## 241

### PATENT DUCTUS ARTERIOSUS – IS SURGICAL LIGATION NECESSARY? THE WESTERN AUSTRALIAN EXPERIENCE

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Patent ductus arteriosus (PDA) with a significant left-right shunt is associated with chronic lung disease (CLD), intraventricular haemorrhage (IVH) and necrotising enterocolitis (NEC). Surgical ligation is reserved for PDA refractory to medical treatment, however there is no clear evidence that this improves outcome. WCHS is the only tertiary perinatal/paediatric centre in Western Australia. Geographical isolation from the nearest cardiac surgical centre (3,500kms) has meant that ductal ligation has not been an option until recently. A retrospective data analysis was undertaken to test the hypothesis that outcomes of infants with persistent PDA were no worse than that of those with a closed duct. Patients and Methods: Infants born < 28 weeks gestation between 1/1/2000 and 30/6/2002 were included and divided into three groups: Group 1 - no significant PDA; Group - 2 significant PDA which closed after medical treatment; Group 3 - significant PDA remaining patent after medical treatment. Those outborn or dying within 72 hours of birth were excluded. A significant PDA was defined by a left atrium aortic root ratio > 1.4 or a ductal diameter of > 1.5 mm with a left-to-right shunt. Continuous data is summarised as median (IQR) and analysed with Mann-Whitney and Kruskal-Wallis tests. Duration of ventilation, oxygen and hospital stay were estimated using Kaplan-meier probability estimates and analysed using Cox proportional hazards regression model Results Total 284 infants <28 weeks gestation were included and 32 excluded. Twenty-four (10%) infants died at median (IQR) 15.5 (9–35) days. Relative to Group 1, the infants in Group 3 were at increased risk of death (adjusted OR = 4.01 (95% CI 1.12–14.51) p=0.033). Deaths: Group1=6/154; Group2=7/65; Group3: deaths=11/33. There was no significant difference between groups in the incidence of CLD, CLD or death, NEC, IVH, duration of oxygen or hospital stay but duration of ventilation tended to be longer in Group 3 (adjusted HR 0.66 (95% CI 0.41–1.06) p=0.082. Conclusion: The clinical significance of higher mortality is uncertain but we surmise that infants with a persistent PDA had worse lung disease, which may have contributed to their death. A randomised clinical trial is needed to determine whether surgical ligation will reduce mortality in infants with persistent PDA.

## 242

### DURATION OF BREASTFEEDING AND CHILDHOOD OBESITY IN AUSTRALIAN CHILDREN: A PROSPECTIVE COHORT STUDY

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Childhood obesity is increasing in prevalence and leads to morbidity and mortality in later life. Breastfeeding has been suggested to be protective, with an estimated population attributable risk from formula feeding of 15–20%1. We examined associations between breastfeeding and body mass index BMI in a prospective cohort of 2087 Australian children entering the study at 16 to 18 weeks of gestation. Methods: Characteristics of 2,979 mothers recruited from Perth antenatal clinics between 1989 and 1992 were recorded during pregnancy and 8 years later. Children's weight and length or height were measured at birth, 1, 3, 5 and 8 years; information about breastfeeding was collected at birth, 1 and 3 years. We used NCHS standards to define overweight or obesity in 1 year-olds and the standards of Cole et al2 at 3, 5 and 8 years. Analysis excluded children born before 37 weeks gestation or with congenital abnormalities. Associations between obesity and breastfeeding duration were examined in linear and logistic regression. Findings: Surveys included 1710, 1184, 1480 and 1430 children at 1, 3, 5 and 8 years, respectively. At 8 years 19.6% of girls and 15.4% of boys were overweight or obese. Maternal obesity and smoking during pregnancy were each associated with significantly shorter breastfeeding duration; tertiary education was significantly related to longer breastfeeding duration. In multivariate regression, maternal BMI, education, smoking and parity were significant simultaneous predictors of breastfeeding duration. Breastfeeding duration was inversely related to children's BMI at 1 year (coefficient -0.031,95% CL -0.042,-0.020;p<001) with adjustment for sex, birthweight, gestational age and ethnicity, and remained significant after adjustment for maternal BMI, smoking status, age, parity and education (-0.028,95%CL -0.040,-0.016;p<0.001). Breastfeeding duration was unrelated to BMI in 3 year-olds but was a significant predictor at 5 and 8 years, although not independent of maternal factors. In logistic regression, risk of overweight or obesity at 1 year was lower with breastfeeding for at least 12 months, relative to never breastfeeding, before (OR=0.48,95% CI 0.31,0.76) or after (OR=0.37,95% CI 0.30,0.77) adjustment for maternal factors; associations were not statistically significant at 3, 5, or 8 years. Conclusion: Beyond infancy, genetic factors and health-related behaviours within families may be more influential determinants of BMI than breastfeeding history. 1 Dietz WH JAMA. 2001;16:285:2506–7 2 Cole TJ et al BMJ 2000;320:1240–3

