

Session 4

Session 4A BMFMS: Fetal Medicine

4.1 LOCAL DELIVERY OF VASCULAR ENDOTHELIAL GROWTH FACTOR ADENOVIRUS TO THE UTERINE ARTERY INCREASES VASORELAXATION AND BLOOD FLOW TO THE PREGNANT SHEEP UTERUS LONG TERM

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Introduction: Impaired uteroplacental perfusion causes fetal growth restriction. Our work aims to treat fetal growth restriction by increasing uteroplacental perfusion. Using Doppler ultrasound we previously showed significantly increased uterine blood flow (UBF) 5 days after adenovirus vector-mediated overexpression of vascular endothelial growth factor (VEGF) in the uterine artery. This study investigated the long-term effect of this vector.

Methods: We implanted ultrasonic flow probes (Transonic Inc, USA) around both uterine arteries in mid-gestation pregnant sheep ($n = 6$, 90 days of gestation, term 145 days) and measured UBF telemetrically to obtain baseline data. Five days later we injected adenovirus vectors (5×10^{10} particles) containing the VEGF (Ad.VEGF-A) gene into one uterine artery and β -galactosidase (Ad.lacZ) into the other. UBF was monitored daily until term when a postmortem examination was performed. Uterine artery sections were taken at four levels and studied in an organ bath. We assessed VEGF expression in the uterine artery by ELISA and immunohistochemistry 5 days ($n = 6$) and 30 days ($n = 6$) after vector injection.

Results: By term, (30 days post-injection) UBF increased by 33.3% from baseline in Ad.VEGF-A-injected vessels compared with 16.9% in Ad.LacZ-injected vessels. Ad.VEGF-A-transduced vessels contracted significantly less with phenylephrine (E_{max} 135 SE:12.1 versus E_{max} 156.1 SE:23.3, $p < 0.05$) than Ad.LacZ-injected vessels. The bradykinin relaxation response was not significantly different. VEGF expression was detected by ELISA and was observed in the uterine artery perivascular adventitia by immunohistochemistry at 5 days but not at 30 days after injection.

Conclusions: Adenovirus-mediated overexpression of VEGF increases UBF and uterine artery relaxation long term.

4.2 AMNIOCENTESIS FOR SOFT MARKERS: A 6-YEAR REVIEW 2000–5

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The West Midlands regional policy for the incidental detection of soft markers at mid-trimester ultrasound was introduced in 2002. This comprised karyotyping for either an isolated nuchal pad, multiple other soft markers (echogenic bowel, echogenic cardiac

foci, short femur, pyelectasis and choroid plexus cysts), or a single marker with high previous risk for Down's syndrome. Within the region, all women are offered a dating scan, triple test and an 18–20-week anomaly scan. Routine screening for soft markers is not performed.

All amniocenteses following abnormal scan findings were reviewed, 3 years before and after the introduction of the policy. The indications for karyotyping were grouped into categories summarising the presence of single or multiple soft markers according to the policy. The rates of aneuploidy were generated for each group.

14 875 amniocenteses were performed in a birth population of 381 127 (39.0 per 1000 births); 357 were performed following the finding of one or more soft markers.

In categories in which karyotyping was indicated by the policy, the aneuploidy rate was 14% (7.5% trisomy 21). The highest aneuploidy rate (21%) was in cases of nuchal pad as an isolated ultrasound finding.

There was one Down's syndrome pregnancy in the 6-year period with a single soft marker (excluding nuchal pad). This case had translocation trisomy 21 associated with echogenic bowel following a very low-risk result from private combined first trimester screening.

The policy has been successful in both limiting the number of amniocenteses and in identifying cases with abnormal karyotype.

4.3 FETAL TROPONIN-T AND PRO-BRAIN NATRIURETIC PEPTIDE IN FETUSES OF MOTHERS WITH TYPE 1 DIABETES

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Objective: To determine if fetal serum markers of cardiac function differ between normal and type 1 diabetic pregnancy.

Methods: This is a prospective observational study of 45 type 1 diabetic pregnancies and 39 normal pregnancies with ethics approval. Cord bloods were taken at the time of delivery, centrifuged immediately and stored at -20° until analysis by electrochemiluminescence immunoassay (ECLIA, Roche).

Results: The cord blood pro-brain natriuretic peptide (BNP) and troponin-T levels were higher in the diabetic cohort than in the normal cohort ($p < 0.005$). Pro-BNP correlates positively with troponin-T ($p < 0.0001$), birthweight (0.157, $p < 0.05$) and birthweight centile (0.174, $p < 0.05$). There was no correlation between either fetal troponin-T or fetal pro-BNP and booking or third trimester haemoglobin A1c (see table).

Conclusions: Cord blood pro-BNP and troponin-T are higher in fetuses of diabetic mothers than in the normal population. These data suggest that maternal type 1 diabetes is associated with significant effects on fetal cardiac function, consistent with findings of studies that show fetuses of type 1 diabetes demonstrate cardiomyopathy. Consistently higher values in fetal troponin and pro-BNP in type 1 diabetes suggest that the effects on cardiac function are significant and may contribute to the susceptibility to hypoxia seen in these pregnancies.

4.4 THREE-STAGE CONTINGENCY SCREENING FOR DOWN'S SYNDROME: THE STAFFORD PILOT

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Background: The National Screening Committee (NSC) recommends combined first trimester screening, which requires routine nuchal translucency (NT) scans. Our ultrasound services are, however, constrained by shortages of trained staff and/or funding. We piloted an alternative model that requires less ultrasound resources.

Abstract 4.3

	Normal	T1DM	p Value
Number	39	45	
Pro-BNP (pmol/l)	108 \pm 71	365 \pm 1066	0.005
Troponin T (ng/ml)	0.01 \pm 0.02	0.04 \pm 0.07	0.004
Birthweight (g)	3578 \pm 492	3800 \pm 424	0.035
Birthweight centile	60 \pm 31	84 \pm 18	0.000

BNP, brain natriuretic peptide; T1DM, type 1 diabetes mellitus.

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.¹ 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.² 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.¹ 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 $x(y - z)^2$ %¹ of cooling period.³ 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;¹ 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

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

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.

Abstract 6.1

Causes of stillbirths	IMD 1 N = 80 (%)	IMD 3–9 N = 42 (%)	Odds ratio (95% CI)
Placental abruption	14 (17.5)	4 (9.5)	2.02 (0.62 to 6.56)
Congenital anomaly	15 (18.8)	11 (26.2)	0.65 (0.27 to 1.58)
Fetal growth restriction*	23 (28.8)	5 (11.9)	2.99 (1.04 to 8.55)
Infection	3 (3.8)	2 (4.8)	0.78 (0.13 to 4.86)
Intrapartum asphyxia	2 (2.5)	1 (2.4)	1.05 (0.09 to 11.94)
Maternal reason	3 (3.8)	2 (4.8)	0.78 (0.13 to 4.86)
Placental insufficiency	5 (6.3)	2 (4.8)	1.33 (0.25 to 7.18)
Other specific causes	4 (5.0)	4 (9.5)	0.50 (0.12 to 2.11)
Unclassified	11 (13.8)	11 (26.2)	0.45 (0.18 to 1.15)

IMD, index of multiple deprivation. *Statistically significant.

to increase the awareness of fetal growth restriction in the community and to identify methods to diagnose which fetal growth restriction babies are at risk of stillbirth.

6.2 ADVERSE PERINATAL OUTCOMES AND RISK FACTORS FOR PRE-ECLAMPSIA IN WOMEN WITH CHRONIC HYPERTENSION: A PROSPECTIVE STUDY

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Objective: Prospective contemporaneous data on pregnancies in chronic hypertensive women are sparse; the purpose of this study was to characterise pregnancy outcome and risk factors for superimposed pre-eclampsia.

Methods: Indices of maternal and perinatal morbidity and mortality were ascertained in 822 women with chronic hypertension with data prospectively collected and rigorously validated.

