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; PPROM, 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 feticides 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 PPROM ($p = 0.05$, $p = 0.002$, 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 PPROM) 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 PPROM (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 ressentiment, 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 $VEGF_{165}b$ isoforms, formed by alternatively splicing exon 8 of the VEGF gene, are not described in pregnancy. $VEGF_{165}b$ inhibits conventional $VEGF_{165}$-mediated vasodilatation and angiogenesis and increases vessel permeability.

Materials and Methods: We developed an ELISA to measure plasma $VEGF_{165}b$ concentrations using a $VEGF_{165}b$-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 $VEGF_{165}b$ from first trimester to pre-delivery, compared with a twofold increase in normotensive plasma ($p<0.0012$). At 12 weeks, $VEGF_{165}b$ was lower in patients who later developed pre-eclampsia compared with normotensive patients. Low first trimester $VEGF_{165}b$ predicts the elevated pre-delivery sFlt1 of pre-eclampsia. sFlt1 and sEng are not useful predictors of pre-eclampsia 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 $VEGF_{165}b$. $VEGF_{165}b$ (but not sFlt1 or sEng) may be a clinically useful first trimester serum marker for increased pre-eclampsia risk. The role of $VEGF_{165}b$ in disease pathogenesis remains unknown.

Abstract 8.1

Mean 12-week concentration (ng/ml)	Pre-eclampsia	Normotensive	p Value
$VEGF_{165}b$ (±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.

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 Enquires 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