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0008NEO

PRESCHOOL OUTCOME IN CHILDREN BORN VERY PREMATURELY AND CARED FOR ACCORDING TO NIDCAP

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Background/aim: Care based on the Newborn Individualized Developmental Care and Assessment Program (NIDCAP) has been reported to exert a positive impact on the development of prematurely born infants. The aim of the present investigation was to determine the effect of such care on the development at preschool age of children born with a gestational age of less than 32 weeks. **Method:** All surviving infants intended to treat in a randomized controlled trial (11 in the NIDCAP group and 15 in the control group) were examined at 66.3 (6.0) months corrected for prematurity, mean (SD). In the assessment we employed the Wechsler Preschool and Primary Scale of Intelligence-Revised (WPPSI-R) for cognition, Movement Assessment Battery for Children (Movement ABC) for motor function, subtests of the NEPSY test battery for behavior, and the WHO definitions of impairment, disability and handicap. Mann Whitney test was employed for the continuous variables and an exact logistic regression for the Odds Ratios, correcting for gender, gestational age, relative birthweight and levels of parental education. **Results:** There were no significant differences between the intervention group in Full-Scale IQ 93.4 (14.2) [mean (SD)] vs. the control group 89.6 (27.2), Verbal IQ 93.6 (16.4) vs. 93.7 (26.8) or Performance IQ 94.3 (14.7) vs. 86.3 (24.8). The Odds Ratio (OR; 95% CI) survival without overall disability was 14.7 (0.8->100) in favor of the NIDCAP group. The corresponding OR for surviving without mental retardation was 3.5 (0.7->100) and for surviving without abnormal behavior 19.9 (1.1->100). **Conclusion:** Although we could show a significant impact on the NIDCAP group only in the behavioral aspect of development there were tendencies in the same direction for general cognition and incidence of disability.

0009NEO

PARENTERAL NUTRITION ASSOCIATED CHOLESTASIS(PNAC) IN LBW NEONATES.

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Background/aims: PNAC, though multifactorial in etiology, may be associated with abnormal aminoacid (AA) intake, excess or deficiency, & an excess of Intralipid (IL). Prolonged administration of IL in premature baboons resulted in steatosis, cholestasis (CH), & proliferation of bile ducts in the liver in a dose dependent manner. In neonates receiving PN, possible relationships between serum direct bilirubin(DB) & AA or IL amounts have not been evaluated. We hypothesized that low birth weight (LBW) infants with CH would have received higher amount of AA or IL than those without CH. **Methods:** Twenty two newborns with CH(ges. 29.8±1.6wk, bir wt 1298±217g) were compared with 22 without CH (29.5±1.7wk, 1286±363g). CH was defined as a direct bilirubin(DB) >2mg/dl.; other causes of CH including primary liver disease or mechanical causes were excluded. In CH vs non-CH, peak DB was higher(4.6±2.4 vs 1.2±0.2mg/dl, p<.0001), & PN dur was longer(36.5±1.4 vs 19.2±9.8d, p<.0001). Clinical risk factors were analyzed by multiple logistic regression analysis, & amounts of AA & IL, average daily or total, were analyzed. **Results:** Dur of fasting & PN, (+)C-reactive protein, feeding intolerance, average daily IL amount, total AA & total IL amount were significantly associated with PNAC. Average daily AA amount was similar between groups, whereas average daily IL amount was significantly higher in CH vs non-CH(2.2±0.3 vs 1.8±0.4g/kg/d, p=0.002). Total AA & total IL amounts were significantly higher in CH vs non-CH, respectively(AA, 66.8±24.1 vs 35.6±21.2g/kg, p<.0001;IL, 81.2±29.1 vs 36.5±21.5, p<.0001). Serum peak DB was positively correlated with total AA amount [DB=0.865+0.044xAA(g), r=.500, p=.0014], total IL amount [DB=0.204+0.048xIL(g), r=.677, p<.0001], or average daily IL amount [DB= -3.67+3.36xIL(g/kg/d), r=.529, p=.0006]. **Conclusions:** Since serum DB increased with increasing total infusion of AA or IL in a dose dependent manner, we suggest that cumulative toxicity of AA & IL may result in PNAC in LBW infants. We speculate that decreasing the cumulative load of AA & IL could possibly attenuate severity of hepatic pathology in PNAC.

0011NEO

EFFICACY OF ERYTHROPOITIN IN PREMATURE INFANTS

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Objective: To identify the effect of early of parentral recombinant human erythropoitin (r-HuEPO) and iron administration on blood transfusion requirement of premature infants. **Methods:** In a controlled clinical trial conducted at the Neonatal Intensive Care Unit, Al-Hada Military Hospital, Taif, Kingdom of Saudi Arabia over a 16 month period. We assigned 20 very low birth weight infants (VLBW) with gestational age of (mean ± SEM 28.4 ± 0.5 weeks and birth weight of (mean ± SEM 1031 ± 42 gm), to receive either intravenous (r-HuEPO 200 U/kg/day) and iron 1mg/kg/day or conventional therapy over 21 days study period. Blood transfusion administration under goes a strict protocol in our nursery. **Results:** During the three weeks study period, the hemoglobin and heamatocrit remained similar in the two groups while the reticulocyte counts were greater in the (r-HuEPO) recipients on day 14.The number and volume of blood transfusions were similar in both groups. **Conclusion:** VLBW infants receive fewer blood transfusions than the number previously reported. Strict pheloptomy and transfusion criteria could minimize the need r-HuEPO.

0012NEO

TITLE:ENDOTHELIAL ACTIVATION IN PRETERM INFANTS WITH CHORIOAMNIONITIS AND FUNISITIS

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Aims: Chorioamnionitis and funisitis are associated with preterm labour and postnatal morbidity. Endothelial cell adhesion molecules play a crucial role in transmigration of leukocytes. E-selectin is involved in rolling whereas ICAM-1 and VCAM-1 are essential for adhesion. We investigated whether chorioamnionitis in preterm infants induced the expression and shedding of adhesion molecules in the umbilical cord and increased the concentrations of E-selectin, ICAM-1, interleukin (IL)-1 beta, IL-6 and IL-8 in the cord blood. **Methods:** Immunohistochemistry was performed on paraffin-embedded umbilical cord sections. For E-selectin and VCAM-1 the positive cells per vessel were counted, for ICAM-1 the intensity of staining was measured by a four-step semi-quantitative scale. Concentrations of cytokines, E-selectin and ICAM-1 were measured by ELISA. The patients were divided into 3 groups according to histology: chorioamnionitis with funisitis (n=11; birth weight (BW) median 860g, 95% confidence interval (CI) 588-1516g; gestational age (GA) median 26 wks, CI 22–31 wks), chorioamnionitis without funisitis (n=9; BW median 950g, CI 632-1704g; GA median 28 wks, CI 24–31 wks) and a control group without infection (n=12; BW median 865g, CI 581-1596g; GA median 26 wks, CI 23–31 wks). **Results:** E-selectin expression on arterial and venous endothelium was restricted to 3 cases, all in the chorioamnionitis and funisitis group. VCAM-1 was detected in 8 out of 11 cases with chorioamnionitis and funisitis (median artery 1.3 pos. cells, CI 0–20.2 pos. cells), in 4 out of 9 cases with chorioamnionitis alone (median artery 0 pos. cells, CI 0–0.4 pos. cells; p<0.05) and in 1 out of 12 cases in the control group (median artery 0 pos. cells, CI 0–0.4 pos. cells; p<0.005). The expression on the venous endothelium showed an identical distribution between groups. ICAM-1 was expressed on the endothelium of all investigated vessels, but arterial expression was higher with chorioamnionitis and funisitis (median 2.5, CI 2.3–3.4) compared to chorioamnionitis alone (median 2.1, CI 1.6–2.5; p<0.001) or control group (median 2.0, CI 1.4–2.5; p<0.005). Similar expression patterns were found in the venous endothelium, vascular walls and Wharton's Jelly. The concentrations of soluble ICAM-1 and E-selectin in cord blood were higher with chorioamnionitis and funisitis (median 242.3 ng/ml, CI 111.5–509.4 ng/ml and median 66.3 ng/ml, CI 27.1–245 ng/ml, respectively) than with chorioamnionitis alone (median 123.5 ng/ml, CI 98.2–206.3 ng/ml; p<0.005 and median 43.1 ng/ml, CI 14.8–117.3 ng/ml; p=0.05, respectively) or in the control group (median 116.3 ng/ml, CI 77.4–163.8 ng/ml; p<0.001 and median 19.1 ng/ml, CI 9.3–84.8 ng/ml; p<0.005, respectively). Similarly, concentrations of IL-1 beta, IL-6 and IL-8 were increased with chorioamnionitis and funisitis. **Conclusion:** Chorioamnionitis alone did not cause an up-regulation of adhesion molecules or an increase in proinflammatory mediators. However, chorioamnionitis with funisitis resulted in systemic inflammation and endothelial activation with expression of E-selectin and VCAM-1 on the endothelium of vessels and up-regulation of ICAM-1 expression in all compartments of the umbilical cord. Shedded ICAM-1 and E-selectin resulted in higher concentrations in the cord blood. We speculate that the activation of endothelium in chorioamnionitis and funisitis may not be limited to the umbilical cord but may also involve other organs of the preterm infant and may therefore play a crucial role in neonatal morbidity.

0019NEO

EEG ABNORMALITIES PRECEED IVH IN VERY LOW BIRTH WEIGHT INFANTS

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Background: Neurological morbidity has been linked to the extent of intraventricular haemorrhage (IVH) in very low birth weight infants. About half of IVHs occur more than 24 hours after birth. Changes in cerebral blood flow may be one of the risk factors for IVH. These changes may be detected by electroencephalography (EEG). The prolongation of inter-burst interval in EEG of premature infants has been linked to subsequent neurological morbidity. **Aim:**To examine if EEG predicts the occurrence of IVH more than 24 hours after birth in very low birthweight infants. **Methods:** Premature infants with birthweight < 1500 grams and normal cranial ultrasound scan for the first 24 hours after birth were included. Four-channel digital EEG was performed intermittently on the first four days after birth. Silver-silver chloride electrodes were placed at Fp1, Fp2, C3, C4, O1 and O2 positions. Simultaneous ECG was recorded. EEG recordings were reported by two of the authors (MB and REA), who were blinded to the cranial ultrasound scan results. Criteria used to evaluate EEG included asymmetry, asynchrony, amplitude, presence of transients and length of inter-burst interval. Cranial ultrasound scans were performed every day during the first four days after birth. **Results:**17 very low birthweight infants with normal cranial ultrasound scans on the first day after birth were included. Six infants had abnormal EEG. Only four of these infants developed IVH (1- bilateral subependymal haemorrhage; 1- bilateral IVH with no ventricular dilatation; 1- left IVH with ventricular dilatation and right IVH with ventricular dilatation and parenchymal involvement; 1- bilateral IVH with parenchymal extension on the left). None of the infants with normal EEGs developed IVH. The sensitivity and specificity of an abnormal EEG (based on amplitude and degree of inter-burst interval) to detect a subsequent IVH was 100% and 85% respectively. The positive and negative predictive value for an abnormal EEG to predict the occurrence of subsequent IVH was 66% and 100% respectively. Asymmetry, asynchrony and presence of sharp transients by themselves were not useful criteria for prediction of IVH. **Conclusions:** Prolonged inter-burst interval and low amplitude of EEG in the presence of normal cranial ultrasound may predict the subsequent occurrence of IVH in very low birth weight infants. These changes may be due to altered cerebral perfusion. This observation may provide an opportunity for targeted neuroprotective management.

0020NEO

HAEMODYNAMICS, EEG AND OXYGEN EXTRACTION IN PRETERM INFANTS

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Background: Hypotension has been linked with adverse neurological outcome in small sick newborn infants but the level of blood pressure at which brain damage occurs is uncertain. Hypotension by its presumed effect on decreasing cerebral blood flow and oxygen delivery may alter cerebral electrical activity. Prolonged inter-burst interval in electroencephalography (EEG) has been related to adverse neurological outcome. **Aim:** To examine the relationships between haemodynamic variables, background cerebral electrical activity and cerebral fractional oxygen extraction (CFOE). **Methods:** A prospective, observational study on infants between 24 and 30 weeks' gestation. 4 channel digital EEG recordings were performed for 1 hour on the first day after birth. Simultaneous measurements of left (LVO) and right ventricular output (RVO) were made using echocardiography. CFOE was measured by near infrared spectroscopy. The EEG was analysed by (a) spectral analysis by Fast Fourier Transformation to give Relative (RP) and Absolute Power (AP) of delta (0–3.5 Hz), theta (4–7.5 Hz), alpha (8–12.5 Hz) and beta (13–30 Hz) bands, and by (b) manual calculation of median, maximum and percentage inter-burst interval. Multiple stepwise linear regression was used. Gestational age, age at recording, mean blood pressure, LVO, RVO, arterial pH, arterial pO_2, arterial pCO_2, cord base excess, CRIB score, presence of significant intraventricular haemorrhage (grade 2 or more) and use of morphine were entered as predictor variables. RP and AP of each band, inter-burst interval and CFOE were entered as outcome variables. **Results:** 30 infants were studied. Three infants with electrical seizures were excluded. LVO measurements of 6 infants with large patent ductus arteriosus (>2.5mm) were deleted from the analysis. Only 14 infants had CFOE measurements. Changes in arterial pCO_2 were associated with changes in RP of beta ($r=0.6$, $p=0.007$), RP of delta ($r=-0.6$, $p=0.002$), log median inter-burst interval ($r=1$, $p<0.001$), maximum inter-burst interval ($r=0.6$, $p=0.01$) and percentage inter-burst interval ($r=0.6$, $p=0.008$). Changes in arterial pCO_2 was also associated with changes in CFOE when age of recording was considered ($beta=-0.6$;$R=1.0$; $p<0.001$). Fall in blood pressure decreased the RP of delta when changes in pCO_2 and extent of haemorrhage were controlled for ($beta=0.3$, $R=0.9$, $p<0.001$). **Conclusion:** pCO_2 has a powerful effect on CFOE and EEG. EEG becomes more discontinuous with hypercarbia. The premature brain appears to adapt to hypocarbia by increasing CFOE but this response is absent at high levels of pCO_2. Blood pressure had only a small effect on EEG.

