long-term impact of such milder insults is contentious. The aim is to determine whether infants receiving resuscitation after birth have reduced IQ scores in childhood.

**Methods:** The study is based on 11 513 term infants from the Avon Longitudinal Study of Parents and Children. Three groups were defined: infants who received resuscitation at birth but no further neonatal care (n = 818); those receiving resuscitation who developed subsequent encephalopathy (n = 63) and those not requiring resuscitation or further care (n = 10 632). Cognition was assessed at 8 years with a low score defined as an IQ of <80. Results were adjusted for other covariates. Chained equations were used to impute missing values of covariates only.

**Results:** Resuscitated infants without encephalopathy had an increased risk of low global IQ (odds ratio (OR) 1.65 (1.13 to 2.41)) and some evidence for a low verbal IQ (OR 1.41 (0.89 to 2.22)). They had similar performance IQ to the reference group (OR 1.03 (0.75 to 1.42)). Infants with encephalopathy had an increased risk of low global (OR 6.21 (1.59 to 24.33)) and performance (OR 4.60 (1.49 to 14.19)) IQ and weak evidence for an increased risk of a poor verbal IQ (OR 1.95 (0.23 to 16.36)).

**Conclusions:** Infants who received resuscitation had an increased risk of low IQ scores, even if they remained well in the neonatal period. These data are supportive of the "continuum of reproductive casualty" and support the association between mild fetal compromise and cognition.

**4.8 EXTREMELY PRETERM CHILDREN AT 11 YEARS: HOW DO THEY FARE AT SCHOOL?**

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Academic attainment and special educational needs (SEN) were assessed in a whole population of children born <26 weeks in the United Kingdom and Ireland in 1995 (EPICure Study). 219 (71%) of 308 survivors were assessed with a comparison group of 153 classmates born at term (mean age 10 years 11 months). Standardised tests of reading and maths were administered and teachers completed questionnaires regarding academic attainment and SEN provision. Extremely preterm children had significantly lower reading (-18 points; -22 to -15) and maths (-27 points; -31 to -23) scores than classmates. 30% of extremely preterm children were classified with serious impairment (scores -2 SD) in reading and 45% with serious impairment in maths, compared with 1.3% of classmates. 29 (13%) extremely preterm children attended a special school. In mainstream schools, teachers rated 50% of extremely preterm children with performance below the class average in national curriculum subjects compared with 5% of classmates (odds ratio (OR) 18; 8 to 41). 55% of extremely preterm children had SEN compared with 11% of classmates (OR 10; 6 to 18) and 58% received additional educational resources compared with 13% of classmates (OR 10; 5 to 17). 24% of extremely preterm children in mainstream schools in England had a "Statement of SEN" documenting the child's complex learning difficulties and resource needs, compared with 0.8% of classmates (OR 40; 5 to 300). Extremely preterm children are at risk for learning impairments and require a high degree of SEN resource provision at 11 years. Such provision may increase as extremely preterm children approach the transition to secondary education.

**4.9 PATTERN AND TIMING OF BRAIN INJURY ON ADMISSION SCANS ASSESSED USING CRANIAL ULTRASOUND IN INFANTS WITH NEONATAL ENCEPHALOPATHY COMPARED WITH LOW-RISK INFANTS IN MULAGO UNIVERSITY HOSPITAL, KAMPALA, UGANDA**

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**Introduction:** The incidence of term neonatal encephalopathy (NE) in low-resource settings is 8/1000 livebirths.<sup>1</sup> A safety and feasibility study of hypothermia for NE was undertaken at Mulago Hospital.

**Aims:** To assess, using cranial ultrasound (cUS), the pattern and timing of brain injury on admission in infants with NE compared with controls.

**Abstract 4.9**

Results	Study infants (n = 35)	Normal term infants (n = 31)
GA (mean (SD) weeks)	38.1 (1.4)	38.3 (1.3)
Birthweight (mean (SD) kg)	3.27 (0.45)	3.15 (0.6)
Age at scanning (mean, range)	19.84 (1.2–59.1) hours	1.7 (1–4) days
Normal	7 (20%)	25 (83%)
Abnormal WM	6 (17%)	0
Abnormal WM + BG/thalami	16 (46%)	0
Abnormal BG/thalami	6 (17%)	0
Unilateral focal BG/thalami injury	0	5 (17%)
Abnormal scan <24 h	11/24	–
Atrophy	0	0

BG, basal ganglia; GA, gestational age; WM, white matter.

**Methods:** Term infants with NE admitted to the special care baby unit were screened for eligibility and scanned after random assignment using the z.oneUltra cUS machine. Normal term infants were recruited from postnatal wards. cUS data were classified by consensus into one out of eight injury categories from the predominant pattern and severity of change.<sup>2</sup> Abnormality equal to or greater than category 4 within 24 h of delivery suggested injury starting before birth; scans >24 h were not used for such comment.