Results: The incidence of superimposed pre-eclampsia was 22% (n = 180) with early-onset pre-eclampsia (≤ 34 weeks' gestation) accounting for nearly half. Delivering an infant <10 th customised birthweight centile complicated 48% (87/180) of those with superimposed pre-eclampsia and 21% (137/642) of those without (relative risk (RR) 2.30; 95% CI 1.85 to 2.84). Delivery at <37 weeks' gestation occurred in 51% of those with superimposed pre-eclampsia and 15% without (RR 3.52; 95% CI 2.79 to 4.45). Using multiple logistic regression, black ethnic origin, raised body mass index, current smoking, booking systolic blood pressure of 130–139 mm Hg and diastolic blood pressure of 80–89 mm Hg, a previous history of pre-eclampsia and chronic renal disease were identified as risk factors for pre-eclampsia.

Conclusions: In the largest study of its kind in chronic hypertensive women, these data demonstrate that the prevalence of infants born small for gestational age and preterm is considerably higher than background rates and is increased further in women with pre-eclampsia. These rates are higher than those previously reported, suggesting that the use of customised birthweight centiles provides a more accurate determination of fetal growth restriction. Smoking is an independent risk factor for superimposed pre-eclampsia, in contrast to the protective effect in low-risk pregnant women.

6.3 TEENAGE PREGNANCY AND MICRONUTRIENT STATUS: A STUDY OF 500 PREGNANT TEENAGERS FROM TWO UK INNER CITY POPULATIONS (THE ATE STUDY)

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Aims: Pregnancy outcome was assessed prospectively in a cohort of UK pregnant teenagers and associations with nutritional status investigated. 500 pregnant teenagers were recruited from two inner-city populations in the United Kingdom.

Methods: Nutritional status was assessed by dietary 24-h recall interviews and measurement of relevant indices in blood samples obtained in the third trimester. Associations with pregnancy outcome were explored using univariate and multiple regression analysis.

Results: 17.6% of babies were born small-for-gestational age (SGA) as assessed by customised birthweight centiles (<10 th centile). 9.0% of infants were born preterm. Maternal iron deficiency anaemia in late pregnancy was highly prevalent (52.1%) and 30.4% of participants had 25-hydroxyvitamin D concentrations <25 nmol/l indicating vitamin D insufficiency. Univariate logistic regression identified several predictors of SGA birth, including low folate status (red cell folate, $p = 0.003$; serum folate, $p = 0.016$; serum total homocysteine, $p = 0.025$) as well as folate dietary intake and raised serum ferritin. Maternal smoking, higher maternal age, low BMI, low gestational weight gain, high BMI at booking were also predictive of SGA birth. Serum total homocysteine was a predictor of preterm birth.

Conclusions: This study suggests that dietary factors may play an important role in poor pregnancy outcome in teenagers from inner-city UK populations. Dietary interventions that increase folate and vitamin D intake in pregnant teenagers should be evaluated in prospective studies.

6.4 MATERNAL OBESITY AND THE RISK OF STILLBIRTH IN SMALL-FOR-GESTATIONAL AGE BABIES IDENTIFIED BY CUSTOMISED BIRTHWEIGHT CENTILES

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Background: Maternal obesity is a risk factor for adverse pregnancy outcome. It is also considered to “protect” against the delivery of a small-for-gestational age (SGA) baby.¹ We wanted to examine this claim by using a customised weight standard.

Methods: The cohort consisted of a comprehensive database of 326 377 routine ultrasound-dated Swedish pregnancies. SGA was defined by two methods: (1) 10th centile based on the Swedish population standard (SGApop); (2) 10th centile customised for maternal height, weight, parity, ethnic origin and baby's sex. Maternal obesity was defined as BMI ≥ 30 . Outcome was assessed by rates of stillbirth.

Results: 22 083 mothers had a BMI ≥ 30 (6.8%) and this group had a significantly elevated risk of stillbirth compared with the non-obese population (odds ratio (OR) 1.99, CI 1.62 to 2.43). This risk was still elevated when babies that were SGA by either method were excluded (OR 1.48, CI 1.16 to 1.88). Being small by both methods (SGApop and SGAcust) resulted in a higher risk of stillbirth (n = 1342; OR 6.06, CI 3.87 to 9.48). However, a similar number of cases was additionally identified by SGAcust and these also had an elevated risk of stillbirth: n = 1332; OR 5.49, CI 3.43 to 8.78.

Conclusions: Maternal obesity represents an increased risk factor for stillbirth, which is much higher when the fetus is SGA. Obesity does not “protect” against SGA, but in fact hides a substantial proportion of babies that can be identified as SGA by a customised standard. These previously unrecognised SGA babies of obese mothers have a high risk of intrauterine death.

1. Cnattingius S, Bergstrom R, Lipworth L, et al. Prepregnancy weight and the risk of adverse pregnancy outcomes. *N Engl J Med* 1998;**338**:147–52.

6.5 MATERNAL AND OBSTETRIC ASSOCIATES OF BEING IN GOOD CONDITION FOLLOWING SINGLETON EXTREMELY PRETERM BIRTH

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Background: A heart rate >100 bpm 5 minutes after birth (HR $>100/5$ min) is independently associated with survival to discharge

Oral presentations

Abstract 6.5 Statistically significant associations from the logistic regression analysis for the outcome livebirth with HR >100/5 min

Item	OR (95% CI)	p Value
PPROM	0.74 (0.55 to 0.99)	0.04
Abruption	0.43 (0.27 to 0.68)	<0.001
Any antenatal steroid	2.09 (1.51 to 2.89)	<0.001
GA per week	1.96 (1.77 to 2.22)	<0.001
Birthweight for GA per 100 g	1.44 (1.26 to 1.64)	<0.001
Cephalic presentation	2.36 (1.80 to 3.09)	<0.001
Vaginal delivery	0.58 (0.39 to 0.86)	0.01
Presence of any paediatric staff	2.64 (1.92 to 3.63)	<0.001

GA, gestational age; HR >100/5 min, heart rate >100 bpm 5 minutes after birth; OR, odds ratio; PPRM, prolonged pre-labour rupture of membranes.

for extremely preterm livebirths in the national datasets collected for the EPICure studies in both 1995 and 2006.

Objective: To identify predictors of favourable neonatal outcome (HR >100/5 min) following extremely preterm birth.

Methods: An extensive dataset of maternal demographic, obstetric and neonatal factors was collected for all births 22 + 0 to 26 + 6 weeks in all English hospitals in 2006. Gestational age was validated using a hierarchical classification of scan dates, certain last menstrual period and working gestation.

Results: Data were collected for 1590 singleton births either born by Caesarean section or alive at the onset of labour of whom 1049 (66%) were liveborn with HR >100/5 (see table).

Conclusions: The only intervention highly associated with a favourable outcome for extremely preterm babies is the administration of antenatal steroids. Babies with placental abruption were much less likely to have HR >100/5 min. The incorporation of this information into clinical decision making remains a challenge for both obstetricians and neonatologists.

Session 6B BAPM/NNS: Lungs and Infection

6.6 A RANDOMISED COMPARISON OF WIDE VERSUS NARROW SATURATION MONITOR ALARM LIMITS FOR CONTROLLING OXYGEN THERAPY IN PRETERM INFANTS

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Background: Saturation monitoring is used widely to guide oxygen therapy. The optimal target ranges are unknown. There is a general aim to minimise hyperoxia, hypoxia and variability. Chosen alarm limits may influence stability because alarm soundings prompt alterations to oxygen therapy.

Aim: To determine whether the width of the alarm limits influences the stability of oxygenation in oxygen-dependent preterm infants.

Methods: Infants born at <29 weeks' gestation and receiving supplemental oxygen were studied between days 3 and 14. Each infant was studied for two consecutive 3-h periods allocated in random order. During one period the alarm limits were set at 80–94%

Abstract 6.6

	Wide (80–94%)	Narrow (86–94%)	Median difference
Mean SpO ₂ (%)	89.3 (88.1 to 90.5)	89.0 (88.6 to 91.8)	0 (–1.9 to 1.7)
% Time SpO ₂ >94%	8.8 (5.3 to 20.4)	12.9 (6.3 to 31.0)	3.8 (–0.9 to 10.2)*
% Time SpO ₂ <86%	16.0 (5.8 to 24.7)	14.4 (9.1 to 24.3)	0 (–8.4 to 6.9)
% Time SpO ₂ <80%	3.8 (0.5 to 7.9)	4.2 (2.0 to 11.8)	0.5 (–1.0 to 6.2)
SpO ₂ variability	5.0 (3.3 to 7.3)	6.2 (4.2 to 10.7)	0.7 (–0.4 to 3.8)*

SpO₂, oxygen saturation.