0024NEO

CONTINUOUS MEASUREMENT OF THE CEREBRAL FRACTIONAL OXYGEN EXTRACTION

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Objective: To evaluate the relation between cerebral tissue oxygenation index (TOI), measured with spatially resolved spectroscopy, and the different oxygenation parameters. To describe the influence of $PaCO_2$, arterial haemoglobin concentration (Hb), temperature and mean arterial blood pressure (MABP) on cerebral TOI. A new parameter, FTOE, is introduced as a measure of the fractional oxygen extraction (FOE). **Methods:** Six newborn piglets were measured at 33°C, 35°C, and 37°C and in normocapnia and hypocapnia. MABP, Hb, peripheral oxygen saturation (SaO_2) and $PaCO_2$ were measured at each step. Cerebral blood flow (CBF) was measured by injection of coloured microspheres. Jugular bulb oxygen saturation (JVS), cerebral arterial and venous oxygen content (CaO_2 and CvO_2) and fractional oxygen extraction (FOE) were calculated. TOI of the brain was calculated using spatially resolved spectroscopy and a new parameter FTOE (fractional tissue oxygen extraction) was introduced as (SaO_2-TOI)/SaO2. **Results:** There was a positive correlation between TOI and JVS in both the rewarming (r=082) and hypocapnia ($r = 0.90$) procedure. No correlation was found with CBF, mean arterial blood pressure or haemoglobin. There was a positive correlation between $PaCO_2$ and cerebral TOI in both the rewarming ($r=0.78$) and hypocapnia ($r=0.88$) procedure.FTOE correlated well with FOE calculated as (CaO_2–$CvjO_2$)/CaO2 in both the rewarming ($r=0.8$) and the hypocapnia ($r=0.89$) procedure. There was a negative correlation between FTOE and $PaCo_2$ in both the rewarming (-0.77) and the hypocapnia ($r=-0.88$) procedure. **Conclusion:** The measurement of TOI and FTOE by spatially resolved spectroscopy correlates well with the cerebral venous saturation and FOE respectively. Continuous measurement of FTOE is feasible and can be a stable and well validated parameter for measuring the balance between oxygen delivery and oxygen consumption in the brain.

0025NEO

MEASUREMENT OF THE LIVER TISSUE OXYGENATION BY NIRS.

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Objective: To evaluate the relation between the liver tissue oxygenation index (TOI), measured with spatially resolved spectroscopy, and mixed venous oxygen saturation (MVS). To evaluate the relation between TOI and the blood flow in the different parts of the splanchnic circulation. **Design/methods.** Six newborn piglets were measured at 33°C, 35°C, 37° C and in hypocapnia. MVS, arterial oxygen saturation, Mean Arterial Blood Pressure (MABP), haemoglobin (HB), peripheral oxygen saturation (SaO_2) and $PaCO_2$ were measured at each step. Gastric arterial flow (GF), proximal jejunal flow (PF), midgut flow (MF), distal ileal flow (IF), splenic flow (SF) and hepatic flow (HF) were measured by injection of coloured microspheres into the left atrium. Fractional oxygen extraction (FOE) was calculated and the fractional tissue oxyegen extraction was calculated as (SaO_2-TOI)/SaO_2. NIRS optodes were attached at the skin above the liver and TOI was calculated. **Results.** TOI of the liver correlated well with MVS (r=0,85). There was a good correlation with MF ($r=0.55$) and IF ($r=0.8$). No correlation was found with SF,GF,PF or HF. A good correlation was found between TOI of the liver and MABP ($r=0.84$). No significant relation was found with $PaCO_2$, temperature and haemoglobin. A strong correlation was found between the FOE and FTOE ($r=0.8$). There was a negative correlation between FTOE and $PaCO_2$ ($r=-0.77$) and FTOE and the distal ileal blood flow ($r=-0.8$). **Conclusion.** The measurement of TOI of the liver can give us a continuous measurement of changes in mixed venous saturation. When liver oxygen consumption remains stable, changes in TOI of the liver can reflect changes in the ileal blood flow. Measurement of FTOE can give information about the balance between oxygen delivery and oxygen consumption in the splanchnic circulation

0028NEO

SMALL THYMUS SIZE AND NEONATAL OUTCOME IN VERY-LOW-BIRTH-WEIGHT INFANTS

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Background: Acute thymic involution in the human fetus and newborn is associated with histological chorioamnionitis, a leading cause of prematurity, neonatal morbidity and mortality. Although a small thymus size at birth has been shown to be an accurate predictor for bronchopulmonary dysplasia (BPD-28d) in very-low-birth-weight (VLBW) infants, to date no information exists on the relationship between thymus size and other adverse neonatal outcomes. **Methods:** A total of 326 VLBW newborns, admitted to the neonatal intensive care unit and surviving for at least 36 weeks' postconceptional age were examined (157 males, 169 females; gestational age: 28.9 ± 3.1 weeks, range: 24–32; birth weight: 1205 ±235 g, range: 550-1490. Over the last 16 years, a minimal handling policy, i.e., nasal Continuous Positive Airway Pressure and/or nasal Intermittent Positive Pressure Ventilation for the treatment of RDS has been used in the Brindisi NICU. Thymic size was measured on chest radiographs routinely performed for clinical reasons, and expressed as the ratio between the transverse diameter of the cardiothymic image at the level of the carina and that of the thorax (CT/T). A CT/T $<$ 0.28 was considered to indicate a small thymic size. Data were analyzed by multiple logistic regression models, with each of the end-points (RDS, BPD-28d, PDA, ROP, PVL, IVH, NEC, sepsis, seizures) as the dependent variable. Predictive accuracy for identifying VLBW newborns with adverse neonatal outcome for different cut-off values of CT/T was calculated using receiver-operating characteristic (ROC) curve analysis. **Results:** Gestational age, birth weight and the proportions of BPD-28d, RDS, PDA, ROP, PVLM, sepsis, and IVH of the two groups were significantly different at univariate analysis, whereas no significant differences in gender, NEC and seizures were present. The results of multiple logistic regression analysis, indicated a significant relationship between a small thymic size at birth and BPD-28d (OR: 7.56 ; 95%CI: 3.94 -14.47, p$<$0.00001), RDS (OR: 2.44; 1.59–3.47, p $<$0.00001) , PDA (OR: 1.83; 1.19–2.8, p=0.0058) , ROP (OR: 1.86; 1.19–2.88, p=0.0059), PVLM (OR: 1.75;1.15–2.65, p=0.0093 , and sepsis (OR: 1.69;1.10–2.59, p=0.016). The results of a ROC curve analysis indicated that using a CT/T ratio cut-off $<$ 0.28 a small thymus at birth predicted the subsequent development of BPD-28d with 84% sensitivity (95% C.I.: 63.9–95.4) and 96.3% specificity (95% C.I.: 93.6–98.2) (area under the curve: 0.902±0.041; 95% C.I.:0,864–0.932; P$<$0.05). In contrast, CT/T was found to be a specific (specificity range: 93.0 - 96.3%), but not sensitive (sensitivity range: 23.6–35.6%) predictor for RDS, PDA, ROP, PVLM and sepsis. **Conclusion:** These findings, while confirming a close relationship between small thymus and BPD-28d, indicate that a small thymic size at birth is significantly associated with adverse neonatal outcome.

0035NEO

SURVEILLANCE OF CONGENITAL ANOMALIES AT THE DR. TRUETA HOSPITAL OF GIRONA

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Background/Aims: We analysed the data gathered by the ECEMC Program since 6–1976 till 12–2001 in order to determine the prevalence of congenital defects (CD) in our Hospital(Dr Trueta Hospital) its evolution over the time, and compare our data with the overall population surveyed by de ECEMC. **Material and methods:** The study was based on the data from the malformed newborns identified through the ECEMC (Estudio Colaborativo Español de Malformaciones congénitas). This is an ongoing hospital-based case-control study and surveillance system with a methodology that is aimed not only at the surveillance of congenital anomalies, but also at investigating their characteristics and causes. Detailed descriptions of the ECEMC methodology have been published previously (Martínez-Frías:1994–2000). **Results:** Between 1976 and 2001, we surveyed 43515 (liveborns+stillborns) 1276 of them were malformed (2.932 %), and 43637 (live borns+stillborns+VIGs: voluntary interruption of gestation of them 1398 malformed (3.204 %), in our Hospital

	1980-1985			1986-2000			2001			86-00	2001
											(n e w b + VIRGs)
	total	malform		total	Malform		Total	malform			
	newborns	number	%	newborns	num	%	Newborns	num	%	%	%
A	11,116	402	3.62	23,349	743	3.18	1,431	50	3.49	3.32	3.83
B	382,390	8,488	2.22	1241,906	19,648	1.58	103,404	1,175	1.14*	1.62	1.19*

A: Dr. Trueta Hospital. B: ECEMC * decreasing trend statistical significance: χ^2 p $<$ 0.05
Conclusions: We think that the obseved differences can be due to: 1.- Impact of VIGs on the birth prevalence of DC (Only in a few out of 86 hospitals that integrate the ECEMC register the VIGs) 2.- Influence of immigrant population (In 2001 at Dr. Trueta Hospital), 50 malformed, 23 of them (46%) were not caucasians. 3.- Differences in the implementation in each region, of the primary prevention of neural tube defects and other anomalies with periconceptional intake of folic acid. However, this effect is still very low.

0031NEO

INHALED NITRIC OXIDE BY PULMONARY HYPERTENSION: COMPARISON PRETERM INFANTS VERSUS NEWBORN INFANTS

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Background: Inhaled nitric oxide (iNO) is used as a vasodilator in pulmonary hypertension (PH) of the newborn infants Patients and **Methods**: Retrospective analysis of patients, who were treated in the period from 1994–2001 at our department with iNO. Response was defined as an increase of the paO_2/FiO_2 Ratio ≥ 20% and/or a decrease of the oxygenation index (OI) ≥ 20% after 2h (early response), and consecutively after 24h (late response). The patients were divided into a) primary persistent pulmonary hypertension of the newborn (PPHN), or b) pulmonary hypertension secondary to meconium aspiration syndrome (MAS), sepsis or congenital diaphragmatic hernia (CDH). **Results:** Between 1994 and 2001 we treated 47 patients with iNO at our neonatal intensive care unit. We included 16(35%) preterm infants (GA 34,5 (25–37) weeks, GG 2061 (680–3410)g) (Median/Range) and 31(65%) newborn (GA 40 (38–42) weeks, GG 3510 (2550–4560)g). In regard to iNO response, there was neither a significant difference at 2hours, nor at 24hours between term and preterm infants. 18 (38%) patients suffered from primary PPHN, 29 (62%) from secondary PPHN (14 MAS (30%), 8 sepsis (17%), 4 CDH (8%)). 28 (60%) patients showed an early response, 28 (60%) patients showed a late response. The patients with early response did not differ from the patient without response in regard to the oxygenation parameters (median OI: 20,0 versus 21,8, median paO_2/FiO_2 Ratio: 59,3 versus 55,0 mmHg at the start of the iNO therapy). After 2hours even 10 patients changed the response group in the further course of the disease. 5(18%) patients with early response showed a significant degradation after 24h, whereas 5(26%) of the patients without early response showed a significant improvement of the oxygenation after 24h. Altogether 13 (72%) patients with PPHN, 8 (57%) with MAS, 2 (67%) with CDH, 4 (50%) with sepsis showed a response after 24 hours. **Conclusion:** In regard to iNO response, there was no significant difference between term and preterm infants. The therapy response after 2h had no predictive value for the further prognosis of the oxygenation situation under iNO therapy.

00037NEO

RENAL FAILURE: ANOTHER RISK FACTOR FOR THRESHOLD RETINOPATHY?

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Background: Until strategies are available to prevent preterm birth, caretakers will have to focus on other risk factors to prevent threshold retinopathy. Indicators available in early neonatal life might serve to further discriminate the relative risk to develop threshold ROP associated with a given birth weight or gestational age (GA). **Methods:** Retrospective analysis of clinical characteristics in survivors of the EpiBel study (1999–2000, 22–26 GA at birth, n=175). Characteristics in survivors (n=35) who developed threshold ROP were compared to survivors who did not develop threshold ROP (n=140). After monovariate analysis, multiple and logistic regression analysis (MedCalc) were performed. **Results:** Birth weight and GA were significantly lower (p$<$0.004 and p$<$0.02) in threshold cases while CRIB score was significantly higher (p$<$0.03). Besides length (days) of respiratory disease (supplemental oxygen, respiratory support) (at least p$<$0.001), incidence of renal insufficiency (creatinaemia $>$ 1.5 mg/dl) was significantly higher in infants who developed threshold ROP (p$<$0.002). Renal insufficiency remained a significant risk factor after correction in a multiple regression model for maternal hypertension, amnionitis, growth restriction, pharmacological treatment of PDA. In a logistic regression model, duration of respiratory support (OR 1.02), the number of blood transfusions (OR 1.12) and renal insufficiency (OR 3.31) were independent risk factors to develop threshold ROP. **Conclusions:** Renal insufficiency (crea $>$1.5 mg/dl) is a significant and independent risk factor to develop threshold ROP in this cohort of survivors (22–26 GA). Disturbed renal and retinal microperfusion might explain this association.

0039NEO

ORAL VASCULAR NETWORK ABNORMALITIES AND ACHONDROPLASIA

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Background: Approximately 90% of achondroplasia (ACH) cases are the result of a de novo mutation, with no phenotypical markers for the unaffected ACH parents being known to date. Angiogenesis plays a key role for the normal development of the endochondral bone, and an abnormal vascularization in the growth plate of ACH patients and ACH animal models has been reported. In the present study, the hypothesis of the presence of a systemic vascularization abnormality in the ACH children and unaffected ACH parents was tested. **Methods:** The lower gingival and vestibular oral mucosa was chosen as study-area, due to the high vasculature pattern visibility and easy accessibility. 1:1 ratio, orthogonal projection photographs of the oral mucosa were taken in fifteen children with sporadic ACH, thirty unaffected parents of children with typical ACH phenotype, and forty-five genetically unrelated sex- and age-matched control subjects. The 2-D vascular network geometry [overall complexity (fractal dimension, D, at two scales: D 1–46, and D 1–15) and relative Lempel-Ziev complexity, L-Z), tortuosity (minimum-path dimension, Dmin), and vessel-free area size distribution of the vascular loops] were analysed. **Results:** The ACH-related vascular networks exhibited higher D 1–46 ($P \leq 0.013$) and D 1–15 ($P \leq 0.0032$) fractal dimensions, higher Dmin ($P \leq 0.0013$), higher L-Z complexity ($P < 0.0001$), and lower vessel-free area size ($P < 0.00001$) than control networks. A blood vessel growth comparable to those of ACH patients and unaffected ACH parents ($P \geq 0.35$) was reproduced by computer simulation based on the concepts of iteration, stochastic fractal distribution, Voronoi diagrams, and non-Euclidean distance. A vessel-free area size $\leq 56{,}832\ \mu m^2$ and L-Z complexity > 0.62 showed 100%-sensitivity and 100%-specificity in identifying unaffected ACH parents. **Conclusion:** These findings indicate the presence of a previously unrecognized vascular network abnormality of the oral mucosa in both ACH children and unaffected parents of children with de novo mutation ACH, thus providing the first phenotypical marker for identifying couples potentially at risk for ACH offspring.