**Results:** See table.

**Conclusions:** White matter (WM) plus basal ganglia (BG)/thalamic injury is the predominant pattern of abnormality; BG/thalamic or WM abnormality alone occurred less often. Such abnormality did not occur in controls. No established atrophy was seen but the data suggest that injury affecting BG/thalami plus WM may start before birth in 45% of infants with early scans.

1. Ellis. *Paediatr Perinat Epidemiol* 2000;**14**:39–52.
2. Van Wezel-Meijler. *Neuropediatrics* 2007;**38**:1–10.

**4.10 PROTON MAGNETIC RESONANCE SPECTROSCOPY AND THE FETAL BRAIN IN NORMALLY GROWN AND GROWTH-RESTRICTED FETUSES**

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**Introduction:** Proton magnetic resonance spectroscopy (MRS) is a non-invasive technique for assessing the metabolism of human tissue. Brain proton MRS can predict prognosis after perinatal hypoxic ischaemia in neonates: decreased levels of N-acetyl aspartate (NAA), a neuronal marker and high lactate being associated with poor neurodevelopmental outcome.

This study uses advanced MRI techniques to investigate the effects of intrauterine growth restriction (IUGR) on fetal brain development and hypothesises that IUGR will be associated with lower NAA levels and increased lactate in the brain.

**Methods:** Women are scanned at 1.5 Tesla, following conventional imaging, spectra are acquired with a PRESS\_SV sequence at three echo times of 270, 136 and 42 ms. Spectral analysis is performed using JMRUI software. Signals are summed, spectra phased and referenced to the water peak and peaks identified by their chemical shift.

**Results:** To date 13 fetuses have been scanned, four controls and nine with IUGR, one a recent intrauterine death. Median gestational age was 28 + 4 weeks (range 23–34). 13 acquisitions were analyzable, four normal fetuses, nine with IUGR. Demonstrable peaks included NAA, choline, creatine and Myo-inositol in all spectra. Lactate was identified in three fetuses: all severe IUGR including the recent intrauterine death.

**Conclusions:** MRS of the fetal brain is a challenging technique because of fetal motion but shows promise for studying the in-vivo metabolism of the fetal brain. The significance of lactate and its relationship to other parameters of fetal growth and development and placental function is being investigated.

**4.11 TREATMENT WITH COOLING FOLLOWING PERINATAL ASPHYXIA: PRELIMINARY DATA FROM THE UK TOBY COOLING REGISTER**

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The UK TOBY Cooling Register was established in December 2006, following completion of recruitment into the TOBY study. The TOBY study is a randomised trial of whole-body cooling to 33.5°C rectal for 72 h after perinatal asphyxia. 325 babies were recruited to the TOBY study over 4 years and the results of the study will be available after the 18-month follow-up assessment data have been analyzed, late in 2008.

Following completion of recruitment, many TOBY study investigators intended to offer cooling as a treatment for babies

born with neonatal encephalopathy on the basis of existing evidence from published studies.<sup>1</sup> The UK TOBY Cooling Register of treatment with moderate hypothermia was set up in order to collect data about all episodes of induced hypothermia for the treatment of neonatal encephalopathy in the United Kingdom.

The aims of the register are: to determine the likely demand in the United Kingdom for treatment of newborn infants with cooling; to identify adverse events associated with treatment with cooling; to ensure uniform clinical management to a high standard in a high-risk group of infants; to support further clinical trials of neuroprotection after asphyxia.

Since the inception of the register in December 2006, 132 infants have been notified (up to January 2008) from 28 centres. Cooling was initiated at  $x(y - z)^2$  h after birth, and was maintained within the target range of 33–34°C rectal  $x(y - z)\%$ <sup>1</sup> of cooling period.<sup>3</sup> Details of patient characteristics, neurological state, complications and outcome at discharge from hospital will be discussed.

- ▶ 74.3 (interquartile range 61.6–84.9)%.
- ▶ 4 h 15 min (20 min–11:00 h).
- ▶ Data analyzed on 107 patients so far.

**4.12 A RANDOMISED PILOT FEASIBILITY STUDY OF THERAPEUTIC HYPOTHERMIA FOR NEONATAL ENCEPHALOPATHY IN A LOW-RESOURCE SETTING IN EQUATORIAL AFRICA**

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**Background:** Therapeutic hypothermia is a promising therapy for neonatal encephalopathy (NE) in the developed world;<sup>1</sup> results cannot be directly transferred to low-resource settings.

