

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<sub>165b</sub> isoforms, formed by alternatively splicing exon 8 of the VEGF gene, are not described in pregnancy. VEGF<sub>165b</sub> inhibits conventional VEGF<sub>165</sub>-mediated vasodilatation and angiogenesis and increases vessel permeability.

**Materials and Methods:** We developed an ELISA to measure plasma VEGF<sub>165b</sub> concentrations using a VEGF<sub>165b</sub>-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<sub>165b</sub> from first trimester to pre-delivery, compared with a twofold increase in normotensive plasma ( $p < 0.0012$ ). At 12 weeks, VEGF<sub>165b</sub> was lower in patients who later developed pre-eclampsia compared with normotensive patients. Low first trimester VEGF<sub>165b</sub> 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 <sub>165b</sub> (±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<sub>165b</sub>. VEGF<sub>165b</sub> (but not sFlt1 or sEng) may be a clinically useful first trimester serum marker for increased pre-eclampsia risk. The role of VEGF<sub>165b</sub> 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<sup>+0</sup>–24<sup>+0</sup> 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.<sup>1</sup> 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.<sup>2</sup> 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/cm<sup>5</sup>/m<sup>2</sup>, 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 EPICUR 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% (EPICUR2, 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