0041NEO

TITLE :THE EFFECT OF CO-ADMINISTRATION OF INTRAVENOUS IBUPROFEN ON SERUM HALF LIFE OF AMIKACIN IN THE FIRST DAY OF LIFE

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Background: Bactericidal efficacy of amikacin (Ak) is related to peak serum concentration while mean levels of the drug are related to the toxic side-effects. This lead to the concept of administration of relative larger doses of the drug with longer time intervals. Variability in pharmacokinetics (PK) of newborns make it difficult to achieve effective and save treatment. Part of this variability might be explained by co-administration of other drugs who might influence PK. **Methods:** Retrospective analysis of PK of Ak in a cohort of preterm infants (<31 GA) who received either ibuprofen-lysine or normal saline in the multicenter ibuprofen prophylaxis study (MIPS), Leuven cohort. During the MIPS study, Ak dose was 20 mg/kg with an interval of 24 hours in infants of 30 weeks and 36 hours in infants below 30 weeks GA. PK were calculated assuming a one-compartment model with instantaneous input and first order output. **Results:** PK of Ak data could be calculated in 73 infants. A reversed correlation of t1/2 on GA ($r = -0.18$) was documented. In infants who also received ibuprofen (n=34), median T ½ (h) was significantly longer (16.4, range 7.8–92.1 to 12.4, range 6.7–60.3, $p<0.02$) and median total body clearance (ml/kg/min) was significantly lower (0.36, 0.14–0.84 to 0.6, 0.03–2.6, $p<0.005$) while relative distribution volume (L/kg) was not significantly different (0.63, range 0.27–3.1 to 0.59, range 0.19–1.24). **Conclusions:** T ½ of Ak is increased and CLt of Ak is decreased without changes in Vd by co-administration of ibuprofen-lysine in preterm infants in the first day of life. The interval between consecutive administrations should be increased if ibuprofen is prescribed in preterm infants (<31 weeks GA) in the first day of life.

0044NEO

NATURAL AND SYNTHETIC SURFACTANT PREPARATIONS INDUCE CHEMOTAXIS

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Background/aims: Respiratory distress syndromes (RDS) occur at all ages. Although etiology varies markedly, pulmonary inflammation with neutrophil influx is a common feature. Inflammatory mediators will damage pulmonary surfactant. A decrease in functional surfactant impairs lung compliance leading to the clinical picture of RDS. Exogenous surfactant treatment of patients with RDS does not resolve the inflammatory process. We hypothesized that exogenous surfactant preparations induce neutrophil chemotaxis and thus contribute to a sustained inflammatory response. The aim of our in vitro study was to assess chemotactic activity of surfactant preparations on rabbit and human neutrophils in vitro. **Methods:** Chemotactic activity of Curosurf, Survanta and Exosurf (concentration range 0.1- 4 mg/L) on rabbit and human neutrophils was assessed with the Boyden chamber technique: a filter separates the two compartments of the chamber. Neutrophils were incubated in the upper compartment and surfactant suspensions in the lower compartment. The neutrophil migration distances (μm) in the filter were measured and fMLP served as a positive control. **Results:** Curosurf, Survanta and Exosurf showed a dose-related chemotactic response; rabbit neutrophil migration distance increased from 42 ± 7.1, 43 ± 6.1, 62 ± 4.9 μm without surfactant to 80 ± 4.6, 72 ± 4.1 and $106 \pm 7.4 \mu m$ with 0.1mg/L of Curosurf, Survanta or Exosurf respectively. With human neutrophils, migration increased from 49 ± 3.6, 62 ± 4.1 and 72 ± 2.3 μm without surfactant to 91 ± 4.5, 77 ± 3.9 and $106 \pm 7.5 \mu m$ with 4mg/L of Curosurf, Survanta or Exosurf. **Conclusion:** Exogenous synthetic and natural surfactant preparations induce rabbit and adult neutrophil chemotaxis in vitro. Surfactant administration to neonates and adults with respiratory distress syndromes may sustain the inflammatory response and thus explain the variable response of this treatment.

0046NEO

VASCULAR ENDOTHELIAL GROWTH FACTOR AND RECEPTORS IN PRETERM CLD

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Background/aims: Arrested airway and vascular development is a characteristic pathological finding in preterm infants dying with CLD. Vascular Endothelial Growth Factor (VEGF) is an endothelial specific mitogen which is important in physiological and pathological angiogenesis. VEGF concentrations in bronchoalveolar lavage fluid (BALF) are decreased during the first week of life in infants who subsequently develop CLD. Levels of soluble VEGF receptors 1 and 2, naturally occurring inhibitors of VEGF activity, have not been reported previously. The aims of our study were to measure plasma and BALF concentrations of VEGF, VEGFR-1 and VEGFR-2 in preterm infants, and compare levels in infants with established CLD and preterm controls**. Methods:** Three groups were studied: Group 1 (study group) comprised preterm infants with established CLD ventilated at 28 days of age; Group 2 (control group) were ventilated preterm infants < 7 days of age; Group 3 were healthy non-ventilated preterm infants at 28 days of age. BALF and/or plasma samples were taken and VEGF, and VEGFR-1 and VEGFR-2 concentrations measured using an ELISA technique.

Results:

	Group 1 (N=7)	Group 2 (N=15)	Group 3 (N=9)
BAL fluid			
VEGF (pg/ml)	1890 (480-2190)	1200 (190-1940)	N/A
VEGFR-1 (pg/ml)	670 (300-920) *	1640 (970-2160)	N/A
VEGFR-2 (pg/ml)	290 (170-610)	410 (340-580)	N/A
Plasma			
VEGF (pg/ml)	540 (440-840) *	400 (280-450)	530 (460-710)
VEGFR 1 (pg/ml)	150 (140-160) *	280 (230-550)	120 (70-160)
VEGFR 2 (pg/ml)	6730 (1410-7980)	6690 (5720-9440)	6750 (6550-9690)

Values expressed as median (IQR); * $p < 0.01$, Mann Whitney test compared to group 2

Conclusions: VEGF, VEGFR-1 and VEGFR-2 were measurable in both BALF and plasma from preterm infants. VEGF concentrations were approximately three-fold higher in BALF compared to plasma suggesting VEGF local synthesis in the preterm lung. Infants with established CLD tended to have higher plasma and BALF VEGF, but lower VEGFR-1 levels, compared to ventilated control infants < 7 days. VEGF and VEGFR-1 may play a role in preterm lung injury.

0048NEO

HEALTH HAZARDS FOR PRENATAL EXPOSURE TO DI-(2-ETHYL-HEXYL)-PHTHALATE

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Objective: Di-(2-ethylhexyl)-phthalate (DEHP), the most commonly used plasticiser in flexible polyvinylchloride (PVC) formulations, is a widespread ubiquitous environmental contaminant. Over the years, an increasing number of toxic effects from DEHP exposure have been reported. However, to date, no information exists on the potential health hazards for exposure to DEHP and/or its main metabolite, mono-ethylhexyl phthalate (MEHP) in high-risk conditions, such pregnancy and neonatal period. Aim of this study was to evaluate the prenatal exposure to DEHP and/or MEHP and its possible biological effects. **Methods:** Plasma DEHP and MEHP concentrations were measured in the cord blood of 84 consecutive newborns by High Performance Liquid Chromatography (HPLC). Relationships between DEHP/MEHP and infant characteristics were tested using Fisher's exact test, unpaired t-tests and univariate linear regression analyses and significant differences on univariate analysis were evaluated using multiple logistic regression analysis. **Results:** Detectable cord blood DEHP and/or MEHP were found in 88.1% of the samples. Either DEHP or MEHP were present in 65/84 (77.4%) of the examined samples. Mean concentrations of DEHP and MEHP were 1.19 ± 1.15 μg/ml (95% CI for the mean:0.93–1.44) (values range: 0–4.71) and 0.52 ± 0.61 μg/ml (95% CI for the mean:0.39–0.66) (values range: 0–2.94), respectively. MEHP-positive newborns showed a significantly lower gestational age compared to the MEHP-negative infants ($P=0.033$). Logistic regression analysis results indicated a positive correlation between absence MEHP in cord blood and gestational age at delivery (OR=1.50;95% CI=1.013–2.21,P=0.043). **Conclusions:** These findings confirm that human exposure to DEHP can begin in utero, crossing the placental barrier and firstly indicate that phthalate exposure is significantly associated with a shorter pregnancy duration.

0054NEO

DETERMINATION OF PRINCIPAL DRUGS ABUSE IN MECONIUM

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Background: Drug abuse during pregnancy is a major problem because of associated high incidence of perinatal complication of newborns. Recently, investigators have reported the utility of meconium as test specimen in the screening of fetal chronic exposure to drug abuse. Meconium is the first fecal matter passed by a neonate and its analysis extend the window of detection of drug use approximately the last 20 weeks of gestation, being more informative than urine for the detection of drug exposure in pregnancy. **Methods:** We describe sensitive and selective analytical method based on LC-MS for the determination of opiates, cocaine and metabolites, and amphetamines in meconium samples collected at the Hospital del Mar in Barcelona. One gram of meconium was extracted by Bond-Elut Certify solid-phase extraction columns with standardised methodologies for different drugs. Chromatographic separation was achieved at ambient temperature using a reverse phase column and a mobile phase consisting of 97% acetic acid (1% aqueous solution) -3% acetonitrile in a linear gradient for opiates and cocaine and 94% 0.01 M ammonium bicarbonate -6% methanol for amphetamines. The mass spectrometer was operated in positive electrospray ionization mode and selected ion monitoring (SIM) acquisition mode. **Results:** Up to 177 samples have been analyzed from the second half of 2002. 6.2% of the samples resulted positive to cocaine and 7.3% to opiates, while all the samples resulted negative for amphetamines. The range of found concentrations was 0.07 μg/g- 0.87 μg/g for cocaine, 0.13 μg/g – 0.84 μg/g for benzoylecgonine, 0.005 μg/g-0.017 ug/g for cocaethylene, 0.005 μg/g-0.142 μg/g for monoacetylmorphine, 0.005 μg/g-0.396 μg/g for morphine, 0.01 μg/g- 0.049 μg/g for codeine. **Conclusion:** The LC-MS method reported to analyze opiates and cocaine in meconium was validated according to internationally accepted criteria. Meconium analysis by LC-MS - a versatile analytical tool- can provide a wide window for the detection of fetal exposure to various drugs and xenobiotic agents.

0055NEO

BIOMARKERS AND BIOLOGICAL MATRICES FOR ASSESSEMENT OF FETAL EXPOSURE TO TOBACCO SMOKE

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Background: The accurate assessment of exposure to environmental tobacco smoke through the objective measure of a biomarker could be of major importance in newborns and children for the investigation of the effects of pre- and post-natal environmental exposures to pollutants, including tobacco smoke, in the inception of respiratory diseases. **Methods:** Foetal exposure to cigarette smoke is usually assessed by questionnaires administered to mothers during or after pregnancy. However, difficulties in recognising a smoking behaviour, recalling smoking exposure or changes in smoking habits during gestation could bias these assessments. We measured nicotine and its metabolite cotinine in foetal biological matrices (cord blood, new-born urine, foetal hair, meconium) and assessed the association between these biomarkers of exposure to tobacco smoke and the quantitative measurement of smoking intake and exposure during pregnancy measured through questionnaire. **Results:** Cotinine in body fluids resulted an adequate biomarker to assess exposure to environmental tobacco smoke (ETS) in newborns during a short period of time (days). The geometric mean of cotinine concentration in cord serum statistically discriminated between new-borns from non-exposed and exposed non-smoking mothers, and between these two classes and smokers; and furthermore was able to differentiate levels of exposure to tobacco smoke and levels of intake stratified in tertiles. Urinary cotinine levels in new-borns from non smoking mothers exposed to more than 4 mg nicotine daily were statistically different from levels in two other categories of exposure. Cotinine concentration in urine from new-borns and from mothers did not differentiate between exposure and non-exposure to environmental tobacco smoke (ETS) in non-smoking mothers. As a biomarker of chronic exposure to smoke during gestation, nicotine concentration in fetal hair discriminated new-borns from smoker and non smoker mothers, but did not differentiate between exposure and non-exposure to environmental tobacco smoke (ETS) in new-borns from non-smoking mothers. **Conclusions:** Preliminary results of nicotine and cotinine measurement in meconium show that this biological matrix, differently from fetal hair, can be a promising tool to validate information of cumulative exposure to environmental smoke during the majority of fetal life.

0056NEO

THE INNOVO MULTICENTRE RANDOMISED CONTROLLED TRIAL: PRETERM BABY RESULTS

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Background: Existing data from randomised trials provides no clear evidence of benefit from the use of nitric oxide in preterm infants with severe respiratory failure. Randomised studies to date have included only small numbers and the Cochrane review highlights the need for further trials in this group of babies. **Methods:** The INNOVO Trial (ISRCTN 17821339) was a multicentre randomised controlled trial, funded by the UK Medical Research Council, that recruited preterm babies in 15 neonatal units in the UK and Ireland. All ventilated preterm infants (≤34 weeks gestation) with severe respiratory failure, despite surfactant and optimisation of ventilation, were eligible for trial entry provided they had no evidence of uncontrollable bleeding, no parenchymal brain lesions and no contra-indications to continuing intensive care. The two treatment arms were: nitric oxide added to the ventilator gases vs no use of nitric oxide. No blinding was attempted. The primary outcome was death or severe disability (the latter defined to be roughly equivalent to a DQ of<50) at one year (corrected) in the two arms, with assessment at one year by the child's local paediatrician. Trial size was estimated on the basis of a reduction in the primary outcome from 60% to 40% which gave a recruitment target of 200 babies. The suggested starting dose level was 5 ppm, doubling to 10 ppm if no satisfactory response was achieved, and if necessary doubled again to 20 ppm, then again if required to 40 ppm. A satisfactory response was defined as an increase in post ductal PaO_2 of more than 3 kPa (22.5 mmHg) in the initial 15 minutes of giving iNO. In 13 babies a formal dose response study was performed to determine the best dose. Telephone randomisation was used with minimisation by hospital of care, postnatal age, respiratory disease severity and principal diagnosis at trial entry. **Results:** Despite a variety of startegies the recruitment target was not reached. 108 babies were recuited (55 in the NO arm and 53 controls). Three babies in the NO arm did not receive NO as they either died before it could be given or improved spontaneously. Four babies in the control arm were given NO at the direction of the clinician looking after the baby. The groups were generally well matched but the babies in the NO arm were more mature and heavier at birth (27.4 weeks vs 26.3 weeks and 1,066g vs stays despite similar outcomes. Preliminary health economic assessment indicated that the cost of care for each baby in the NO arm was approximately £10,000 (16000 Euros) greater than that of babies in the control arm and a full cost effectiveness analysis is being undertaken. **Conclusions:** Based on these findings it is hard to justify a policy of using nitric oxide in the managment of preterm babies with severe respiratory failure. Caution must be exercised however in interpreting these results as the original recruitment target was not met.890g respectively). The majority of babies had an oxygenation index >30 at the time of randomisation. Most of the babies (based on clinical judgement) in the NO arm showed improvement in oxygenation (≥ 3kPa) in the first hour following randomisation (31/55). However there was no significant difference in the longer term outcomes: Death or severe disability at 1 yr corrected RR = 0.99 (95% CI 0.76–1.29; p=0.89); Death RR=0.85 (95% CI 0.62–1.16; p=0.41); Death or supplemenary oxygen at EDD RR= 0.84 (95% CI 0.68–1.02; p=0.13). Babies allocated to receive NO had longer hospital