**Aims:** To determine the feasibility of whole-body cooling to 33–34°C for 72 h using simple methods and the temperature profile over the first 80 h in term NE infants undergoing standard care in Mulago Hospital, Kampala, Uganda.

**Methods:** The local ethics committee approved the study. After informed consent, babies were randomly assigned to standard care plus cooling with “cool” water bottles or standard care.

**Results:** Between 27 July 2007 and 31 October 2007, 110 term infants with NE admitted to the neonatal unit were screened. 36 infants were eligible for inclusion (see table).

**Conclusions:** Initial rectal temperatures were similar in therapeutic hypothermia and standard care groups. Screening, randomisation and cooling to 33–34°C over 72 h with water bottles was feasible in this low-resource setting. Suggestions of adverse outcomes make

**Abstract 4.12**

Mean (SD) unless stated	TH (n = 21)	SC (n = 15)
GA at birth (weeks)	38 (1.45)	38 (1.38)
Birthweight (g)	3300 (550)	3200 (268)
Apgar score at 5 minutes	4.7	5.2
Age (min) at randomisation	115	100
Rectal temp at randomisation	33.66 (1.04)	34.43 (1.12) p = 0.06
Mean rectal temperature over 72 h	33.62 (0.69)	36.29 (0.64) p<0.001
HIV-positive (mother) %	14%	13%
Seizures day 2%	29%	13%
Sarnat stage II/III %	43%/33%	57%/0%
Death %	33% (n = 7)	7% (n = 1)

GA, gestational age; SC, standard care; TH, therapeutic hypothermia.

rigorous randomised trials to determine safety and efficacy of therapeutic hypothermia in low-resource settings imperative.

1. **Jacobs S.** *Cochrane Syst Rev* 2007;4(CD003311).

**Session 4C NNA: Positive Parenting**

**4.13 A CRITICAL INCIDENT REPORTING SYSTEM AND AN ANALYSIS OF CRITICAL INCIDENTS IN A LEVEL 3 NEONATAL INTENSIVE CARE UNIT**

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**Introduction:** Critical incident reporting in a neonatal intensive care unit is a vital part of clinical governance to improve the safety and quality of healthcare. Unfortunately these incidents are not analyzed regularly in any meaningful way to get feedback and effect improvements.

**Methods:** At this level 3 neonatal intensive care unit, a critical incident reporting system has been developed in which all reported critical incidents are analyzed at monthly multidisciplinary meetings. They are then entered on a database. Incidents are categorised into classes A–E (A, death/risk of death through to E, incident no injury or inconvenience). This database of 2 years (1 January 2005 to 31 December 2006) was analyzed to determine the causes and patterns in critical incidents.

**Results:** There were 256 discrete incidents reported during this period. Class A incidents accounted for 0.78%, class B 71.5%, class C 8.6%, class D 5.5% and class E 13.7%. 73.4% of incidents were reported by nurses and the rest by doctors. “Clinical” incidents accounted for 86.3% of all incidents, “non-clinical” for 12.1% and “organisational” for 1.5%. “Drug errors” accounted for 47.5% of “clinical” incidents and all were class B category. These included incorrect administration (34.3%), prescription errors (25.7%), missed doses (20.9%) among others. Root cause analysis showed that “accident” (8.6%), “non-adherence to protocol” (8.2%), “communication breakdown” (6.6%) were the commonest reasons for the incidents.

**Conclusions:** In our experience, the critical incident reporting system has been very effective in understanding the reasons for incidents and subsequent handling of such events. In the future it is hoped that the system will be instrumental in reducing them.

**Session 6**

**Session 6A BMFMS: Pregnancy Outcome**

**6.1 THE RELATION BETWEEN SOCIAL DEPRIVATION AND STILLBIRTH CAUSES**

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Social deprivation is an important determinant of poor health. We aimed to identify appropriate health targets by investigating associations between social deprivation and causes of stillbirth in Liverpool Women's NHS Foundation Trust.

**Methods:** All stillbirths occurring between 2004 and 2006 were included in the study and classified with ReCoDe. Maternal postcode was used to determine the index of multiple deprivation (IMD) for each patient. Women in IMD decile 1 (poorest 10% of England) were compared with women in IMD deciles 3–9. Results were analyzed using RevMan v4.2 (see table).

**Results:** 55% of our antenatal population are from IMD 1. We investigated 152 stillbirths. The numbers of observed and expected stillbirths in each IMD decile are similar. 46% of women from IMD 1 are smokers compared with only 7% in the least deprived group. There is a significant difference in the specific causes of stillbirths.

**Conclusions:** Current antenatal management is preventing an excess of stillbirths in the most deprived women. However, to make an impact in decreasing stillbirth rates in the next decade, we need