Data are median (interquartile range). *p<0.05.

and during the other at 86–94%. Saturation values were downloaded to a PC every second. For each period the percentage of time spent with saturation >94%, <86%, <80% and saturation variability (standard deviation) were calculated. Differences within babies between the two periods were analyzed by Wilcoxon test.

Results: See table.

Conclusions: When wider saturation alarm limits were used, babies spent less time with high saturations but no more time with low saturations. These results will facilitate improved oxygen saturation targeting.

6.7 COMPARISON OF LEFT AND RIGHT VENTRICULAR FUNCTION IN TERM AND PRETERM NEONATES USING TISSUE DOPPLER IMAGING

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Background: Tissue Doppler imaging (TDI) enables the measurement of myocardial velocities and calculation of the myocardial performance index.¹² Preterm infants are at risk of cardiac dysfunction but the aetiology and most effective treatments are not clear. This is the first study comparing TDI data from preterm and term neonates.

Methods: 30 neonates (25–41 weeks' gestation) were scanned by a single investigator (RN) on day one of life. TDI waveforms were acquired from an apical four-chamber view using a Doppler pulse-wave sample gate at the lateral tricuspid (right ventricular) and mitral (left ventricular) annuli. Peak systolic, early diastolic and late diastolic velocities were measured. Pulse-wave Doppler data of tricuspid, mitral and left ventricular outflow were obtained from an apical view. Right ventricular outflow was assessed from a parasternal view. Average readings were taken from three to five cardiac cycles. South Birmingham REC gave ethical approval.

Results: Patient data were compared from three gestational groups (n = 10 in each). Myocardial velocities decreased and the derived myocardial performance index increased with decreasing gestation (see table).

Conclusions: TDI enables the quantification of neonatal myocardial function. Velocities from term babies are consistent with published data¹³ and this study provides evidence of relative myocardial dysfunction in preterm infants.

1. Mori K, et al. *Heart* 2004;**90**:175–80.
2. Roberson DA, Cui W. *J Am Soc Echocardiogr* 2006;**19**:1438–45.
3. Ekici, et al. *Echocardiography* 2007;**24**:61–7.

Abstract 6.7

	Tricuspid annulus velocity (mean, SD) (cm/s)			Mitral annulus velocity (mean, SD) (cm/s)		
	S	E	A	S	E	A
Term	6.7 (1.2)	7.2 (1.2)	7.9 (1.7)	5.0 (1.2)	6.2 (1.0)	7.6 (2.5)
32–36 weeks	6.0 (0.9)	6.2 (0.9)	7.9 (1.6)	4.4 (0.7)	5.8 (1.6)	6.2 (2.1)
<30 weeks	4.8 (0.6)	4.0 (1.1)	7.4 (1.6)	3.7 (0.6)	4.3 (0.8)	5.4 (2.5)

6.8 LOW CORD BLOOD MONOCYTES MHC CLASS II EXPRESSION IS ASSOCIATED WITH SEPSIS IN TERM AND PRETERM NEONATES

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Hypothesis: MHC class II expression on monocytes is necessary for immune competence and can be downregulated after an inflammatory stimulus. We hypothesised that MHC class II expression would be decreased in preterm neonates and that low expression would increase the risk of subsequent sepsis.

Abstract 6.8

Patient groups	N	GA (median days)	Median monocyte MHC class II expression % (IQR)
Term labour	33	282	93.9 (84.8 to 97.5)
Term elective Caesarean section	25	272	92.9 (86.8 to 96.7)
Fetocide	20	164	82.7 (75.6 to 89.4)
IUGR	13	201	86.7 (86.3 to 89.6)
PTL	42	186	80.8 (67 to 81.8)* ***
PPROM	48	191	64.6 (39.5 to 72.2)** ***

GA, gestational age; IQR, interquartile range; IUGR, intrauterine growth restriction; PPRM, prolonged pre-labour rupture of membranes; PTL, preterm labour.

* $p < 0.05$, ** $p < 0.005$ compared with fetocide, *** $p < 0.001$ compared with term controls.

Methods: Umbilical cord blood was collected from 181 fetuses born: (1) at term after labour or elective delivery; (2) at < 32 weeks following preterm labour (PTL) and/or prolonged pre-labour rupture of membranes (PPROM); (3) fetal blood taken before fetocides for major anomalies. Inflammatory status was determined from monocyte MHC class II expression, measured using flow cytometry; whole blood was stimulated with *Escherichia coli* lipopolysaccharide and cytokine production quantified at 24 h. Placental histology, neonatal sepsis, morbidity and mortality were recorded.

Results: Monocyte MHC class II expression was lower in all preterm fetuses compared with term controls ($p < 0.001$). Furthermore, MHC class II expression was lower in neonates born after PTL or PPRM ($p = 0.05$, $p = 0.002$, respectively) than fetocide and also in PTL/PPROM with chorioamnionitis ($p = 0.0001$) (see table). In the term control groups seven neonates admitted for investigation of sepsis had significantly reduced class II expression (non-sepsis versus sepsis, median percentage 93.4 (97.4–86.1) versus 41.6 (59.7–38.9) $p = 0.0001$). The septic neonates in the preterm group (PTL and PPRM) also showed significantly low class II expression on cord monocytes (non-septic versus septic preterm neonates, 69 (80.9–46.8) and 49.2 (62.2–30.1), respectively ($p = 0.009$). Lipopolysaccharide stimulation of whole blood from PTL/PPROM groups resulted in significantly lower levels of TNF- α (median and range 265.9 pg/ml (82–389) and IL-6 3493 pg/ml (2423–7893) than term controls (TNF- α 698 pg/ml (279–2633), IL-6 50 000 pg/ml (10 000–66 006) $p < 0.05$) for both fetocide and term). TNF- α production was further reduced in preterm samples when the neonates became septic (41.3 pg/ml (31–127)) compared with gestational matched controls (265.9 pg/ml (82–389) $p < 0.05$).

Conclusions: Monocyte MHC class II expression was lower in premature compared with term neonates and was particularly low after PTL or PPRM (compared with fetocide samples) or exposure to chorioamnionitis. As the MHC class II molecule is important in antigen presentation by monocytes, these low levels of expression may partly explain the immaturity of the neonatal immune system and its susceptibility to infection. In addition, endotoxin hyporesponsiveness in preterm neonates with sepsis suggests immunoparalysis. Reduced expression of monocyte MHC class II and endotoxin tolerance could make the neonate more vulnerable to sepsis.

6.9 UREAPLASMA SPP. OR BACTERIAL COLONISATION ARE ASSOCIATED WITH THE DEVELOPMENT OF CHRONIC LUNG DISEASE OF PREMATURITY

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Antenatal and postnatal infections have been linked to the development of chronic lung disease (CLD) of prematurity. We aimed to determine whether the presence of microbial 16s ribosomal (16s rRNA) genes or *Ureaplasma* spp in lung lavage fluid from preterm neonates is linked to the development of CLD.

Sixty-seven infants < 32 weeks' gestation, ventilated for neonatal respiratory distress syndrome (RDS), underwent serial bronchoalveolar lavage (BAL). BAL fluid was cultured for *Ureaplasma* spp and microbial 16s rRNA genes sought by PCR.

Fourteen infants (21%) had *Ureaplasma* spp in BAL. Two died, 11 developed CLD and three recovered from RDS ($p = 0.012$ CLD versus RDS). The mean gestational age of babies with *Ureaplasma* was $26 + 3$ weeks ± 2 days and of uncolonised babies was $27 + 5$ weeks ± 1 day, supporting the hypothesis that *Ureaplasma* is implicated in the pathogenesis of preterm labour. Culture was the best method of detecting *Ureaplasma*; however, PCR is effective in detecting 16s rRNA genes of other bacteria.