0065NEO

PERFUSION INDEX AT BIRTH AND EARLY DIAGNOSIS OF HISTOLOGIC CHORIOAMNIONITIS

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Background: Chorioamnionitis (CA) is known to be associated with increased risk for fetal /neonatal morbidity and mortality and/or long term brain damage. However, a large fraction of CA remains subclinical, with no recognizable predictive clinical signs at birth being known to date. Here, we tested the hypothesis that the pulse oximetry perfusion index (PI) is an early predictor of CA. **Methods:** In a prospective study, 45 consecutive term newborns with histologically documented CA (M:25, F:20; gestational age, M±SD: 38.1±1.4 weeks; birth weight: 3,035±620 g), infection before birth, were compared to a control group of 45 consecutive term newborns without CA (M:22, F:23; gestational age, M±SD: 38.3±1.3 weeks; birth weight: 3,055±515 g). Clinically evident CA were excluded. For both groups, PI was assessed using a Masimo SET Radical pulse oximeter (Masimo Corp., Irvine, CA, USA) with the sensor placed randomly on either of the feet, and artifact-free values were captured for at least 5 minutes after delivery. Core and peripheral temperature were also measured (Datascope Passport YSI 700, Datascope Co., Mahwah, NJ, USA). **Results:** Significantly lower PI values at 1-min (1.74 ± 0.32 vs. 4.50 ± 0.83; $p<0.0001$) and 5-min (2.18 ± 1.02 vs. 4.42 ± 2.10; p0.0001) after delivery were observed in the CA-positive group, together with a significantly lower 1-min Apgar score (median-interquartiile range, 6 [5- 7] vs. 9 [8–10]; $p<0.0001$). On the other hand, birth weight, 5-min Apgar score, 1-min and 5-min SpO2, 1-min and 5-min pulse rate, 1-min and 5-min skin temperature, as well as 1-min and 5-min core temperature were not significantly different between the groups (p≥ 0.32). **Conclusion:** These findings suggest the use of PI in monitoring of infants in the delivery room for the early screening of perinatal inflammatory disease. Although the mechanisms underlying the significantly lower PI readings remain to be elucidated, local skin vasoconstriction and/or peripheral microcirculatory changes are suggested. An early CA / antenatal infection diagnosis by measuring low PI may make possible to improve the outcome of affected neonates.

0074NEO

TITLE:PAIN EXPRESSION IN FORMER PRETERMS IN THE FIRST YEAR OF LIFE

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Background: Pain expression in former preterm infants at time of immunisation might not only be related to findings at time of immunisation (post conceptional age, preprocedural state), but might also relate to experiences in earlier neonatal life (GA, surgery, length of stay, duration of ventilation, gender) and findings at time of immunisation We therefore investigated pain expression in former preterm infants during first immunisation with Palivisumab (Synagis®). **Methods:** Videotapes were made in former premature infants before, during and after the first intramuscular administration of Palivisumab (15 mg/kg). Heart rate, crying time and maximal pain expression (Modified Behavioural Pain Scale, MIBS) were registered based on video recordings. Characteristics during neonatal stay and at time of immunisation were collected. Data were reported by median and range. Correlations of PCA (postconceptional age) on pain expression characteristics (heart rate variation, crying time, MIBS) were calculated. Gender and surgery-related differences were studied. **Results:** Videotapes were analysed in 49 infants (24 girls, 25 boys). Median GA (gestational age) at birth was 28 (range 25–32) weeks, median length of stay (LOS, level III) was 66 (31–206) days and median duration of neonatal ventilation was 10 (0–46) days. 13 infants had at least one surgical intervention during neonatal stay. Median PCA at immunisation was 52 (36–90) weeks. Median % increase in heart rate was 28 % (5 % to 99 %). Median crying time was 30 (0–112) seconds. Median MIBS scale increased from (0–6) to 8 (2–10). A correlation of PCA on relative increase of heart rate (r=0.6) and on crying time (r=0.23) but not on MIBS was documented. Correlation of crying time on LOS was 0.37. No gender-related or surgery-related differences were documented. **Conclusions:** A weak to moderate maturational trend of PCA on relative increase in heart rate and on crying time but not on MIBS was documented in former preterm infants after first immunisation with Palivisumab in the first year of life. No gender-related or surgery-related differences were documented.

0077NEO

A NEW CLINICAL SIGN IN DOWN SYNDROME PATIENTS AND THEIR UNAFFECTED PARENTS

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Background: Down Syndrome (DS) is a leading genetic cause of mental retardation, and a significant medical and social problem. No clinical markers for identifying couples at risk for having a DS child exist to date. Generalised ligament laxity has been associated with bone-collagen type disorders, including DS. As extracellular matrix is known to play an important role on angiogenesis and blood vessel geometry, we tested the hypothesis of the presence of an abnormal vascularization in both DS patients and unaffected DS parents. **Methods:** Thirteen genetically unrelated patients with documented free trisomy 21 (M: 7, F: 7; age 16.4 ± 8.5 years; range: 0.25–25), their unaffected parents (M:14, age: 50.2 ± 11.8 years; F:14, age: 48.1 ± 12.7 years; normal karyotype), and forty-two genetically unrelated sex- and age-matched control families (control subjects, M:7; F:7; age 16.0 ± 8.0 years, n=14; control fathers, age: 49.8 ± 10.5 years, n=14; control mothers, age: 47.8 ± 12.2 years, n=14) were enrolled in the study. Informed consent was obtained from all the subjects or their parents, and the investigation was approved by the local ethical committees. The lower gingival and vestibular oral mucosa was chosen as the study-area, due to the high vasculature pattern visibility and easy accessibility. Fractal dimension (D) at two scales (D 1–46, and D 1–15), tortuosity (minimum-path dimension, Dmin), and relative Lempel-Ziev complexity (L-Z) of the vascular networks from the lower gingival and vestibular oral mucosa were measured. **Results:** The vascular networks of DS patients and their unaffected parents exhibited significantly higher fractal dimensions D 1–46 (1.80 ± 0.02 vs. 1.65 ± 0.13; difference: 0.15, 95% C.I.: 0.11–0.19; t=7.39, df=82, P<0.0001) and D 1–15 (1.59 ± 0.09 vs. 1.21 ± 0.12; difference: 0.38, 95% C.I.: 0.33–0.43; t=16.42, df=82, P<0.0001), and L-Z complexity (0.87± 0.07 vs. 0.51 ± 0.09; difference: 0.36, 95% C.I.: 0.32–0.39; t=20.46, df=82, P<0.0001), together with a lower Dmin (1.00 ± 0.034 vs. 1.07 ± 0.04; difference: 0.07, 95% C.I.: 0.054–0.086; t=8.64, df=82, P<0.0001) than the control networks. Conversely, no statistically significant differences in the examined vascular pattern characteristics were observed between the networks of the DS children and those of their unaffected parents (P ≥0.42), or between control children and control parents (P ≥0.35). **Conclusion:** Our findings indicate the presence of a previously unrecognised vascular network abnormality of the oral mucosa in both DS patients and unaffected parents, thus providing a useful phenotypical marker for identifying couples potentially at risk for a DS offspring.

0093NEO

IGF-I AND NEONATAL MORBIDITY IN VERY PRETERM NEWBONS

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Background/aims: IGF-I plays an essential role in the regulation of foetal growth and tissue-specific growth. It is hypothesized that low IGF-I levels compromise tissue growth and contribute to tissue injury and overall morbidity in preterm infants. The importance of IGF-I for the vascularisation of the human retina and the association of low IGF-I levels with ROP are well known. We therefore investigated the relation between IGF-I levels, birth weight and birth weight for gestational age, neonatal mortality and morbidity. **Methods:** As part of a larger study on the clinical and endocrine effects of L-thyroxine and hydrocortisone treatment, IGF-I levels were measured on cord blood, and weekly for six weeks in 80 preterm infants with a gestational age < 30 weeks. We investigated the relation of IGF-I levels with birth-weight, birth-weight for gestational age (GA), neonatal mortality and the incidence of hyaline membrane disease (HMD), bronchopulmonary dysplasia (BPD), retinopathy of the prematurity (ROP), necrotising enterocolitis (NEC), intraventricular haemorrhage (IVH), septicaemia and death. Results: Cord blood IGF-I levels did not correlated with GA or birth weight (for GA). The postnatal IGF-I course was not influenced by L-thyroxine nor hydrocortisone treatment. Low IGF-1 levels were related with increased incidence of HMZ ($p<0,05$) and BPD ($p<0,05$), not with other neonatal morbidity, in particular ROP. **Conclusion:** Low IGF-1 levels are related with increased respiratory morbidity after preterm birth. Whether this relationship is causal or not remains to be explored. Those findings hold promise for potential therapeutic strategies to reduce respiratory morbidity in preterm infants.

0094NEO

EFFECT OF ENDOTRACHEAL $MGSO_4$ IN PIGLETS WITH PULMONARY HYPERTENSION

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Background/aims: Intravenous $MgSO_4$ has been shown to be a non-specific vasodilator in piglets with pulmonary hypertension. It is also used occasionally in infants with persistent pulmonary hypertension of the newborn (PPHN). Systemic hypotension is a serious side-effect which may worsen right-to-left shunting. We hypothesised that endotracheal (ET) MgSO4 will decrease pulmonary arterial pressure selectively without systemic vasodilation. **Methods:** Pulmonary hypertension was induced in 11anaesthetised piglets (age 3–7 days, mean weight 1.8 kg) using hypoxic gas (FiO_2 0.12). Three received iv $MgSO_4$ (25mg/kg x 4 doses each), three ET saline placebo (2ml x 4 each) and five ET $MgSO_4$ (50mg/kg x 4 each). The following were measured: Systemic blood pressure (SBP, femoral arterial line), right atrial pressure (RAP, right internal jugular line), pulmonary artery pressure (PAP, pulmonary artery catheter, thoracotomy)and cardiac output (Q, Transonic perivascular ultrasound flow probe around main pulmonary artery). All measured variables were continuously recorded onto a PC using Powerlab and Chart programs. Pulmonary and systemic vascular resistance index (PVRI, SVRI*) and their ratio (PVRI/SVRI) were calculated. Mean percentage (%) change in the variables before and after each dose was determined. Serum Mg levels were measured at baseline and after each dose.

Results:

Mean % change	After 1st iv Mg	After 1st ET Mg	After 1st ET saline	After 2nd iv Mg	After 2nd ET Mg	After 2nd ET saline
PVRI	-6.6	-10.7	-2.1	-21.1	-8.9	-7.6
SVRI	-4.5	4.6	-12.3	-1.7	9.4	0.1
PVRI / SVRI	-1.7	-13.4	15.5	-17.48	-16.1	-5.8
Mean % change	After 3rd iv Mg	After 3rd ET Mg	After 3rd ET saline	After 4th iv Mg	After 4th ET Mg	After 4th ET saline
PVRI	-12.8	1.9	-1.7	-10.7	13.0	-1.6
SVRI	-12.0	7.6	-1.6	-10.7	-2.7	-2.3
PVRI / SVRI	-1.5	-4.2	0.1	-0.3	16.4	1.3

Baseline serum Mg levels were the same for both iv and ET MgSO4 groups (0.76 mmol/l). At the end of the experiment it was significantly higher in the iv Mg group compared to the ET Mg group (1.73 mmol/l vs. 0.92 mmol/l, p=0.001, t-test) **Conclusions:** In this small exploratory study, we observed that the first and second doses of ET $MgSO_4$ reduced PVRI but not SVRI, suggesting a local vasodilator effect. If confirmed with a larger sample size, ET $MgSO_4$ could potentially be used as a specific pulmonary vasodilator that is very cost effective. *PVRI=PAP/Q, SVRI=(SBP-RAP)/Q

0100NEO

PRE-TERM DELIVERY, LEVEL OF CARE AND INFANT DEATH IN SWEDEN, A POPULATION BASED STUDY

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Aim: To elucidate the role of level of care in combination with other perinatal risk factors for infant death in very preterm deliveries. **Methods:** Live-born singleton infants, born at 24–31 completed weeks of gestation to primiparous women, were identified in Swedish Medical Birth Register during the years 1992 – 1998 (n=2285). Risk of infant mortality (primary outcome) was estimated by odds ratios. Independent variables in the multivariate logistic regression models were mode of delivery, hospital type, gestational age, birth weight for gestational age, infant sex, fetal presentation, placental complications, and hypertensive illness. **Results:** The rate of infant mortality increased from 5% among infants born at 31 weeks to 56% among infants born at 24 weeks. Compared with infants born at university hospitals, the unadjusted odds ratio (95% confidence interval) of infant death was 0.70 (0.54 – 0.90) among infants delivered at county hospitals. However, after adjustment, the odds ratio of infant death shifted to 1.33 (0.98 – 1.81) for preterm births at county hospitals. This shift was primarily due to different gestational age distributions in regional and county hospitals. Due to a significant interaction between gestational age and hospital type with regard to infant mortality (p=0.049), the cohort was stratified according to our present recommendation for antenatal transfer to university hospital, i.e. expected delivery less than 27 weeks of gestational age. Among infants born at 24–26 weeks, infant mortality rates were 29% (76 deaths) in university hospitals and 43% (54 deaths) in county hospitals, giving an adjusted odds ratio of 1.84 for county versus university hospitals (95% confidence interval 1.11 – 3.04). The risk of death at 24–26 weeks in county hospitals was primarily increased in pregnancies with placental complications, normal maternal blood pressure, and in infants with birth weight appropriate for gestational age. **Conclusions:** The excess risk of infant mortality among very preterm infants born at county hospitals is confined to infants born before 27 weeks, but whether this risk is mediated by quality of care remains to be determined.