## 243

### CHANGES IN GAS EXCHANGE AND OXYGENATION DURING SURFACTANT ADMINISTRATION USING CONTINUOUS ARTERIAL BLOOD GAS MONITORING

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**Background:** While prophylactic surfactant is an evidence based treatment for infants less than 28 weeks gestation, problems occuring during administration including changes in arterial partial pressure of oxygen and carbondioxide (PaO2 & PaCO2) and drug reflux through endotracheal tube (ETT) have been reported. The volume of a surfactant is relevant to the ease of administration and acceptability to the neonatal lungs. In our experience, surfactants with larger volume can cause hypercarbia and hypoxia associated with ETT obstruction, more frequently with high frequency oscillatory ventilation (HFOV), requiring prolonged intermittent positive pressure ventilation (IPPV) immediately after administration. Curosurf volume (100mg/1.25ml/kg) is considerably smaller than other surfactants (100mg/3–4ml/kg) and administered as a single dose. Larger volumes with fractional doses do not give same enhancement on gas exchange as same total dose given by a single dose. Continuous blood gas monitoring (CBGM) has been proven to provide continuous records of changes in pH, PaO2 & PaCO2 with acceptable precision compared to standard blood gas measurements.

**Aims:** To stydy the changes in pH, PaCO2 & PaO2 during surfactant (Curosurf) administration using CBGM.

**Methods:** Pretrem infants less than 28 weeks with respiratory distress syndrome requiring HFOV who had a multiparameter intraarterial sensor, placed in an umbilical arterial catheter were studied prospectively. Changes were recorded during and 10 minutes after Curosurf administration. The data together with CBGM record printouts are available for discussion.

**Results:** 5 infants (mean gestation 25.8 weeks) were included in the study. All infants tolerated the administration very well with no significant changes in heart rate. In all infants, there were minimal changes in PaCO2 ( mean + 0.18 kPa) 10 minutes after Curosurf. IPPV was applied only for less than 20 seconds and the change in mode of ventilation was not necessary. FiO2 was lower (mean -0.12) with changes in PaO2 (mean - 0.7 kPa) in 10 minutes after Curosurf.

**Conclusions:** This small but important study provides information on effects of Curosurf while it is being given, proven by CBGM. Minimal changes in PaCO2 and minimal interruption in alveolar recruitment on HFOV while surfactant is administered are important in extremely preterm infants' ventilatory management and cerebral circulation. Further studies in these areas with larger number of infants are indicated.

## 244

### EXPRESSION OF CLASS I MHC IN POSTNATAL RAT HIPPOCAMPUS

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Class 1 major histocompatibility complex (MHC-I), known to be essential for immune responses to antigen, was recently shown to be required for connections between retina and central targets in the developing brain and also to play a role for long term potentiation in mature mouse hippocampus. Here we report the postnatal developmental profile of MHC-I in the hippocampus. The study was prompted by the multiple roles of MHC-I in brain and the impact of infection and hypoxia on hippocampus in infancy. Hippocampus was dissected from 5, 20 and 40 day old rats (P5, P20 and P40 respectively) and MHC-I mRNA was determined. We found a significant increase in MHC-I mRNA from P5 to P20, but no further increase between P20 and P40. In P20, a single intraperitoneal injection of either IL-1â or INF-â triggered enhanced transcription of MHC-I mRNA. In studies of MHC-I protein abundance with Western blot, using the monoclonal antibody OX-18, we found a significant increase in immune reactivity of MHC-I enriched in plasma membrane, i.e. the mature form of MHC-I from P5 to P20. No further increase was noted between P20 and P40. Results may have an impact for the understanding of late developmental processes and for the defense systems in the hippocampus region of the infant brain.

## 245

### PREDICTION OF CEREBRAL OUTCOME AT 24 MONTHS IN PRETERM INFANTS BY NIRS IN THE FIRST 24 HOURS AFTER BIRTH

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**Background:** The prognostic value of cerebral NIRS in preterm infants remains controversial. Impaired autoregulation of brain perfusion quantified as high coherence between oscillations of cerebral intravascular oxygenation and arterial blood pressure in sick preterm infants has been related to intracerebral haemorrhage and hypoxic ischemic encephalopathy (Tsuji 2000).