In the first 3 days of life 16s rRNA genes were present in 6/30 babies with RDS and 8/27 babies who developed CLD ($p = 0.4$); however, by 28 days or extubation, 10/30 babies with RDS and 19/27 babies with CLD had evidence of microbial colonisation ($p = 0.005$). *Staphylococcus epidermidis* was the commonest organism in infants with CLD or RDS. Other bacteria were found only in babies who developed CLD.

Ureaplasma spp is significantly associated with the development of CLD. Along with gestational age, microbial colonisation of the airways of preterm ventilated infants is significantly associated with the development of CLD.

Session 6C NNA: Developmental Care

6.10 NEONATAL NURSES' ATTITUDES TOWARDS EXTREMELY LOW GESTATION INFANTS

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Background: As more infants receive intensive care at extremely low gestations, the attitudes that neonatal nurses hold towards extreme prematurity will have a significant impact upon the nursing care that they provide to infants and families.

Aim: This study investigated the factors that may be impacting upon the attitudes of neonatal nurses towards extremely preterm birth.

Methods: Neonatal nurses from bands 5 to 8 working within the Trent Perinatal Network were recruited into a Q study. Nurses completed a Q Sort and follow-up interview. The Q Sort comprised 53 statements developed from literature surrounding extremely preterm birth. The semi-structured interview discussed participants' attitudes towards the Q statements. Q Sort and thematic analysis were used to analyze the data.

Results: 14 out of 48 nurses have currently undertaken the Q study. Emerging themes indicate nurses believe: disability has a profound impact upon infant and family quality of life and should be a factor in decision making; the impact of disability should be made explicit to parents; primary decision making surrounding treatment withdrawal should be undertaken by healthcare professionals; the care of borderline infants can sometimes conflict with their perception of their nursing role.

Conclusions: Current analysis of the interview data has identified common factors that nurses feel influence their care of extremely preterm infants. In order for nurses to provide optimum care, a more open and inclusive approach is needed when dealing with decisions about disability and care withdrawal.

6.11 "THE PROMISE OF CATCH-UP": MATERNAL EXPECTATIONS REGARDING THE NOTION OF "CATCH-UP" IN THE DEVELOPMENT OF PREMATURELY BORN INFANTS

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This presentation explores the phenomenon of catch-up, a term used in relation to the development of prematurely born children. It

discusses how catch-up influences the mothering of children born prematurely at or before 32 weeks of gestational age.

It will provide a definitional drift of catch-up highlighting how the term has drifted from the original specific meaning. It outlines a doctoral study into catch-up in which a thematic analysis associated with the term was developed from Internet discussion boards and e-mail groups that support families with children born prematurely; these themes were tested in interviews with 17 mothers whose children were aged 3, 5 or 7 years living in five primary care trusts in south-west England.

The central analytical theme interprets catch-up as hope, either supporting the mothers' hopes for their children or as a myth that can lead to the promotion of false hopes. This paradox of hope is discussed, referencing Gabriel Marcel, and considers catch-up as a trial with characteristics of captivity, duration, endurance and fluidity.

The presentation concludes by exploring catch-up in relation to amor fati and the associated idea of resentment, as described by Nietzsche, and considers whether amor fati can offer a different way of thinking for mothers and health professionals involved in the care of these children. This way of thinking challenges the more analytical approach currently characterising the life of children in the 21st century in western society and prematurely born children in particular.

Session 8

Session 8A BMFMS: Maternal Medicine

8.1 VASCULAR ENDOTHELIAL GROWTH FACTOR165B AND PRE-ECLAMPSIA

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Introduction: The vascular endothelial growth factor (VEGF) family of glycoproteins plays a key role in the regulation of angiogenesis, vascular permeability and vasodilatation, with high levels occurring in pre-eclamptic plasma. Novel VEGF_{165b} isoforms, formed by alternatively splicing exon 8 of the VEGF gene, are not described in pregnancy. VEGF_{165b} inhibits conventional VEGF₁₆₅-mediated vasodilatation and angiogenesis and increases vessel permeability.

Materials and Methods: We developed an ELISA to measure plasma VEGF_{165b} concentrations using a VEGF_{165b}-specific capture antibody (R&D MAB3045) and a biotinylated pan-VEGF detection antibody. The ELISA is sensitive to 30 pg/ml. We quantified soluble fms-like tyrosine kinase (sFlt1) and soluble endoglin (sEng) concentrations in the same plasma by ELISA.

Results: Pre-eclampsia is associated with an eightfold increase in plasma VEGF_{165b} from first trimester to pre-delivery, compared with a twofold increase in normotensive plasma ($p < 0.0012$). At 12 weeks, VEGF_{165b} was lower in patients who later developed pre-eclampsia compared with normotensive patients. Low first trimester VEGF_{165b} predicts the elevated pre-delivery sFlt1 of pre-eclampsia. sFlt1 and sEng are not useful predictors of pre-eclampsia

Abstract 8.1

Mean 12-week concentration (ng/ml)	Pre-eclampsia	Normotensive	p Value
VEGF _{165b} (±SEM)	0.47 (±209)	4.90 (±1664)	0.0047
sEng (±SEM)	4.11 (±0.54)	4.44 (±0.18)	0.33
sFlt1 (±SEM)	1.27 (±1.76)	1.20 (±73.2)	0.18

VEGF, vascular endothelial growth factor.

at 12 weeks' gestation, because there were no concentration differences in either molecule between the two groups (see table).

Conclusions: Pregnant women who later develop pre-eclampsia have low first trimester VEGF_{165b}. VEGF_{165b} (but not sFlt1 or sEng) may be a clinically useful first trimester serum marker for increased pre-eclampsia risk. The role of VEGF_{165b} in disease pathogenesis remains unknown.

8.2 HAEMODYNAMIC AND PLACENTAL MARKERS TO PREDICT PRE-ECLAMPSIA

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Early identification of women at risk of pre-eclampsia facilitates targeted surveillance and intervention. Changes in some haemodynamic and vascular markers precede the onset of clinical pre-eclampsia.

In a longitudinal study, we prospectively measured uterine artery Doppler pulsatility index (UAD PI), augmentation index (AIx-75—a measure of arterial stiffness) using pulse wave analysis, blood pressure (BP), placental growth factor (PlGF), soluble fms-like tyrosine kinase-1 (sFlt-1), soluble endoglin (sEng), inhibin A and activin A at 22⁺⁰–24⁺⁰ weeks' gestation. We evaluated the ability of these markers, alone and in combination, to predict pre-eclampsia. We measured serum markers using specific ELISA.

Of 205 women recruited, 14 developed pre-eclampsia. Pre-eclampsia cases were matched 1 : 2 to controls.

The data were normally distributed after logarithmic transformation. PlGF was significantly lower and all other markers were higher in women who subsequently developed pre-eclampsia. Data are presented as receiver operator characteristic areas for those variables that best predicted pre-eclampsia: UAD mean PI 0.91 (CI 0.85 to 0.96); AIx-75 0.92 (CI 0.87 to 0.96); PlGF 0.84 (CI 0.72 to 0.97); sFlt-1 0.71 (CI 0.59 to 0.80); sEng 0.79 (CI 0.66 to 0.92); mean BP 0.78 (CI 0.65 to 0.91); sFlt-1/PlGF 0.86 (CI 0.74 to 0.98); sFlt-1+sEng/PlGF 0.85 (CI 0.72 to 0.97); inhibin A 0.72 (CI 0.59 to 0.87); activin A 0.87 (CI 0.8 to 0.94). Multiple logistic regression of different combinations of parameters found that the combination of mean PI, log PlGF and AIx-75 was the best predictor of pre-eclampsia (receiver operator characteristic area 0.98 (CI 0.96 to 1)). For a false positive rate of 5%, this combination has a detection rate of 93%.