0101NEO

SIMPLE SCORING METHOD FOR PREDICTION OF NEONATAL CHRONIC LUNG DISEASE

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Objectives: To predict the neonatal chronic lung disease(CLD) early and identify the high-risk infants for development of neonatal CLD using a simple score method. **Method** From January 1, 1997 to December 31, 1999 (Phase 1), inborn infants of estimated gestational age (GA) < 32 weeks and survived over 28 days after birth at Asan Medical Center were included. Retrospectively collected perinatal and neonatal data including gestational age, birth weight, 5 minute Apgar score, peak inspiratory pressure(PIP) divided by birth weight at 12 hours of age, mean airway pressure(MAP) divided by birth weight, and modified oxygenation index, and ventilatory modalities were used as the parameters for prediction of CLD and, by means of the results, a simple score method was developed. Predictive scores, based on the score table, were obtained prospectively for all live inborn infants of GA < 32 weeks between January 1, 2000, and August 31, 2001(Phase 2), and compared the calculated results including area under the curve(AUC), sensitivity, specificity between the two phases. The diagnosis of CLD was made either at 28 days of age or 36 weeks postconceptual age(PCA). **Results** Of 256 infants < 32 weeks' gestation recruited during phase 1, 212 infants survived over 28 days after birth. 58(22.7%) and 33(12.9%) infants of CLD were identified at 28 days of age and 36 weeks PCA, respectively. In phase 2, 138 infants < 32 weeks' gestation were evaluated and 25(18.1%) and 9(7.1%) infants were diagnosed as CLD at 28 days of age and 36 weeks of PCA, respectively. When defining the CLD at 28 days of age, AUC was 0.932(95% CI;1.278–1.508) and 0.943(95% CI;1.303–1.567) at 7 and 10 days of age, respectively, for phase 1 group. The AUC was 0.910(95% CI;0.833–0.951) and 0.931(95% CI;0.885–0.978) at 7 and 10 days of age, respectively, for phase 2 group. When defining the CLD at 36 weeks of PCA, AUC was 0.845(95% CI;0.775–0.914) and 0.863(95% CI;0.795–0.931) at 7 and 10 days of age, respectively, for phase 1 group and 0.935(95% CI;0.869–1.001) and 0.958(95% CI;0.869–1.016) at 7 and 10 days of age, respectively, for phase 2 group. The infants with CLD defined at 28 days of age, sensitivity, specificity, and predictive values at the specific cut-off points of phase 2 showed similar results compared with those of phase 1. The infants who classified into the high-risk group in phase 2 showed 11.1–14.3 times higher mortality than those of control group. **Conclusion** This score method provides reliable estimating values in predicting development of CLD in premature newborn < 32 weeks of gestation. It can be applied at the bed side through a simple calculation regardless of ventilatory modalities and can be a useful tool in predicting neonatal CLD in NICU. The scores when used within 10 days of life better predicted the CLD at 28 days after birth than those for CLD at 36 weeks PCA. Other kinds of postnatal variables, such as late-onset sepsis, should be considered as the risk factors for development of CLD at 36 weeks PCA. Consenting sponsor ; Christian P. Speer, MD, FRCPE Director and Chairman University Children's Hospital Josef-Schneider-Str. 297080 Würzburg/Germany

0104NEO

SURFACTANT PROTEIN D IN NEWBORN INFANTS

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Background/aims Surfactant is synthesized and secreted by alveolar type II epithelial cells and consists of aproximately 90% lipids and 5–10% surfactant specific proteins (SP). Four specific proteins called A-D are identified. SP-B and SP-C are hydrophobic polypeptides accellerating the adsorption of lipid to the surface of the alveoli, while SP-D and SP-A are hydrophilic and participate in the innate host defence system. SP-D and SP-A is very similar to complement protein C1q and belong to the group of collectines. Studies of amniotic fluid and lung tissue shows increasing values of SP-D with increasing gestational age. SP-A and D in amniotic fluid is therefore used as a measure of lung maturation. The levels of SP-A in umbilical cord blood as well, depend on gestational age and perinatal conditions, but in terms of SP-D, this is not investigated. The aim of the study is to find the normal range of SP-D in newborn infants and to elucidate the role of surfactant protein D in respiratory distress and neonatal infections. Matherial Infants born at the Odense University Hospital, 01.08.00 – 28.02.02 Methods Serum SP-D was measured by enzyme-linked immunosorbent assay (ELISA) in umbilical cord blood and capillary blood from 458 mature and 254 premature infants. **Results** Umbilical cord levels of SPD was < 20 - 1544,7 ng/ml (mean 470,5 ng/ml) in infants born at term and 140,1 - 2551,6 ng/ml (876,0 ng/ml) in infants born prematurely. Capillary SPD was 195,5 - 2669,1 ng/ml (861,9 ng/ml) in mature and 197,7 -17783,0 ng/ml (2114,7 ng/ml) in prematures. Mode of delivery and length of labor influenced the capillary levels of SPD, but not the umbilical cord blood levels. In infants with premature rupture of the membranes (PROM) for more than 24 hours, the umbilical cord blood level of SPD was lower than in infants without PROM. Infants who later developed respiratory distress or infections had significantly higher levels of SPD in umbilical cord blood and capillary blood the first days of life. **Conclusions** SPD-levels in umbilical cord and capillary blood are highly variable. The levels are depending on both maternal, perinatal and neonatal factors.

0112NEO

THE EFFECT OF HUMAN RECOMBINANT ERYTHROPOIETIN ON PREVENTION OF ANEMIA OF PREMATURITY.

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Backgroud and objective: Premature infants often developes significant anemia that requires blood transfusion, which carry a significant risk. Recombinant human erythropoietin by stimulation of erythropoiesis could reduce the occurence of anemia of prematurity in premature infants. **Material and Method:** From April 2001 to march 2002, 24 neonates in newborn services at Amirkola children hospital randomly asigned to erythropoietin group and control (no treatment) group. Inclusion criteria were a birth weight ≤1750 grams and a gestationa age≤ 34 week. Exclusion criteria were neonate with a problem of hemolytic anemia,congenital infections, congenital malformation, severs asphyxia, intraventricular hemorrhage(grade III and IV), need for exchange transfusion and death during the first week of life.Erythropoietin group recieved rHEPO400 unit/kg/dose subcutaneously three timea week plus 4 mg/kg/day iron orally. WBC, Hb. Hct, Reticolucyte count were obtained every 2 week until the 42 days of life, Anemia defined as a Hb≤ 8gr/dl and a Hct≤ 24%. Student t test and fisher exact used to evaluate the differences between tow groups. **Results:** Hb and HCt values were significantly higher in erythropoietin group than the control group after the 14th day of the study ($P < 0.04$) and this differences was getting higher until the end of the trial. ($P < 0.0001$). Five neonates developed anemia which all of them were from control group. None of the erythropoietin group developed anemia. **Conclusion:** The results of this study confirm the efficacy of recombinant human erythropoietin in the prevention of anemia of prematurity. *Keywords:* Neonate, anemia, prematurity, anemia of prematurity, prevention

0113NEO

HOW CAN WE IMPROVE COMMUNICATION WITH PARENTS ON THE NEONATAL UNIT? – PARENTS DECIDE

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Introduction: Good communication by neonatal staff reduces stress experienced by parents of neonates receiving intensive care. Our aim was to assess the effectiveness of communication on a neonatal unit and identify ways to make improvements. **Methods:** A retrospective study was preformed over a period of one year in infants below 33 weeks gestation and all babies requiring intensive care for over 24 hours. Infants who died were excluded. A postal questionnaire was sent to parents for their opinion on various aspects of communication by staff using satisfaction evaluation scores. Parental attendance during ward rounds in other units was assessed by telephone survey. **Results:** Questionnaires were sent to parents of 133 infants and a return of 88 (71.5%) was obtained. Over 90% of parents gave high scores for the welcome they received on the unit and for the explanation of their infants' condition. Communication by nurses scored high by 83% of parents, whereas that by doctors scored high by 63% ($P<0.001$). Parents remembered meeting the consultant in 73% cases. Parents appreciated a visit from medical staff before birth, but this was done only in 31%. Many parents suggested that a counsellor be provided to discuss their concerns freely. 34% of parents felt unhappy to leave during ward rounds. A telephone survey of 40 UK neonatal units showed that most (95%) allowed parents to stay when their infant was discussed. **Conclusion:** Most parents were happy with the quality of communication by neonatal staff. This could be further improved by increasing the number of prebirth visits, increasing consultant presence on the unit, allowing parents to attend when their infant is discussed on ward rounds and having a counsellor on the unit.

0116NEO

FACTORS ASSOCIATED WITH EARLY CATCH UP GROWTH OF VLBW SGA INFANTS

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Background/aims: Intrauterine growth retardation is often a factor leading to preterm delivery to allow for early postnatal nutritional intervention. Nevertheless, clear recommendations about nutritional management of these infants are still lacking. We conducted a retrospective cohort study to evaluate early catch up growth (CuG) of VLBW SGA infants and identify possible factors that might contribute to its success. **Methods:** All SGA infants (2 among Weight, Length, Head Circumference $<10^{th}$percentile) admitted during 1996–2002 to our NICU were included in the study if they had birth weight <1500 g, no major congenital anomalies and were still hospitalized at 36 wks post-menstrual age. Data collection included demographics, anthropometry, nutritional intakes and major neonatal complications. Z scores for weight (ZsW), length (ZsL) and head circumference (ZsHC) were calculated for each infant at birth and every week thereafter until discharge. An infant was considered to have had CuG if her/his Zs were higher at discharge than at birth. Multiple logistic regression analysis was used to identify factors that might influence CuG during hospitalization. **Results:** 90 infants (GA 31.3±2.3 wks, BW 1047±310 g) met the inclusion criteria. Mean intakes during hospital stay (58.6±26.5 days) were 159.7±5.3 ml/kg/d for fluids (45.9±36.3 ml/kg/d of human milk), 99.4±5.0 kcal/kg/d for metabolizable calories and 2.7±0.3 g/kg/d for metabolizable proteins. Mean weight loss was 8.1±3.9%; BW was regained after 9.,7±3.1 days of life; total enteral nutrition (150 ml/kg/d) was reached after 27.0±22.8 days of life. W gain resulted in 17.5±3.3 g/kg/d; L and HC gain were 1.16±0.25 and 0.96±0.22 cm/wk, respectively. Zs at birth were -1.92±0.53 for W, -2.38±0.85 for L, and -2.18±0.62 for HC; Zs at discharge were -2.05±0.70 for W, -1.99±0.95 for L, and -1.07±0.78 for HC. Mean weekly Zs changes were -0.01±0.06 for W, 0.06±0.12 for L, and 0.16±0.12 for HC. At discharge there were 91.7% SGA infants for W, 78% for L and 35.9% for HC. During hospitalization, 48,8% of infants experienced CuG for W, 64.6% for L and 94.6% for HC. Multiple logistic regression analysis identified gestational age as an independent positive predictor of both W CuG (OR 2.7 CI 95% 1.5, 4.8) and L CuG (OR 1.8 CI 95% 1.1, 2.8); human milk was a negative predictor of W CuG (OR 0.98 CI 95% 0.96, 0.99) and metabolizable proteins were a positive predictor of L CuG (OR 1.06 CI 95% 1.01, 1.12). No significant factors were found for HC CuG. Zs at birth, enteral intake, metabolizable calories, exposure to dexamethasone, days of oxygen, or sepsis were not found to be significant predictors for any CuG. **Conclusions:** VLBW SGA infants could show CuG already during hospitalization, expecially in HC. Prematurity was identified as the main independent factor associated with CuG; among nutritional factors, the positive role of metabolizable proteins on L CuG is consistent with results showing the benefits of aggressive protein intake. Further studies are needed to establish the effects of early CuG on long term growth and morbidity.

0117NEO

LACTATIONAL EXPOSURE TO DI-(2-ETHYLHEXYL)- PHTHALATE

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Background/aims: Since the 1930s, plasticisers have been used to impart flexibility to an otherwise rigid polyvinylchloride (PVC). Di-(2-ethylhexyl)- phthalate (DEHP) is the most widely used plasticiser in PVC formulations. However, DEHP leaks out from PVC items with time and use, and consequently it is an ubiquitous environmental contaminant. Babies are exposed to DEHP for their whole lifetime via the environment, consumer products and medical devices, but foodstuffs represents a main source. Since very few information exists on lactational exposure to DEHP and/or its main metabolite MEHP, we tested their presence in milk from healthy mothers. **Methods:** DEHP and MEHP concentrations in colostrums or milk samples from 17 healthy mothers (age, M ± SD: 30.8 ± 4.3 yr, range: 23–39) breastfeeding their infants (N=17, vaginal delivery: 29.4%; gestational age: 36.4 ± 3.3 wk, range: 29–41) were measured by High Performance Liquid Chromatography (HPLC). **Results:** Detectable DEHP and/or MEHP were found in 16/17 (94.1%; $\chi^2=11.53$, df=1, P=0.0007) and 2/17 (11.8%; $\chi^2=8.47$, df=1, P=0.0042) of the samples, respectively. Either DEHP or MEHP were present in all the examined samples. Mean concentrations of DEHP and MEHP were 1.01±0.27 μg/ml (95% C.I. for the mean:0.86–1.15) (value range: 0.57–1.44) and 0.68± 0.56 μg/ml (value range: 0.28–1.08), respectively. **Conclusions:** These findings indicate that human exposure to DEHP can occur during breastfeeding . Further research is needed to clarify its possible biological effects.

0118NEO

GI AND GENETIC ANOMALIES IN INFANTS EXPOSED PRENATALLY TO METHAMPHETAMINE

Jan Sherman [1] and Michael P Sherman [2]. [1]School of Nursing, Family Health Care, University of San Francisco, CA and [2]Pediatrics, University of California, Davis, CA. City: San Francisco, California, USA **Background:** Prenatal cocaine use has been associated with an increased risk of birth defects. In the past decade there has been a surge in prenatal methamphetamine (meth) use. No study has compared the adverse outcomes associated with prenatal meth and cocaine use. **Objective:** The purpose of this study was to compare the type of newborn abnormalities associated with prenatal meth and cocaine use. Design/Methods: A Level III NICU admission database was reviewed from 1990 to 2002. Infants were divided into two groups: Illicit prenatal drug exposure (IPDE) and no illicit prenatal drug exposure (NIPDE). Drug exposure was defined as a positive maternal or infant drug screen, and/or a history of illicit prenatal drug use. Infants were then sub-classified by illicit drug. Multivariate analysis was used to determine significant differences between the two groups. **Results:** A total of 6555 infants were admitted to the NICU, with 1103 positive for IPDE (17%). Of these infants, 563 were positive for meth and 325 were positive for cocaine. Infants with IPDE to meth were more likely to have GI ($p = .04$) and genetic ($p = .006$) anomalies when compared to infants with IPDE to cocaine.

GI Anomalies Associated with Prenatal Exposure to Meth and Cocaine		
GI Anomaly	Meth (n = 563)	Cocaine (n = 325)
Gastrochisis	6	
Omphalocele	1	1
Imperforate anus	1	
Atresia	2	
Volvulus/malrotation	2	1
Ileus	2	
TEF/EA	1	
Hirshsprungs	1	
Total	16	2
Genetic Anomalies Associated with Prenatal Exposure to Meth and Cocaine		
Trisomy21	5	
VCF		1
Multiple genetic anomalies	29	5
VATER	1	
Beckwith Weidemann	1	
FAS	3	2
Pierre Robin	2	
Total	41	8

Conclusions: In this NICU population, IPDE to meth was significantly associated with an increased incidence of GI and genetic anomalies. Given the nature of the GI defects, vascular disruption in meth exposed infants may be more prevalent than in cocaine exposed infants.