**Aim:** To compare cerebral NIRS parameters during the first 24 hours of life in sick preterm infants with cerebral ultrasound findings and neurological outcome at 9 and 18 months. Patients: 31 preterm infants admitted to our NICU for respiratory distress. Gestational age ranged from 26 1/7 to 32 2/7 weeks (median: 27 2/7) and birth weight from 690 to 2440 g (median: 1030 g).

**Methods:** Total haemoglobin (tHb) and oxygenaton index (OI) was measured with NIRS using a sensor placed fronto-parietally at three time points: 1) within first 6 h, 2) 12 - 16 h and 3) 24 - 28 h. Heart rate, arterial blood pressure (MAP), arterial oxygen saturation and transcutaneous pO2 and pCO2 were recorded simultaneously. Cerebral ultrasound examination (Acuson 128XP, 7 MHz transducer) was performed at 12 to 24 hours of life, at days 3, 7, 14 and every two weeks until discharge. Psycho-motor-developmental index (Bayley, PDI), mental-developmental index (MDI) and the neurological status were assessed in all surviving infants at nine and 18 months corrected for prematurity. A late follow-up examination was done between 3 and 10 years.

**Results:** Nine infants died within the first 10 days. Nine months after expected date of birth 10 out of 20 survivors were classified abnormal with MDI or PDI <85. (Parents of two infants refused the examination). At 18 months corrected for prematurity 3 out of 18 infants had abnormal neurological status. Coherence between OI or tHb and MAP or heart rate did not change significantly between the three session. Intact survivors had significantly higher coherence with 0.6 (IQR 0.38–0.84) than survivors with abnormal neurological status 0.38 (IQR 0.24 – 0.52) and deaths 0.28 (IQR 0.24 – 0.52).

**Conclusion:** In contrast to previous studies low coherencies in the first 24 hours were associated with intraventricular haemorrhage, death or abnormal neurological outcome at 18 months or later. Consistent predictive results are obtained with coherencies between MAP or HR and OI or tHb analysed at 6, 12 and 24 hours after birth.

## 246

### A RANDOMIZED, CONTROLLED MULTICENTER TRIAL OF PORCINE SURFACTANT® FOR TREATMENT OF SEVERE MECONIUM ASPIRATION SYNDROME

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**Background and objective:** Despite improved perinatal monitoring and respiratory care, severe meconium aspiration syndrome (MAS) remains a life threatening respiratory disorder in early postnatal period. Pathogenesis and pathophysiology of MAS involves surfactant dysfunction due to inactivation by meconium at alveolar spaces. There has been no report about efficacy of Curosurf in MAS although a retrospective study revealed certain benefits. We hypothesized that in severe MAS, meconium-induced lung injury and impaired gas exchange may be altered by exogenous surfactant, and conducted this randomized. Controlled, multicenter study. **Subjects and methods:** Sixty-one term infants with severe MAS within 36 hours after birth were enrolled in this trial in nineteen neonatal intensive care services. The infants in the treatment group (n=31) received an initial dose of Curosurf at 200 mg/kg body weight, and repeated doses were given in 200, 100 and 100 mg/kg if a/A of the infant remained <0.20 at 6–12 hours after the previous dose. The primary evaluated parameters were oxygen requirement, ventilator settings, and incidence of complications.

**Results:** The baseline demographic characteristics of the two groups were similar. There was a trend in favour of Curosurf for a more rapid improvement in blood oxygenation (Figure). The mean oxygenation index (OI) in the Curosurf group was significantly lower than the baseline value starting from the assessment at 1 hour. The number of infants with OI <10 in the Curosurf group was numerically higher than that in the control group ($p<0.05$ at the assessment of 24 hours post-administration). The a/A ratio at 24 hours was increased >100% compared to baseline in 24/29 (83%) infants treated with Curosurf and in 12/25 (48%) infants in the control group ($p<0.05$). Other secondary efficacy variables: reduction of MAP by ≅ 2 cm $H_2O$ at 24 and 72 hours, duration of mechanical ventilation, cumulative exposure to oxygen, did not show significant differences between groups. The survival rate was 30/31 and 27/30 in the Curosurf and control group, respectively. The incidence of complications did not differ between groups.

**Conclusion:** Surfactant replacement therapy improved oxygenation and did not increase complications in the study subjects, suggesting that surfactant is effective and safe for treatment of severe MAS in term infants.