A combination of UAD PI, pulse wave analysis AIx-75 and serum PlGF in the second trimester can achieve a clinically useful prediction of pre-eclampsia.

8.3 MINIMALLY INVASIVE HAEMODYNAMIC MONITORING ACCURATELY DEMONSTRATES THE PROFOUND CARDIOVASCULAR EFFECTS OF A 5-UNIT SYNTOCINON BOLUS AT CAESAREAN SECTION

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Introduction: The cardiovascular effects of standard doses of oxytocin were first displayed in a study over 30 year's ago.¹ The potentially dangerous consequences of these effects in pregnant women with either cardiac disease or hypovolaemia secondary to blood loss was highlighted by two related mortalities in the Confidential Enquiries into Maternal Deaths 1997–1999.² Non-invasive tests do not show the true extent of the haemodynamic effects of syntocinon, therefore we used the LidCO Plus system to provide continuous cardiovascular data during Caesarean delivery.

Methods: The trial was approved by the local research ethics committee and 35 uncomplicated healthy women gave written consent to participate. All the women had Caesarean section at

39 weeks under standard spinal anaesthetic and an intravenous bolus of 5 units of syntocinon after delivery of the fetus. Arterial lines were needed for calibration and pulse contour analysis used to obtain continuous data from the LidCO Plus system.

Results: Baseline was defined as the mean value during the last 20 s before the injection of syntocinon. Mean baseline values were: cardiac output (CO) 6.6 l/min, systemic vascular resistance 1155 dynes \times s/cm⁵/m², heart rate (HR) 91 bpm and mean arterial pressure (MAP) 94 mm Hg. At 10 s post-injection profound changes were noted: CO +20%, systemic vascular resistance (SVR) -44%, HR +6% and MAP -20%. Maximal effect was seen at 30 s (CO +28%, SVR -83%, HR +10%, MAP -34%) with values returning to baseline within 130 s.

Conclusions: Small doses of intravenous oxytocin produce profound and rapid changes in maternal haemodynamics at Caesarean section.

1. **Weis FR**, Markello R, Mo B, et al. Cardiovascular effects of oxytocin. *Obstet Gynecol* 1975;46:211-14.
2. **Why Mothers Die 1997-99**. The fifth report of the Confidential Enquiries into Maternal Deaths in the UK. London, UK: RCOG Press, 2001:134-49.

8.4 HYPEREMESIS IN PREGNANCY STUDY: A RANDOMISED CONTROLLED TRIAL OF MIDWIFE-LED "OUTPATIENT" CARE

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Background: Nausea and vomiting (NVP) in pregnancy is a frequent debilitating condition resulting in increased healthcare use and reduced quality of life (QoL). The aim of this pilot randomised controlled trial was to investigate the effect of a complex intervention, rapid rehydration combined with ongoing midwifery support, as compared with routine inpatient care.

Methods: 53 women attending the Maternity Assessment Unit with severe NVP were randomly allocated to intervention (rapid intravenous hydration (3 litres over 6 h), intravenous cyclizine, discharge home with advice leaflet, oral cyclizine and ongoing support involving two telephone calls from a specialist midwife; n = 27) or control (admission and routine care; n = 26) groups. Physical symptoms were measured using the pregnancy unique quantification of emesis and vomiting score (PUQE) on admission and for 7 days. QoL was measured on days 1 and 7 via SF36.v2 score and satisfaction with care on day 7.

Results: Groups were comparable at baseline in terms of demographics, blood and urine results, severity of symptoms and reported QoL. Protocol adherence was greater in the intervention group (93% versus 69%, p = 0.04). There were no differences between the groups on day 7 in terms of mean PUQE score, QoL and satisfaction with care. Re-admission rates were similar, whereas total admission time with NVP was higher in the control group (94 h versus 27 h, p = 0.001). Obstetric outcomes were comparable in the two groups.

Conclusions: This study suggests that a policy of rapid rehydration plus ongoing midwifery support is an effective alternative management option for treating women with severe NVP. A larger randomised controlled trial with economic analysis appears justified.

Session 8B BAPM/NNS: Resuscitation, Early Care and Prematurity

8.5 EPIcure 2: INTERVENTIONS TO STABILISE EXTREMELY PRETERM BABIES AT BIRTH

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Background: Survival of liveborn babies at 23 weeks' gestation in England is low at approximately 13% (EPIcure2, unpublished data);

Abstract 8.5

Gestation (completed weeks)	23	24	25	26	p Value
Total livebirths	318	411	492	541	
Interventions and outcomes by gestation (%)					
Active intervention withheld	17	4	1	1	<0.0001
CPR and/or adrenaline*	11	15	11	6	0.002
Successful intubation by 5 minutes*	62	66	64	61	NS
Heart rate >100 at 5 minutes†	83	83	90	92	0.0013
Died following active support*	24	10	4	1	<0.0001

CPR, cardiopulmonary resuscitation.

*% of all actively supported; †% of those intubated by 5 minutes.

this may reflect reluctance to stabilise and provide intensive care for these babies.

Objective: To record interventions at birth and to study differences between management at different gestations.

Methods: Details of signs of life and interventions at birth were recorded for all births 23 + 0 to 26 + 6 weeks in English hospitals in 2006.

Results: 1762 livebirths were recorded; 318 (18%) at 23 weeks. Although statistically fewer than at other gestations, nonetheless 83% of 23-week gestation infants were offered active support. Of these, similar proportions across gestations were intubated by 5 minutes and more extremely immature babies were given cardiopulmonary resuscitation and/or adrenaline. Good response, assessed by heart rate at 5 minutes was associated with increasing gestational age; there was an inverse relationship between gestational age and the proportion of deaths (see table).

Conclusions: These data refute the suggestion of systematic reluctance actively to resuscitate babies at 23 weeks' gestation.

8.6 SEX-SPECIFIC DIFFERENCES IN CIRCULATING CARBON MONOXIDE AND THE INCREASED INCIDENCE OF HYPOTENSION IN MALE PRETERM INFANTS

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Aim: Carbon monoxide (CO)-mediated cGMP release may result in abnormal vascular resistance and hypotension. With male sex a strong predictor of cardiovascular instability we hypothesised sex-specific differences in circulating CO contribute to the increased incidence of hypotension in preterm boys.

Methods: Infants 24-28 (n = 44) and 29-34 (n = 43) weeks' gestation were studied. Haemoglobin-bound CO (% COHb) was measured by spectrophotometry in umbilical arterial blood and at 24, 72, and 120 h postnatally. Blood pressure was measured invasively and microvascular blood flow determined by laser Doppler flowmetry.

Results: Umbilical COHb was higher in the most preterm infants (p = 0.043) and in boys (p = 0.049). Similar gestational (p = 0.011) and sex effects (p = 0.025) were observed over the first 5 days of life. COHb fell over time (p < 0.001). A negative correlation was observed between COHb and mean arterial pressure at 24 (r = -0.393, p < 0.001), 72 (r = -0.436, p < 0.001) and 120 h of age (r = -0.314, p = 0.009). A positive correlation was observed with microvascular blood flow at 24 (r = 0.495, p < 0.001) and 120 h of age (r = 0.548, p < 0.001). Controlling for gestation and sex, COHb was greater in infants who died in the first week of life at 72 h (p = 0.035).

Conclusions: The relationship between CO, blood pressure and microvascular blood flow are novel findings, not confined solely to sick preterm infants. CO was greatest immediately after birth. Both

inducible heme-oxygenase and non-heme oxygenase-dependent pathways related to oxidative stress may initially play a more central role in carbon monoxide production, with boys more susceptible to oxidative injury and its sequelae.

8.7 PREDICTING NEONATAL MORTALITY: A COMPARISON OF THE CRIB-II SCORE WITH AND WITHOUT TEMPERATURE AT ADMISSION

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Introduction: In 2003 the Clinical Risk Index for Babies was updated as CRIB-II. However, CRIB-II includes admission temperature, which complicates the use of this score as it can be influenced by early neonatal care. This work investigates the ability of CRIB-II with and without admission temperature (CRIB-II_(-T)) to predict in-hospital mortality among very preterm infants.