0121NEO

T_{H1}/T_{H2} AND OTHER T CELL SUBPOPULATIONS IN BREAST FED AND ARTIFICIALLY FED NEONATES

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Background/Aim: Experimental and in vitro clinical studies give evidence that biological products present in human milk may have an immuno-modulatory effect on the neonatal immune system promoting a T_{H1} type immune response. The purpose of this study was to investigate the effect of breast feeding on lymphocyte subpopulations and the T_{H1}/T_{H2} type deviation during the 1st month of life, when exogenous antigen stimulations are very limited. **Material-Methods:** The study population was consisted of 79 inborn, healthy term neonates, 41 exclusively breast fed for at least 1 month and 38 artificially fed. Immunological investigation was performed on the 1st and 30th days of life and included measurement of the total T cells and T cell subpopulations (CD3+CD4+, CD3+CD8+, CD8+CD45RA, CD4+CD29+), natural killer cells (NK) and measurement of intracellular production of IL-2 (T_{H1} immune response) and IL-4 (T_{H2} immune response) by the T helper cells, using flow-cytometry and the appropriate monoclonal antibodies. **Results:** Comparison of values between day 1 and day 30 showed a significant decrease in the absolute numbers of total T cells, CD3+CD4+ cells, CD8+CD45RA and CD4+CD29+ cells, as well as in the CD3+CD4+/ CD3+CD8+ ratio and the IL-2/IL-4 ratio on the 30th day, in both groups. Comparison between breast fed and artificially fed neonates revealed no significant difference in any of the parameters measured either on the 1st or on the 30th day of life. **Conclusions:** During the 1st month of life a decrease of the total T cells and most T cell subpopulations, along with a predominance of T suppressor/cytotoxic cells and T_{H2} profile is observed. Our findings do not support the view that breast feeding affects the T_{H1}/T_{H2} T cell profile during the first month of life.

0123NEO

OUTCOMES IN <1000G INFANTS USING A NASAL CPAP-BASED STRATEGY

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Aims: To compare outcomes for infants <1000g treated with a predominantly nasal CPAP approach (modelled on that of Columbia University, New York) with outcomes recorded by the Australian and New Zealand Neonatal Network (ANZNN). **Methods:** Data on all infants <1000g admitted for intensive care was collected prospectively for the 29 neonatal units contributing to the ANZNN database (i.e. all level 3 units in the region). Outcomes for infants treated at Middlemore Hospital over a 3 year period (1998–2001) were compared with the ANZNN data for 1999. **Results:** 64 infants were admitted to Middlemore Hospital and 954 to the 29 neonatal units. The 2 groups were similar with respect to birth weight, Apgar scores, sex and delivery method. Gestational age was lower in the Middlemore infants and outcome variables were adjusted for this difference. Fewer babies at Middlemore were born to mothers who had completed antenatal corticosteroids ($p<0.001$). The Middlemore Hospital group spent longer on CPAP ($p<0.001$) and had less time in oxygen (median 4 days compared to 54 days; $p<0.001$). Fewer of the Middlemore cohort were in oxygen at both 28 days and 36 weeks corrected gestation (Odds ratio 0.15; 95%CI 0.07–0.32) and fewer infants were discharged home on oxygen (Odds ratio 0.38; 95%CI 0.16–0.90). Other outcomes were a significant reduction in the number of infants with culture proven sepsis at Middlemore Hospital (Odds ratio 0.42; 95%CI 0.25–0.73). There was a higher rate of necrotising enterocolitis at Middlemore Hospital (Odds ratio 2.4; 95%CI 1.11–5.17). Rates of severe intraventricular haemorrhage (grade 3 or 4) and requirement for laser therapy for retinopathy of prematurity, length of hospital stay and survival rates were not significantly different. Results of follow up at 18months corrected age were available for 89% of the Middlemore group. 12.5% had either severe cerebral palsy (CP), blindness or a developmental quotient (DQ) <50, 10% had either moderate CP, deafness or DQ 50–69, 42.5% had either mild CP or a DQ 70–84 and 35% had no CP and DQ 85 or above. **Conclusions:** Improved respiratory outcomes for infants <1000g were evident at Middlemore Hospital inspite of a lower rate of antenatal steroid use. The rate of culture proven infection was lower although there were more cases of necrotising enterocolitis. Developmental outcome was comparable with that of other neonatal units. The use of a nasal CPAP-based respiratory support system appeared to have beneficial effects without adversely affecting neurodevelopmental outcome.

0125NEO

LACTOFERRIN AND LACTOBACILLUS ENHANCE NEONATAL ANTIBACTERIAL GUT DEFENSES.

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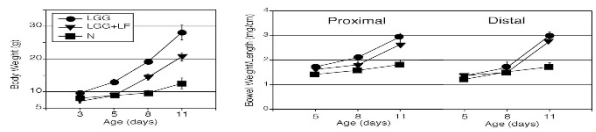
Background and Aims: Extremely preterm human infants have increased susceptibility to small bowel invasion by bacteria. We hypothesized that the type of commensal bacteria that initially colonize the immature gut may program epithelia for enhanced growth and maturation of their anti-bacterial host defenses. We also theorized that the major milk protein, lactoferrin, would act as an adjuvant and would facilitate growth of a "bifidus flora" in the small bowel. **Methods:** Newborn rats were given enteral recombinant human lactoferrin (rhLF) to augment colonization of the small bowel with Lactobacillus GG (LGG). Pups were treated with nothing, LGG, or rhLF + LGG from 3 through 7 days of age. Gut colonization by LGG was quantified in lavaged jejunal and ileal fluid and gut wall homogenates. The former specimens showed planktonic and the latter samples demonstrated adherent growth of gut-related LGG. The 3 groups of pups also had enteral infection with Escherichia coli (10^{12} CFU/kg) induced on day 5 of life. Sixteen h later, the numbers of E. coli were measured in small bowel fluid and in the gut wall. **Results:** Control pups not treated with LGG initially had lactic acid bacteria colonize the bowel, but these bacteria did not persist. Pups treated with LGG or rhLF and LGG had persistent ileal colonization with LGG at 8 and 11 days of age. The Figure shows treated versus non-treated neonatal rats had significantly accelerated proximal (jejunal) and distal (ileal) small bowel and somatic growth ($P<.05$).



After E. coli-related gut infection, planktonic and epithelia-adherent growth of E. coli in the small bowel was effectively reduced by treatment with rhLF and LGG ($P<.05$). Small bowel histopathology in rhLF + LGG-treated and infected pups showed several beneficial features: 1) intact Paneth cells with many granules compared to de-granulated, abnormal Paneth cells in non-treated, infected animals, 2) reduced villous edema, and 3) an earlier appearance of domed villi, the precursors of Peyer's patches, in the ileum. Additional studies of rhLF and LGG, alone or in combination, revealed no adverse effects in neonatal rats. **Conclusion:** rhLF and the common probiotic, LGG, promoted gut growth and improved host defenses against invasive E. coli in the nascent small intestine. We propose rhLF and LGG may be prophylactic therapeutic agents that might reduce necrotizing enterocolitis and gut-related sepsis in extremely preterm human infants.

0126NEO

PROOF: NEONATAL PANETH CELLS DEFEND THE SMALL BOWEL FROM ESCHERICHIA COLI.

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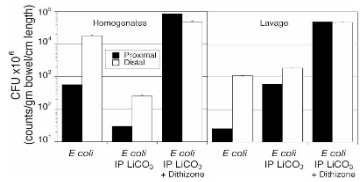
Background and Aims: In adults, the small bowel crypts are lined with special epithelia called Paneth cells (PC). These epithelia contain and secrete many anti-bacterial agents and are believed to protect the small bowel from bacterial invasion. The role of PC in anti-bacterial defense of neonatal small bowel is unknown. We theorized that destruction of PC would result in high numbers of planktonic and epithelia-adherent E. coli after gut infection. **Methods:**Dithizone, a zinc binding dye, was used to rapidly deplete PC from the intestine of 4-d-old rats. Dithizone [75 mg/kg] was ideally dissolved in 50 mM sodium compared to lithium carbonate [CO_3]. Dithizone was given by intraperitoneal injection 6 hours before rat litters were infected with intra-gastric Escherichia coli [~2 x 10^{12} colony-forming units per kg]. Control litters were given either the dithizone vehicle or NaCl i.p. followed by infection with E. coli. Eighteen hours after infection, survival and illness severity were determined using an established scoring system. Small bowel lavage (planktonic or luminal growth) and small bowel homogenates (epithelial gut-related growth) were quantitatively cultured for E. coli. Treated and control pups also had the proximal and distal small bowel fixed in situ and examined microscopically for Paneth cells [hematoxylin and eosin stained sections, 1000x]. **Results:** Deaths were significantly (P<.05) increased in the dithizone treated and infected pups (25/32 pups) compared to the $NaCO_3$- ⅔ and NaCl-treated and infected (3/24) pups [8 pups per litter]. Illness scores were also significantly higher in the dithizone group v. controls. The Figure shows the numbers of E. coli in small bowel lavages [gut fluid] and homogenates [gut epithelia and wall]. The numbers of E. coli were significantly increased in the proximal [jejunum] and distal [ileum] segments of the small bowel (P<.05). In dithizone-treated pups, stained histologic sections revealed no PCs in the crypts v. controls.



Conclusions: A new method of depleting Paneth cells from the small bowel and studying enteric bacterial infection is described. This procedure shows the importance of Paneth cells in neonatal gut-related defense against invasive enteric pathogens.

0127NEO

SEVERE NEONATAL HYPERBILIRUBINEMIA AND BLOOD EXCHANGE TRANSFUSION

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Backgrund: Neonatal jaundice is a common condition that could potentially lead to severe neurotoxicity (kernicterus) and frequent indication for blood exchange transfusion(BET). The aim of this study was to determine the correlation between the causes of neonatal jaundice and need of blood exchange transfusion. **Methods:** From junuary of 1998 to December 2000, 100 neonate treated by blood exchange transfusion (BET) in NICU of Amirkola Children Hospital (Babol-Iran).Indication of BET were serum bilirubin level(SBR) of ≥ 20mg/dl in thigh risk term neonate and ≥ 25 mg/dl in no risk one. For low birthweight(LWB) infants a SBR mg/dl ≥ 1% of body weight in gram was an indication for BET. Data were analyzed by the X2 and Z statistic test. **Results:** The need for BET in male sex were 12% higher than femals. 41.25% were due to ABO incompatibitity, 23.75% G6PD defficiency, 13.75% idiopathic, 12.5% prematurity, 5% Rh incompatibility, 2.5% sepsis and 1.25% polycythemia. ABO incompatibility and G6PD defficiency were the most common causes P<0.001 .Need for BET in LBWinfants were higher than term neonate P<0.001.**Conclusion:** According to the high incidece of ABO incompatibility and G6PD defficiency in this region , for prevention of sever neonatal hypebilirubinemia we suggest to do the umbilical cord G6PD screening and blood group typing in neonates who have a mother with O blood group .Key words:Neonates, hyperbilirubinemia, blood exchange trasfusion, G6PD

0133NEO

SURFACTANT REPLACEMENT WITH AND WITHOUT MECHANICAL VENTILATION

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Background: In neonates with respiratory distress syndrome (RDS) surfactant replacement is usually given in conjunction with mechanical ventilation. Alternatively, surfactant can be administered during a short intubation, followed by immediate extubation to spontaneous breathing with nasal continuous airway pressure (nCPAP). This treatment reduces the requirements of subsequent mechanical ventilation and also appears to reduce the need for repeated doses of surfactant. **Aim:** Develop an animal model to compare lung mechanics and bioavailability of exogenous surfactant after spontaneous breathing or mechanical ventilation. **Methods:** Preterm rabbits with a gestational age of 28.5 days were treated with pharyngeal deposition of 200 mg/kg radiolabeled porcine surfactant (^{14}C-DPPC- Curosurf®) and randomised to spontaneous breathing or mechanical ventilation for 4 hours. Measurements of lung-thorax compliance, radioactivity in bronchoalveolar lavage (BAL) and homogenized lung tissue, the degree of lipid peroxidation in BAL and Microbubble Stability Test by computerized image analysis were performed. **Results:** Dynamic lung-thorax compliance was higher in the spontaneously breathing animals compared to the mechanically ventilated animals ($p<0.05$). The recovery of radiolabeled Curosurf in bronchoalveolar lavage was significantly lower in the spontaneously breathing group compared to the mechanically ventilated group ($41\pm11\%$ versus $72\pm9\%$, $p<0.01$), indicating higher degree of tissue association. Microbubbles were predominant in the lavage fluid from both groups, but the degree of lipid peroxidation was higher in mechanically ventilated animals ($p<0.05$), suggesting surfactant inactivation. The estimated pool of endogenous surfactant was equal in both groups. **Conclusion:** We conclude that mechanical ventilation appears to impair the initial lung tissue association of exogenous surfactant and result in lower dynamic compliance and higher degree of surfactant lipid peroxidation compared to spontaneous breathing. This might contribute to the clinical observation that the duration of the effect after surfactant treatment is longer and, subsequently, repeated doses are rarely indicated in infants given surfactant replacement during spontaneous breathing with nCPAP.

0134NEO

RANDOMIZED CONTROLLED TRIAL OF LOW-DOSE ORAL ERYTHROMYCIN IN FEEDING INTOLERANCE IN PRETERM INFANTS

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Background: Erythromycin is a motilin-receptor agonist that has been shown to improve feeding tolerance in adults, children, and infants. **Aim:** To evaluate the effectiveness of low-dose oral erythromycin in the management of feeding intolerance in preterm infants. **Subjects and methods:** a double blind, randomized controlled study was conducted on 60 preterm infants with feeding intolerance. Thirty infants were given erythromycin at a dose of 1 mg/kg tds and 30 infants were given placebo (normal saline). **Results:** Overall, low dose oral erythromycin did not influence the time to full enteral feeds or the number of episodes of gastric aspirates. However, in infants > 32 weeks gestation, infants in the erythromycin group achieved full enteral feeds earlier than placebo group (10.5 ± 4.1 vs $16.3 + 5.7$ days, respectively; $p= 0.01$), had fewer episodes of gastric aspirates ($p= 0.03$) and had shorter duration of total parenteral nutrition (TPN) ($p= 0.03$). In infants with gestational age ≤ 32 weeks, there were no significant differences between erythromycin and placebo groups regarding these variables. None of the infants had adverse effects related to erythromycin therapy. **Conclusions:** Low-dose oral erythromycin had beneficial effects on feeding intolerance and it shortened the duration of TPN in preterm infants older than 32 weeks gestation. A similar effect on younger preterm infants was not found. Erythromycin was well tolerated by all infants in our study.

0135NEO

SURFACTANT METABOLISM IN INFANTS UNDERGOING LUNG TRANSPLANTATION

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Background: We have previously used stable isotope labeled precursors of pulmonary surfactant phospholipid to distinguish normal and disrupted surfactant metabolism in newborn infants. Infants undergoing lung transplantation are a unique population. Pre-transplant they all have irreversible respiratory failure and post-transplant their lung function usually improves dramatically. Whether surfactant metabolism is disrupted in the newly transplanted lungs is unknown. **Aim:** To compare in vivo surfactant metabolism before and after lung transplantation.**Methods:** 2 infants (A - born at term, transplanted at 80 days of age, diagnosis alveolar proteinosis of unknown ethiology and B - born prematurely at 31 weeks gestation, transplanted at 86 days of age, diagnosis hypoplastic lungs secondary to oligohydroamniosis) received 24-hour intravenous infusions of [1-$^{13}C_1$] acetate at 2 week intervals prior to lung transplantation and at 24 hours post-surgery. Disaturated phospholipids (DSPL) were extracted from serial tracheal aspirates (TA). The amount and fatty acid composition of DSPL were measured in each sample with quantitative gas chromatography (GC) and the ^{13}C-enrichment over time was measured with GC/mass spectrometry. For one subject, theses measurements were compared in simultaneous TA and bronchoalveolar lavage fluid (BAL) obtained at transplantation. Fractional synthetic rate (FSR), the proportion of the surfactant pool synthesized de novo (%/day) was calculated. **Results:** The amount of DSPL and the proportion of C16:0 (palmitate) in the DSPL increased in TA obtained before and after transplantation (Table). FSR increased after transplantation in Subject A, but did not change in Subject B. The amount of DSPL in BAL obtained at transplantation was greater than that in a simultaneous TA (68 vs 29 umol), however the ^{13}C-enrichment (BAL: 2.8% vs TA 2.5%) and % C16 (BAL: 90% vs TA 84%) were similar.

	Subject A		Subject B	
	Pre-transplant	Post-transplant	Pre-transplant	Post-transplant
DSPL (nmol)	10±4	65±49	14±11	427±268
Palmitate (% of DSPL)	55±20	89±6	65±14	88±4
FSR (%/day)	2.4	5.3	23.3	23.4

Conclusions: In these two subjects, pulmonary surfactant production was intact in the transplanted lungs in the immediate post-operative period. The greater proportion of palmitate in the DSPL suggests that the surfactant in the newly transplanted lungs is likely to be more effective. The greater amount of DSPL in TA post-transplant suggests a larger surfactant pool size. This would indicate a greater increase in absolute synthetic rate post-transplant than what is reflected in the FSR, but further studies will be necessary to more accurately determine surfactant pool sizes in the pre- and post transplant period. Furthermore, the similarities betweeen TA and BAL in enrichment and fatty acid profile demonstrate that TA derived surfactant is an appropriate representation of alveolar surfactant for in vivo studies of surfactant metabolism using stable isotopes

0143NEO

EARLY ^{1}H SPECTROSCOPY AND BRAIN WATER T2 IN ENCEPHALOPATHIC INFANTS

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Aim: To compare the separate abilities of 1)early quantitative magnetic resonance imaging (MRI) measurements of the spin-spin relaxation time (T2) of brain water and 2)lactate/N-acetylaspartate (Lac/Naa) peak-area ratios measured by proton spectroscopy (^{1}H MRS) to predict adverse neurological outcome in infants with neonatal hypoxic-ischaemic encephalopathy . Subjects 22 infants (37 – 42 weeks gestation) with suspected perinatal hypoxia-ischaemia and signs of acute neonatal encephalopathy were studied within 5 days of birth. **Methods:** Spin-echo images (echo time (TE) 25 and 200 ms; repetition time (TR) 4.5 s) were acquired at 2.4 Tesla and T2 maps calculated. Regions of interest (ROI; 0.2ml volume) were defined within the basal ganglia (BG), frontal and parietal white matter (FWM & PWM). In order to compare measurements from similar regions of tissue, a thalamic (thal) ROI (2 ml volume) was defined as the intersection of the medial imaging slice and the ^{1}H-MRS voxel. Mean T2s were calculated for each ROI. Thal Lac/Naa was determined by single voxel ^{1}H-MRS (PRESS; TE 270ms; TR 2 s; 256 echoes averaged; 8ml voxel volume). In surviving infants neurological assessments and Griffiths developmental assessments at age one year were undertaken by a paediatrician and psychologist who was blind to the clinical history and MR findings. Infants with abnormal neurology and/or Griffiths developmental quotient between 71 and 84 in at least one subscale were classified as being impaired. Infants with disabling neurological signs and/or at least one subscale Griffiths quotient of less than 70 classified as disabled.

Results:

Outcome	Group Median (interquartile range)	Group mean (SD) (ms)			
	Thal Lac/Naa	Thal T2	BG T2	FWM T2	PWM T2
Normal (n=8)	0.24 (0.18-0.40)	142.6 (9.9)	146.8 (10.9)	202.0 (38.2)	168.4 (9.3)
Impaired (n=6)	0.38 (0.22-0.69)	164.6 (9.7)$^+$	176.2 (14.2)$^+$	223.5 (71.6)	206.0 (34.9)$^+$
Disabled/ Dead (n=8)	1.26* (0.81-2.03)	158.9 (22.9)	169.5 (28.7)	214.4 (51.1)	185.0 (36.8)

*$p<0.05$ Mann-Whitney Rank Sum test; $^+$ $p<0.05$ unpaired t-test; all compared to normal outcome group. **Conclusions:** Whilst early Thal ^{1}H MRS is predictive of subsequent disability or death, deep grey matter and PWM brain-water T2 seems better at predicting infants who will develop impairments only. At age < 5 days, FWM T2 was not predictive of outcome. Combining MRI T2 relaxometry with ^{1}H-MRS may improve the prognostic specificity of the neonatal MR examination

0146NEO

CD44-V6 EXPRESSION IN SMOOTH MUSCLE CELLS IN THE POSTNATAL REMODELLING PROCESS OF DUCTUS ARTERIOSUS

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Background: The Ductus Arteriosus (DA) is a special vessel because it forms intimal thickening during the last two trimesters of pregnancy leading to obliteration when the vessel constricts postnatally. This inward vessel remodelling is multifactorial: after birth, the rise in oxygen tension induces contraction of the DA; moreover the slow flow through the DA stimulates vessel smooth muscle cells (SMC) to proliferate and migrate from the media to the intima with neointimal cushion formation. Besides, remodelling involves alteration in the balance between cell proliferation and apoptosis, and matrix production and degradation as well. CD44 is a family of surface cell proteoglycans involved in cellular activation, proliferation and migration. The isoform CD44-v6 is expressed minimally on SMCs in the media of normal arteries, but is expressed highly on SMCs in the neointima and media of injured arteries. After birth, hypoxia within the DA could induce increased expression of CD44-v6 on SMCs; this leads to SMCs phenotypic modulation from "contractile" to "synthetic" with neointimal cushion formation and DA closure. **Methods:** DA were excised from autoptic specimens of 11 infants who died at different ages: five at 2–15 days (all patent), one at 45 days (partially patent), three at 4 – 6 months (all closed) and two at 5 months (both patent). CD44 and CD44-v6 expression was evaluated by immunohistochemistry. The nature of CD44-v6 positive cells was determined with antibodies against SMC-actin and CD45RO (leucocyte antigen). **Results:** CD44 was not expressed by SMCs of any of the DAs tested. Its isoform, CD44-v6, was expressed by SMCs in DA with active inward wall remodelling, i.e. samples between 2 and 15-days. Both media and neointima SMCs showed high positivity. SMCs either of closed DAs or of the late patent DAs were Cd44-v6 negative. CD44-v6 positive cells were SMC-actin positive and CD45RO negative. **Conclusions:** These preliminary results support the hypothesis that the CD44-v6 upregulation after birth, probably due to hypoxic condition in DA, could induce SMC proliferation and migration from the media to the intima, thus allowing DA closure.Vice versa, a reduced or absent CD44-v6 expression could play a role in patent DA persistence. Alternatively, the overexpression of CD44-v6 could reflect the persistency of a fetal upregulation, secondary to the low intrauterine oxygen tension. Further studies, including fetal specimens, are needed to better elucidate the role played by CD44-v6 in postnatal ductal closure. (Supported by grant N° 196/2001 of the Italian Ministry of Health).

0149NEO

OXIDATIVE IMBALANCE IN PRETERMS WITH MECHANICAL VENTILATION

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Background: The reactive oxygen species, the free radicals can cause pathology. Exposition to high oxygen concentrations would cause a greater production not compensated by the preterms immature enzymatic systems and their nutritional and surfactant deficiency. **Aims:**1. To assess the oxidant-antioxidant status in a two healthy newborns groups: term (TN) and preterm (PTN). 2. To assess the oxidative stress situation in a preterm newborn group hyalin membrane disease (HMD) affected with mecanical ventilation. 3. To compare the different groups. **Methods:** Sanguine samples were obtained in 2 and 7 life days in routine studies. Plasmatic malondialdehyde (MDA) and lipid peroxides (LPO) as markers of lipid peroxidation were assessed. We determined plasmatic antioxidants: vitamin E, sulfhydryl groups (SH), and antioxidant plasmatic activity (AOA). Clinical parameters were assessed. **Results:** The preterm newborn with HMD that need mechanical ventilation, show high oxidative stress parameters and low antioxidants defenses in relationship to the full-term and premature babies without respiratory pathology.

Table 1	2 Days			7 Days		
	TN	PTN	HMD	TN	PTN	HMD
MDA (µM)	1,1±0,5	1,8±1,7 ns	2,9±1,9 p< 0'01	0,9±0,4	1,4±1 p<0'05	2,4±2 p<0'01
LPO (µM)	2,6±1,3	4,4±2,6 p<0'01	7,2±2,7 p<0'0001	1,47±0,9	2,9±1,8 p<0'01	5,5±3,8 p<0'001
Vitamin E (µM)	14±5,6	10,7±4,8 p<0'05	7,7±4 p<0'01	29±12	27±10 ns	22,4±3 p<0,05
AOA (µM)	2158±130	1889±377 p<0'01	1978±427 ns	2136±149	1968±215 p<0'01	1998±239 ns
SH (µM)	735±269	632±145 ns	530±126 p<0'01	830±300	692±220 ns	608±195 p<0'01

Conclusions: Oxidative stress is increased in preterm newborns. This oxidant-antioxidant imbalance is more severe in the prematures mechanically ventilated by their HMD. Specific antioxidant therapy, aimed at reducing oxidative stress in preterms with HMD needs to be assessed.

0154NEO

CHANGING MORTALITY AND NEONATAL MORBIDITY IN VERY PRETERM INFANTS.

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Aims: To investigate the relation between changes in perinatal risk factors and short term outcome in very preterm (VPT) infants (gestational age (GA) <32 weeks). **Methods:** Comparison of perinatal risk factors and their impact, estimated as Odds ratio's (OR's), on mortality and morbidity (BPD and IVH) in two geographical surveys of VPT infants born in 1983 and in 1993. OR's were estimated using a logistic regression model with backward stepwise procedures in which antenatal, perinatal and postnatal factors were introduced and significant factors were retained in a chronological way. To answer the question whether the OR of each risk factor changed over time, we included year of birth (Timefactor) and its interaction terms with the perinatal risk factors in a model fitted to the combined populations. Significance of the interaction term corresponds to a significant change in the magnitude of the effect between 1983 and 1993. **Results:** The 1983 population consisted of 1007, the 1993 population of 727 VPT infants, GA's 29.1 ± 2.0 and 29.4 ± 1.8 weeks and BW's 1247 ± 349 and 1238 ± 363 grams respectively. Neonatal mortality decreased from 28.0 to 15.3 percent (P<.000) and one-year mortality from 32.3 to 17.8 percent (P<.000). Of all perinatal risk factors, the OR of sex (male versus female) changed significantly from 1.35 in 1983 to 2.30 in 1993 and the OR of multiple birth (multiplet versus singleton) from 1.68 to 0.92, corrected for all other perinatal factors. The incidence of BPD in infants discharged alive from hospital increased from 13.6% to 18.2% (P=.026). The OR on BPD of sex changed significantly from 2.36 in 1983 to 1.12 in 1993 and of birth weight (BW) from 0.96 to 0.85 for each increase of 100 grams BW, corrected for all other perinatal factors. The incidence of IVH grade 2–4 in 1983 was 11.3% and in 1993 8.5% (P=.115). Introduction of the Timefactor did not change the OR′s of the perinatal risk factors. **Conclusions:** The magnitude of the OR′s of the factors sex and multiple birth on mortality changed over time. In infants discharged alive from hospital, the magnitude of the OR′s of sex and BW on BPD changed over time. The OR′s of perinatal risk factors on IVH did not change over time.

0160NEO

OLIGODENDROCYTE APOPTOSIS CAUSED BY GLUTARIC ACID AND ITS METABOLITES

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Background: Glutaryl-CoA dehydrogenase deficiency is an inherited metabolic disease characterized by elevated concentrations of glutaric acid (GA) and its metabolites glutaconic acid (GC) and 3-hydroxy-glutaric acid (3-OH-GA). Its hallmarks are striatal and cortical degeneration which have been linked to excitotoxic neuronal cell death. However, magnetic resonance imaging studies have revealed also widespread white matter disease. We therefore investigated the effects of GA, GC and 3-OH-GA on the rat immature oligodendroglia cell line, OLN-93. For comparison, we also exposed the neuroblastoma line, SH-SY5Y, and the microglia line, BV-2, to GA, GC, and 3-OH-GA. **Methods:** Flow cytometry was used to assess apoptosis via annexin-V, anti-active caspase-3 antibody, and propidium iodide staining, while cell viability was measured by metabolism of 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyl tetrazolium (MTT). **Results:** Apoptosis but not necrosis was detected at various stages (early: annexin-V, effector: caspase-3) after 24–48 h incubation with GA, GC or 3-OH-GA in OLN-93 but not in neuroblastoma or microglia cells. This pattern was confirmed in MTT assays. **Conclusion:** GA, GC and 3-OH-GA directly initiate the apoptotic cascade in oligodendroglia cells. This mechanism may contribute to the white matter damage observed in glutaryl-CoA dehydrogenase deficiency.

0162NEO

LIPID PEROXIDATION PRODUCTS IN PRETERM INFANT PLASMA WITH RETINOPATHY.