Methods: All infants born ≤ 32 weeks' gestation and admitted for neonatal care were identified from the Neonatal Survey 2005–2006. Infants with lethal congenital malformations were excluded. Predictive probabilities for mortality were calculated for each infant using the published algorithm for CRIB-II and then recalibrated for CRIB-II and CRIB-II_(-T) using the study data. The predictive abilities of the scores, investigated overall and by groups defined by gestational age and admission temperature, were summarised by c -statistics, Cox's regression and Brier scores.

Results: 3268 infants were included: 317 (9.7%) died before discharge. Using the published algorithm both versions of the score showed excellent discrimination ($c = 0.92$) but under-predicted the total number of deaths (CRIB-II, 255.2: CRIB-II_(-T), 216.6). After recalibration CRIB-II and CRIB-II_(-T) displayed excellent predictive characteristics both overall and for the groups defined by gestation. Whereas CRIB-II_(-T) also displayed excellent predictive characteristics for the groups defined by temperature, CRIB-II showed a statistically significant lack of calibration (Cox's regression 36.1°C to 37.5°C , $p = 0.021$; $\geq 36.0^{\circ}\text{C}$ or $> 37.5^{\circ}\text{C}$, $p = 0.011$).

Conclusions: After recalibration CRIB-II without temperature showed excellent predictive qualities and should be used when benchmarking neonatal care to avoid the risk of results being influenced by early neonatal care.

8.8 THE BLISS CLUSTER RANDOMISED CONTROLLED TRIAL OF THE EFFECT OF "ACTIVE DISSEMINATION OF INFORMATION" ON STANDARDS OF CARE FOR PREMATURE BABIES IN ENGLAND (BEADI)

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Background: Traditional dissemination of information has limited impact on change in practice. Clarification of which dissemination strategies work best in neonatal units is needed. The trial aim was to assess the effectiveness of an innovative active strategy for dissemination of neonatal recommendations.

Methods: Cluster randomised controlled trial, all English neonatal units, randomised by hospital ($n = 182$), stratified by networks and unit level of care. Multifaceted intervention: audit/feedback, interactive educational meetings, organisational changes. Outcomes: hospital policies (hypothermia prevention, resuscitation team at birth) and practices in preterm babies (resuscitation team and surfactant in labour ward, admission temperature). Data: EPICure2 study (baseline), CEMACH survey (post-intervention). Statistical analysis (intention to treat): post-intervention differences between active and control group accounting for clustering effect (practice outcomes).

Results: There were no differences between active/control units in level of care, number of admissions or babies < 1.5 kg per year and between preterm babies in active/control groups in relevant baseline demographics characteristics. There were no significant post-intervention differences between active/control units in hospital policies. There were post-intervention differences in practice for preterm babies: eg, mean admission temperature higher in the active group, mean difference 0.29°C (95% CI 0.22 to 0.55), more use of polyethylene occlusive wrapping 79% versus 62% ($p = 0.05$), more surfactant given in labour ward 78% versus 60% ($p = 0.04$) and a trend to more ideal birth resuscitation teams composition 68% versus 57% ($p = 0.09$).

Conclusions: An innovative "active" strategy for dissemination of neonatal recommendations is more likely to lead to practice changes in preterm babies than current knowledge transfer mechanisms in England.

Session 8C NNA: Feeding Difficulties

8.9 NASAL INJURIES IN PRETERM INFANTS ASSOCIATED WITH CONTINUOUS POSITIVE-AIRWAYS PRESSURE

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Background: Nasal trauma is a recognised complication of nasal continuous positive-airways pressure (CPAP) therapy, but its prevalence and severity has not been compared in controlled trials.

Methods: Preterm infants < 30 weeks gestation and/or < 1500 g at birth, randomly assigned to infant flow driver CPAP (IFD) or bubble CPAP (BCPAP) were followed to assess the incidence and severity of nasal injury. Nasal injury data on all babies were recorded prospectively on a nasal injury scoring chart devised for this study. The severity of nasal injury was graded as mild (1–4), moderate (5–8) or severe (≥ 9). Data were analyzed using t-tests and χ^2 tests.

Results: Records were obtained on 85 infants (IFD 46, BCPAP 39). There was no difference in the gestational age (27.7 weeks in IFD versus 27.6 weeks in BCPAP) and birthweight (1046 g in IFD versus 1024 g in BCPAP) between the two study groups. Half of the study infants sustained moderate (31.8%) to severe (24.7%) nasal injuries. This was similar in the two groups (54.3% on IFD versus 59.0% on BCPAP; $p = 0.668$). The time of worst nasal injury was similar (IFD 4.2 ± 3.9 days versus BCPAP 4.5 ± 5.1 days, $p = 0.813$).

Conclusions: Nasal injury was equally common in babies receiving CPAP with either IFD or BCPAP devices and requires further intervention to reduce its frequency and severity.

Session 9

Session 9A BMFMS: Labour and Delivery

9.1 MYOMETRIAL CONTRACTILITY STUDIES IN DIABETIC PREGNANT WOMEN

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Several studies worldwide have shown a higher Caesarean section rate in diabetic compared with non-diabetic women. Local audit conducted at our hospital revealed an emergency Caesarean section rate of 37.4% compared with 13.2% for non-diabetic women. We

have investigated whether there is an intrinsic contractility problem in the myometria of pregnant diabetic women.

Methods: Myometrial biopsies were obtained during term elective Caesarean section from 20 diabetic and 68 non-diabetic women and were subjected to in-vitro laboratory testing. All the diabetic women had good antenatal glycaemic control. Contractility was measured simultaneously with intracellular calcium signalling using fluorescent Indo-1. Contractility was also measured in 0-glucose solutions and with the addition of 700 pM insulin. Myometrial glycogen content was measured in millimoles.

Results: The entire set of diabetic samples contracted worse than the non-diabetic samples. The amplitude and the duration of contractions were significantly reduced (to $76.6 \pm 6\%$ and $44 \pm 10\%$, respectively, relative to control 100%). Similar changes were observed in intracellular calcium transients. A significant reduction in the glycogen stores (11.3 ± 1.3 mmol) occurred in diabetic samples compared with 16.6 ± 2.0 mmol in non-diabetic samples. In 0-glucose solution, a more rapid reduction in force amplitude and cessation of contractility was observed in the diabetic compared with paired control samples. Myometrial contractility was reduced in both control and diabetic samples exposed to insulin.

Conclusions: Even under standardised conditions, myometrial contractility is worse in term diabetic uteri and may underlie the increased risk of emergency Caesarean section. This may be exacerbated by decreased metabolic reserves.

9.2 A PHYSIOLOGICAL APPROACH TO STIMULATING LABOUR: PULSE, A RANDOMISED CONTROLLED TRIAL OF PULSATILE VERSUS CONTINUOUS OXYTOCIN ADMINISTRATION

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Introduction: Induction and augmentation of labour are associated with high rates of medical intervention. Continuous oxytocin infusion protocols are routinely used to stimulate uterine contractions, but can cause uterine hyperstimulation and fetal distress. As continuous exposure to oxytocin is associated with oxytocin receptor downregulation, pulsatile oxytocin infusion protocols may provide an effective and more physiological approach to stimulation of uterine contractions.

Aim: To improve the current method of oxytocin induction and augmentation of labour. We hypothesised that low-dose pulsatile infusion of oxytocin is associated with lower Caesarean section and intervention rates compared with a continuous oxytocin infusion protocol.

Methods: A randomised controlled trial ($n = 1031$ women) was conducted in two large UK maternity units with local ethics committee approval. Pregnant women requiring oxytocin for induction or augmentation were recruited, with written informed consent, and were randomly assigned to either a continuous or pulsatile (discrete 10 s boluses every 6 minutes) oxytocin infusion protocols. The infusion dose was increased every 30 minutes according to NICE guidelines. Primary outcome measures were Caesarean section rate (induction group) and intervention rate (Caesarean section/instrumental delivery rate for the augmentation group).

Results and Conclusions: In the induction group, Caesarean section rates (38% versus 38%, $n = \text{NS}$) and spontaneous vaginal delivery rates are similar in the pulsatile and continuous infusion groups. As the low-dose pulsatile infusion is as effective as the standard continuous infusion, our results suggest that current clinical protocols for induction should be reassessed.

Funding: GlaxoSmithKline Giving Committee/Tommy's the baby charity).

9.3 RESIDENT OBSTETRIC CONSULTANT COVER: DOES IT MAKE A DIFFERENCE TO VAGINAL DELIVERY RATES OR PERINATAL MORBIDITY?

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NICE and the RCOG recommend 24 h resident consultant cover on the labour ward. At Nottingham City Hospital there was resident on-call consultant cover for 2 days of the week. This study reviews the vaginal and operative delivery rates and perinatal morbidity on the nights with resident consultant cover compared with senior specialist registrar cover.

Methods: Between January 2004 and November 2006 consultants covered 2 nights a week. Nights covered by a consultant were compared with nights covered in the same week by a specialist registrar. We calculated the number of Caesarean sections, operative vaginal deliveries, fetal blood sampling, unexpected admissions to the neonatal unit, arterial cord pH < 7.1 and major post-partum haemorrhage (>1000 ml). Non-parametric tests were used to compare the two groups.

Results: There was a significant increase in the vaginal delivery rate with consultant cover (65% versus 50.9%; $p < 0.05$). There was no difference in the operative vaginal delivery rates, although there were significantly more forceps deliveries with consultant cover. There were more category 2 Caesarean sections with consultant cover, although a reduction in the category 1 Caesarean section rate. There were significantly less fetal blood sampling. There was a lower incidence of low Apgar (7 versus 11; $p > 0.05$), neonatal unit admissions (3 versus 6; $p > 0.05$) and cord pH < 7.1 (4 versus 6; $p > 0.05$) associated with consultant cover, although these changes were not significant. There was a significant reduction in the incidence of post-partum haemorrhage (10 versus 14; $p < 0.05$).

Discussion: Resident consultant labour ward cover is associated with an increase in the normal vaginal delivery rate. This is associated with lower neonatal and maternal morbidity. There is, however, an overall increase in Caesarean sections.

9.4 THE EFFECT OF BARUSIBAN ON PLASMA CONCENTRATIONS AND UTERINE CONTRACTILITY IN THREATENED PRETERM LABOUR: A RANDOMISED, DOUBLE-BLIND, PLACEBO-CONTROLLED TRIAL

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Objective: Atosiban is a mixed oxytocin/vasopressin antagonist with marked tocolytic activity. Preclinical studies suggest that barusiban, a specific oxytocin antagonist, also markedly reduces uterine contractility. The object was to determine plasma concentrations, contractions and side effects following barusiban or placebo in threatened preterm labour (PTL).

Methods: 163 women in threatened PTL (34 + 0–35 + 6 weeks) with cervix ≤ 15 mm were randomly assigned to a single intravenous dose of barusiban (0.3, 1, 3, 10 mg) or placebo. Rescue tocolytics were prohibited. The primary endpoint was women who did not deliver within 48 h. Plasma concentrations were determined by mass spectrometry. Uterine contractions and maternal/neonatal outcomes were determined.

Results: The mean plasma concentrations at 2 h were 11, 39, 139 and 537 ng/ml in women who received 0.3, 1, 3 and 10 mg barusiban, respectively. The concentration was not related to contraction frequency (mean frequency at 2–2.5 h: 4.4, 5.0, 6.6, 5.9 and 6.1 for placebo and barusiban, respectively). There was no

significant difference in the percentage of women who did not deliver within 48 h (72% for placebo and 65%–88% for barusiban groups). Barusiban was well tolerated, although side effects were increased at higher concentrations. Postpartum blood loss and time to lactation were not significantly increased. There were no major safety concerns.

Conclusions: A single dose of selective oxytocin antagonist barusiban (0.3–10 mg) increased plasma concentrations to those calculated to be effective but did not delay delivery or reduce uterine contractions in women with threatened PTL and short cervical length. The results contrast with those of the mixed oxytocin/vasopressin antagonist, atosiban.

9.5 WITHDRAWN

Session 9B BAPM/NNS: Nutrition

9.6 DIFFERENTIAL EFFECTS OF MATERNAL NUTRIENT RESTRICTION ON INFLAMMATION IN RENAL AND ADIPOSE TISSUE IN OBESE JUVENILE OFFSPRING: THE ROLE OF TLR4 AND CCR2

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Introduction: Obesity is associated with a chronic inflammatory state. Key proinflammatory genes involved include Toll-like receptor 4 (TLR4) and chemokine receptor 2 (CCR2). We have previously shown, in sheep, that early-to-mid maternal nutrient restriction protects the kidney from the deleterious effects of juvenile obesity. The extent to which alterations, or differential tissue regulation, occur in these key genes after adolescent onset obesity is unknown. We examined the combined effects of maternal nutrient restriction during pregnancy and early-onset obesity on their distribution.

Methods: Eighteen pregnant sheep were randomly assigned to a normal (C, 7 MJ/day, $n = 8$) or nutrient restricted diet (NR, 3.5 MJ/day, $n = 10$) from days 30 to 80 gestation (term 147 days). After weaning, offspring had restricted activity and increased energy-dense food to promote obesity. Sheep were humanely killed at 1 year and tissues sampled. mRNA abundance of genes of interest in renal and perirenal adipose tissue were measured by real-time PCR. Animal ethics committee approval was given.

Results: Birthweight and weight at 1 year were not different between groups. Both TLR4 (C 1.0 ± 0.2 , NR 2.0 ± 0.3 , $p < 0.05$) and CCR2 (C 1.0 ± 0.2 , NR 3.9 ± 1.1 , $p < 0.05$) were upregulated in perirenal adipose tissue of nutrient restricted offspring but down-regulated in the kidney (C 1.0 ± 0.2 , NR 0.6 ± 0.1 , $p < 0.05$, C 1.0 ± 0.2 , NR 0.4 ± 0.1 , $p < 0.05$, respectively).

Conclusions: Maternal nutrient restriction adversely affects adipose tissue through key proinflammatory genes but conversely protects the kidney from such effects. Identifying the mechanisms may offer potential tissue-specific therapies aimed at reducing the burden of the metabolic syndrome.

Funding: Funded by the British Heart Foundation

9.7 THE EFFECT OF CAESAREAN SECTION AND A SINGLE ENTERAL FEED ON LIVER METABOLISM IN RESPONSE TO TOTAL PARENTERAL NUTRITION

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Total parenteral nutrition (TPN) in neonates frequently causes liver disorders. We have demonstrated that preterm piglets on

TPN for 7 days develop fatty livers.¹ Despite some evidence of differing metabolism between preterm and term neonates, no study has previously compared liver function during TPN in preterm and term neonates, neither have they studied the effect of limited enteral feeding on liver metabolism during TPN.

Piglets were delivered by Caesarean section 4 days preterm (PT) or vaginally at term (T). They received either a single bolus of milk (F) or no enteral nutrition (UF) before commencing TPN. Jugular catheters were inserted 3 h postpartum and piglets were maintained on TPN plus intralipid 20% for 7 days, killed and tissue sampled.

Liver lipid content in preterm piglets was above 5% (w/w), the definition of steatosis,² but was significantly ($p < 0.05$) reduced by pre-feeding (PT-UF 7.6 ± 0.8 ; PT-F 5.2 ± 0.3 ; T-UF 4.2 ± 0.2 ; T-F $3.5 \pm 0.2\%$ (w/w) \pm SEM). Principal component analysis of NMR spectra of liver extracts showed that vaginal delivery at term and/or pre-feeding increased gluconeogenic precursors and ketone production. Phosphoenolpyruvatecarboxykinase activity was increased by feeding and birth (PT-UF 8.59 ± 0.59 ; PT-F 10.25 ± 2.28 ; T-UF 13.62 ± 0.96 ; T-F 12.00 ± 0.49 mU/mg protein).

This suggests that preterm Caesarean delivery results in a failure to switch between anabolic metabolism, seen in late gestation fetuses and glucagon-stimulated catabolic metabolism in term infants, resulting in increased hepatic lipid and glycogen storage (PT-UF 92.9 ± 22.4 ; PT-F 89.6 ± 30.2 ; T-UF 33.7 ± 8.7 ; T-F 47.5 ± 19.1 mg glucose/g tissue). The effects of Caesarean delivery preterm are partly mitigated by enteral feeding.

1. Hyde MJ, et al. *Neonatology* 2008;**93**:77–86.

2. Cairns SR, Peters T. *Clin Sci (London)* 1983;**65**:645–52.

9.8 DOES POSTNATAL GROWTH AFFECT POST-DISCHARGE MORBIDITY IN PRETERM INFANTS?

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Background: Preterm infants are more likely than term infants to develop ongoing morbidity after initial hospital discharge. It is unclear whether this is associated with specific patterns of postnatal growth.

Aim: To study the association between postnatal growth patterns and post-discharge morbidity in preterm infants born at < 33 weeks' gestation.

Methods: Infants recruited from a tertiary neonatal intensive care unit over a 12-month period were prospectively followed until 18 months corrected age. Infants were stratified depending on their change in weight Z-score at 28 days and 18 months resulting in four groups with differing postnatal growth patterns (see table): group 1 (persisting poor growth), group 2 (poor post-neonatal growth), group 3 (post-neonatal catch-up growth) and group 4 (adequate growth). Prospective data on rehospitalisation, general practitioner and A&E visits were compared using non-parametric tests.

Results: 119 infants were recruited and morbidity was analyzed for 108 (92%). There were no significant differences in morbidity. Logistic regression analyzed the association between rehospitalisation and change in weight Z-score (odds ratio (OR) 1.3, 95% CI 0.9 to 1.8; $p = 0.1$), birthweight < 1000 g (OR 2.9, CI 1.1 to 7.5; $p = 0.03$) and cerebral palsy (OR 8.1, 95% CI 1.7 to 38.2; $p = 0.008$).

Conclusions: Postnatal growth pattern was not associated with measures of post-discharge morbidity in this cohort, suggesting that

Abstract 9.8

	Group 1 (n = 16)	Group 2 (n = 18)	Group 3 (n = 24)	Group 4 (n = 50)	p Value*
Z-score change B-28 days	≥ -1	< -1	≥ -1	< -1	
Z-score change B-18 months	≥ -1	≥ -1	< -1	< -1	
Rehospitalisation	1 (0-7)	0 (0-11)	1 (0-10)	0 (0-11)	0.11
GP visits	5 (1-18)	8 (1-18)	8 (1-40)	4 (0-26)	0.25
A&E visits	1 (0-3)	0 (0-4)	0 (0-5)	0 (0-8)	0.91

B, birth. Values are median (range) number of episodes. *Wilcoxon rank sum test.

improving post-discharge growth may not result in measurable health benefits.

9.9 THE EPICURE STUDY: LONGITUDINAL GROWTH MEASUREMENTS OVER AN 11-YEAR FOLLOW-UP PERIOD

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Background: Prematurity is associated with poor somatic growth in infancy but results of longer follow-up are inconsistent.

Aims: To compare serial height, weight, body mass index and occipito-frontal circumference (OFC) of all children born ≤25 + 6 weeks' gestation from 1 March 1995 to 31 December 1995 in the United Kingdom and Ireland with term born classmates.

Methods: Of 1289 livebirths, 283 of 308 survivors were seen at 30 months and 219 (72% of survivors) at 11 years with 153 age and sex-matched controls taken from randomly selected classmates. Measurements were taken by three paediatricians using a Leicester stadiometer, standardised weighting scales and a Secca head circumference tape measure. Measurements were converted to Z-scores using Child Growth Foundation norms for chronological age.

Results: Height, weight, OFC and BMI were significantly lower among preterm children than in their term born classmates, who differed only slightly from population norms; growth in OFC showed the greatest impairment at 11 years. Only growth in weight (and therefore BMI) showed catch-up between the two assessments in 200 children followed longitudinally (see table).

Conclusions: Infants born ≤25 + 6 weeks remain shorter, lighter and with smaller head circumferences compared with controls and population norms at 11 years. Only weight has shown catch-up over the intervening 8 years but the extremely preterm children remain with lower BMI compared with controls.

Abstract 9.9

	EP children Z-score (SD)	Controls Z-score (SD)	Difference of means (95% CI)	Change in Z-score 30 months to 11 years
Height	-0.55 (1.02)	0.15 (1.01)	0.71 (0.50 to 0.92)**	+0.20 (-0.02 to 0.42)
Weight	-0.42 (1.28)	0.21 (1.17)	0.62 (0.37 to 0.88)**	+0.79 (0.53 to 1.05)**
BMI	-0.22 (1.38)	0.17 (1.26)	0.39 (0.11 to 0.66)*	+0.80 (0.52 to 1.08)**
OFC	-1.27 (1.25)	0.15 (0.99)	1.26 (1.02 to 1.50)**	+0.25 (-0.02 to 0.51)

BMI, body mass index; EP, extremely preterm; OFC, occipito-frontal circumference.

*p<0.01; **p<0.001.

Session 9C NNA: Surgical Interventions

9.10 FIRST IMPRESSIONS: THE EXPERIENCES AND PERCEPTIONS OF FATHERS OF THEIR FIRST VISIT TO THE NEONATAL UNIT

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Most fathers in the United Kingdom are present at the birth and immediate care of their baby. When a newborn baby requires admission to the neonatal unit it is generally common practice for the father either to accompany his baby or to visit shortly afterwards. However, there is limited evidence regarding fathers' experiences and feelings about their first visit to their baby in the neonatal unit. Recent directives in the United Kingdom have identified the need to empower and engage fathers. It is therefore important to understand the father's perspective of an occasion such as this.

The aim of this study was to gain an understanding of the experiences and perceptions of fathers when they first visited their baby in the neonatal unit. Semi-structured interviews were undertaken with 20 first-time fathers recruited from one neonatal unit in the United Kingdom. Fathers were asked to describe what happened and their feelings around this time. Their responses were analyzed using qualitative methods. Themes that emerged from the interviews were: the dilemma about the timing of the first visit; the impact of the sights and sounds of the neonatal unit; their recall of information given; the nature and extent of their interaction with the baby and the overall effect that this first visit had upon them.

Knowledge generated by this study will inform healthcare professional education and training and the development of policy and health education. Consequently, the quality of care provision will be enhanced and the needs of fathers more fully addressed.

9.11 NURSING WORKLOAD IN UK TERTIARY NEONATAL UNITS

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Background: Neonatal intensive care requires adequate numbers of trained neonatal nurses to provide safe, effective care; but existing research into the relation between nurse numbers and the care needs of babies is over 10 years old. Since then, the preterm population and treatment practices have changed considerably.

Aims: To validate the dependency categories of the British Association of Perinatal Medicine (BAPM, 2001) and to revalidate the northern region categories (NR, 1993) in relation to contemporary nursing workload.

Setting: Three tertiary neonatal intensive care services in England.

Methods: Direct observations by trained observers captured nursing activity around each baby every 10 minutes. Time spent on each nursing activity was related to the dependency category of the baby and the grade of the nurse.

Results: Both scales detected differences between categories. Discrimination between individual categories was improved when nasal continuous positive airway pressure (nCPAP) was distinguished from ventilation. All categories attracted more time compared with 1993. Babies in BAPM1/NRA occupied nursing time for a median of 56 minutes per hour (inter-quartile range 48-70); those on nCPAP or BAPM2/NRB for a median of 36 minutes per hour, (27-42); those in BAPM3/NRC

for 20–22 minutes (15–33); and those in BAPM4/NRD for 31–32 minutes (24–36). The NR scale was easier to apply and had greater interobserver agreement (98.5%) than the BAPM scale (93%).

Conclusions: Both scales predict average nursing workload. A revised categorisation that separates nCPAP from ventilation is more robust and practical. Nursing time attracted in all categories has increased since 1993.