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Background: Improvement in neonatal intensive care have resulted in more preterm babies surviving. The incidence of retinopathy appears to be related to birth weight and to these babies being more ill. Oxygen induces aberrant physiologic responses that can be damaging: vasoconstriction in the retina is an early response that can lead to vasoobliteration, neovascularization, and retinal traction (retinopathy of prematurity). Oxygen also causes tissue injury through the formation of reactive oxygen intermediates and peroxidation of membrane lipids. The aim of this study was to assess the oxidant-antioxidant status in preterm babies with retinopathy compared to preterm without it. **Patients and methods:** 18 preterm babies (31'9±2'5 weeks of gestational age and 1813±577g of birth weight) hyalin membrane disease affected with mechanical ventilation were estudied. Five premature developed retinopathy. Sanguine samples were obtained in 2 and 7 life days, during routine studies. Plasma lipid peroxides and oxidability as markers of lipid peroxidation were assessed. We determined plasmatic antioxidants: vitamin E, sulfhydryl groups, selenium and antioxidant plasmatic activity. Transferrin, albumin, bilirrubin, uric acid and copper were assessed. **Results:** Preterm babies with retinopathy to birth show higher oxidative stress parameters (lipid peroxides: 8'1± 2'5 vs. 6'8±2'8μM, ns; and plasma oxidability: 1±0'5 vs. 1'3±0'5nmol dien/min, ns), as well as to 7 days (lipid peroxides: 7'8±4'3 vs. 4'6±3'7μM, ns; plasma oxidability: 1'3±0'6 vs. 2'4±0'5nmol dien/min, p<0'001). Antioxidants defenses to birth are lower in the children that developed retinopathy in relationship to preterm babies without retinopathy (vitamin E: 5±5 vs. 8'6±4μM, ns; antioxidant plasmatic activity: 1806±690 vs. 2051±269μM, ns; sulfhydryl groups: 432±97 vs. 576±115μM, p<0'05; selenium: 31±6'5 vs. 39'2±9μg/L, p<0'05) as well as to 7 days (vitamin E: 21±5 vs. 23±7μM, ns; antioxidant plasmatic activity: 1869±332 vs. 2034±214μM, ns; sulfhydryl groups: 561±229 vs. 626±188μM, ns; selenium: 35'6±13 vs. 40±8μg/L, ns). We don′t find significant differences in the FiO_2 of both groups. **Conclusions:** The retina is an especially susceptible tissue to suffer oxidative damage. Preterm babies with retinopathy show a greater oxidant-antioxidant imbalance than the prematures that did not develop it.

0165NEO

OXIDATIVE STRESS IN THE PREMATURE INFANTS OF PREECLAMPTIC MOTHERS

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Background/aims: Oxidative stress plays an important role in the pathophysiology of preeclampsia. An increase in lipid peroxidation products and a decrease in antioxidant activity in preeclampsia have been reported in many papers. Studies on oxidant/antioxidant status of preeclampsia have been focused on maternal parameters. On the contrary, few studies have been conducted on umbilical cord of the newborn. The aim of this study was to evaluate lipid peroxidation and plasma activities of antioxidant enzymes in the premature infants born to preeclamptic mothers and to compare with the premature infants born to normotensive mothers. **Methods:** Blood samples were obtained from umbilical cord of the premature infants born to preeclamptic (n=18) and normotensive (n=9) mothers. Gestational age was similar in both groups. The cord plasma levels of malondialdehyde (MDA) and glutathione (GSH), and activities of glutathione peroxidase (GPx) and superoxide dismutase (SOD) were measured by a spectrophotometric method. **Results:** Mean gestational age was 32.1±2.1 weeks (range 26–35 weeks, median 32 weeks) in the preeclamptic group and 32.3±2.6 weeks (range 28–35 weeks, median 33 weeks) in the control group. The mean gestational age did not differ significantly among the groups (p=0.76). Mean birthweight was 1492±341 grams (range 1050–2100 grams, median 1425 grams) in the preeclamptic group and 2016±594 grams (range 1000–3050 grams, median 2000 grams) in the control group. The mean birthweight was significantly lower in the preeclamptic group (p=0.007). Cord plasma levels of MDA in the preeclamptic group were similar to the control group (2.34±0.79 versus 2.31±0.85 nanomol/ml); the difference between two groups was not significant (p=0.91). Cord plasma GSH level and GPx activity were found decreased in the preeclamptic group (406±127 μmol/L and 2.17±0.26 IU/ml, respectively) when compared to the control group (462±122 and 2.27±0.12, respectively); but the difference did not reach the significant level (p=0.44 for GSH and p=0.48 for GPx). Cord plasma activity of SOD was significantly higher in the preeclamptic group (0.47±0.29 IU/ml) than in the control group (0.22±0.14), (p=0.01). **Conclusions:** Although cord MDA levels were similar in both the preeclamptic and the control group, increased SOD activity in cord blood might be indicator of increased oxidative stress in the premature infants born to mothers with preeclampsia. Further studies performed on large population are needed to confirm these findings.

0170NEO

MEAN HEART RATE AND HEART RATE VARIABILITY IN PRETERM VENTILATED INFANTS RECEIVING MORPHINE ANALGESIA

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Background: There is no single physiological indicator that can be reliably used to assess pain or the effectiveness of analgesia in the newborn. We utilised a double blind trial investigating the use of morphine in preterm ventilated infants (The NEOPAIN Trial) to investigate the effect of morphine on mean heart rate and heart rate variability and to evaluate the potential value of these parameters in assessing the adequacy of analgesia in the clinical setting. **Methods:** Infants were randomised to receive morphine (n=18) or placebo (n=18) by continuous infusion from birth. Infants of 23–26 weeks gestation received morphine 10mcg/kg/hr, 27–29 weeks received 20mcg/kg/hr and >30 weeks received 30mcg/kg/hr. Mean heart rate and heart rate variability were measured in all babies before and during treatment. Standard deviation about the mean was used as the measure of heart rate variability. **Results:** The two groups were similar before treatment. On starting morphine, both mean heart rate and heart rate variability decreased in the morphine group compared to the placebo group ($p=0.054$ and $p=0.057$ respectively). The change in mean heart rate reached statistical significance in the lowest gestational age subgroup ($p=0.042$). The difference between treatment and placebo groups disappeared by days 3 and 4 of the infusion. **Conclusions:** There is evidence that morphine produces a reduction in mean heart rate in mechanically ventilated infants. This may represent attenuation of pain or stress. The change in heart rate variability lends support to the hypothesis that it may be an indicator of pain or stress that can be relieved by analgesia. Disappearance of these effects by days 3 and 4 of treatment suggests possible development of opioid tolerance by this stage.

0172NEO

A CONTROLLED TRIAL OF DAILY MOTHER-INFANT SKIN-TO-SKIN CONTACT AFTER EXTREMELY PRETERM BIRTH

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Background: Extremely preterm birth may impede the development of the mother-infant relationship and is associated with subsequent altered cognitive and behavioural infant profiles, even in the absence of significant neurological impairment. Skin-to-skin contact has been proposed as a simple intervention to improve infant outcomes and enhance mother-infant interaction. **Aim:** We conducted a controlled crossover trial to address the hypothesis that mother-infant skin-to-skin contact after extremely preterm birth would result in improved outcomes. **Methods:** The study was conducted in two tertiary referral neonatal intensive care units and was approved by the institutional research ethics committee. Infants born below 32 weeks gestation were enrolled within the first week after birth and assigned to either a control group receiving standard care, or to an intervention group in which mothers were encouraged to provide a 20-minute session of skin-to-skin contact once daily for 4 weeks. The study design did not prohibit mothers in the control group from providing skin-to-skin contact if they wished. Quantitative measures were used to assess mother and infant outcomes. Infant behavioural (Modified Behavioural Pain Scale) and salivary cortisol responses to the standardised stressor of routine immunisation were assessed at 4 months and 1 year; the Griffiths neurodevelopmental examination, the Fagan Test of Infant Intelligence and the Hammersmith Infant Neurological examination were conducted at 1 year postmenstrual age. Lactation performance, mother-infant face-to-face interaction, maternal measures of anxiety (State-Trait Anxiety Inventory), depression (Edinburgh Postnatal Depression Scale) and care-giving confidence were assessed at 4 months and 1 year. Monthly telephone contact was maintained following discharge from hospital. Aggregate scores were computed and compared using independent sample T-tests. Data were log transformed if necessary. Analysis was by intention to treat and also by the amount of skin-to-skin contact delivered. **Results:** Seventy-eight infants of mean (SD) gestational age of 28 (2.1) weeks were recruited; 8 infants died and 16 defaulted from follow-up resulting in 54 assessments at 1 year. There was considerable variation in the amount of skin-to-skin contact provided by the mothers in the intervention group (mean (SD) 507 (414) minutes). No mothers in the control group asked to provide skin-to-skin contact. No significant differences were found in infant behavioural and salivary cortisol responses, neurodevelopmental profiles, or in the mother-infant relationship, maternal psychological well-being and lactation duration. **Conclusions:** The active promotion of mother-infant skin-to-skin contact after extremely preterm birth does not result in measurable benefits nor in adverse consequences for the infant, the mother or the mother-infant relationship.

0173NEO

OPIATE WITHDRAWAL FOLLOWING THERAPEUTIC DOSES OF MORPHINE IN PRETERM VENTILATED NEONATES

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Background: Although withdrawal effects of in utero exposure to opiates are well documented, few data are available about the effects of discontinuation of therapeutic doses of opiates in infants. We utilised a double blind trial investigating the use of morphine in preterm ventilated infants to explore the effects of opiate withdrawal on mean heart rate and heart rate variability in this group. **Methods:** Infants <32 weeks gestation were randomly assigned to receive morphine (n=18) or placebo (n=18). Infants of 23–26 weeks gestation received morphine 10mcg/kg/hr, 27–29 weeks received 20mcg/kg/hr and >30 weeks received 30mcg/kg/hr. The infusion was discontinued without weaning in infants who received the study drug for ≤48 hours and weaned slowly over 12–48 hours in those who were treated for >48 hours. Mean heart rate and heart rate variability were measured in all babies during treatment and for up to 48 hours after stopping treatment. Standard deviation about the mean was used as the measure of heart rate variability. The maximum change in heart rate and variability between days 3 and 4 of study infusion and the weaning or post-infusion period were calculated and the treatment and placebo groups were compared. **Results:** There was a trend towards both decreased heart rate ($p=0.054$) and variability ($p=0.057$) in babies during early administration of morphine infusion compared to placebo. On discontinuation of the study drug, a significantly greater increase ($p=0.014$) in mean heart rate was seen in the treatment group (mean diff = 18.22bpm, 95% CI 3.05–23.64) compared with the placebo group (mean diff = 4.87bpm, 95%CI 0.05–26.64). The increase in heart rate occurred between 4 and 20 hours after discontinuation of the study drug and persisted for 12 to 24 hours before the two groups became similar again. There was no significant change in mean heart rate during weaning. There was no significant difference in the change in heart rate variability on weaning or discontinuation. **Conclusions:** The presence of a significant rebound tachycardia on discontinuation of the infusion supports the hypothesis that there may be a recognisable phenomenon of opiate withdrawal associated with discontinuation of therapeutic doses of morphine. Heart rate variability does not seem to provide any additional useful information.

0174NEO

RECTAL NO/H_2 IN NEWBORN: A NEW TOOL TO STUDY HOST-MICROBIAL INTERPLAY?

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Background/aims: The early interplay between intestinal bacteria and the host is thought to play a central role in normal maturation of the immune system as well as in later development of allergy. Intestinal hydrogen, (H_2) is exclusively produced by bacteria whereas nitric oxide, (NO) is produced by the gut mucosa e.g. during inflammation. To further study the host-microbial interactions we have measured the levels of H_2 and NO in newborn babies. **Methods:** We studied 32 healthy term infants delivered vaginally (n=16) or by planned caesarean section (CS) All infants were breast-fed from the first hours. Rectal gas was sampled using a tonometric balloon technique and analysed with chemilumine-scence (NO) or with an electrochemical sensor (H_2). **Results:** H_2 appeared during the first postnatal days, suggesting a relationship with early bacterial colonisation, which was faster in infants delivered vaginally compared to the CS group. NO was low at birth but increased during the following 3–5 days. In 4 babies NO transiently reached > 1000 ppb, i.e., levels similar to those seen in bowel inflammation indicating strong activation of the immune system. **Conclusions:** We have developed a fast and pain-free method to directly measure luminal intestinal gases in newborn infants. This method may be a useful tool to explore the relationship between early intestinal immune activation and later development of allergy. .

0186NEO

ALTERED DEPOSITION OF ADIPOSE TISSUE AFTER EXTREMELY PRETERM BIRTH.

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Background and Aims: Body adipose tissue (AT) content and distribution in adults influence the risk of coronary heart disease, hypertension, and type 2 diabetes. However, the age at which patterns of AT deposition are established and their determinants are unknown. We are evaluating adiposity in infancy and have previously reported data from infants born at term. In this study we aimed to determine whether the preterm baby accumulates adipose tissue in a pattern different to that of the term born infant. **Methods:** Infants underwent whole-body AT magnetic resonance imaging as previously described. Infants born at term were imaged within 5 days of delivery and preterm infants upon reaching term equivalent age. Briefly, infants are positioned supine in natural sleep and a longitudinal series of 5mm thick transverse images optimised for AT differentiation obtained. Images were analysed using a commercial software programme (SliceOmatic, Tomovision). The study was approved by the institutional research ethics committee. Volumes of each AT compartment (total, subcutaneous, visceral and other internal) were quantified and converted to adipose tissue mass (ATM). Visceral AT was obtained by quantifying internal AT in the slices from the sacrum to the to the slice containing the top of the liver or base of the lung. Data are presented as total ATM as a percentage of body weight and subcutaneous (SCAT) and visceral adipose tissue mass (VAT) as a percentage of total ATM. Statistical analyses were performed using StatsDirect version 2.0.1. Results are mean (SD). **Results:** Data for 8 preterm (gestational age range 25–30 weeks) and 25 term babies have been analysed to date. Preterm babies at term weighed significantly less than term born babies. Although there was no difference in percentage ATM, adipose tissue was preferentially deposited in the visceral compartment in the preterm babies. Visceral adipose tissue as a proportion of total ATM was significantly greater in the preterm babies (preterm 15.04% vs term 8.53%, p=0.005). The subcutaneous adipose tissue content in preterm babies was significantly reduced (preterm 85.00% vs term 91.46%, p= 0.005). (Independent sample t-test).

	Term n=25	Preterm at term n=8	p	95% CI for difference
Body weight at scan (kg)	3.19 (0.45)	2.29 (0.39)	<0.0001	0.56 to 1.24
Total ATM / body weight (%)	23.35 (38.8)	21.76 (4.09)	0.35	-1.75 to 4.9
SC AT/Total ATM (%)	91.46 (2.78)	85.00 (4.67)	0.005	2.89 to 10.02
VAT/Total ATM (%)	8.53 (2.78)	15.04 (4.68)	0.005	-10.07 to -2.95)

Conclusions: Optimum nutritional support after preterm birth remains controversial. Compromised growth is associated with adverse neuro-developmental outcome but conversely rapid growth in early infancy may increase the risk of later morbidity. Our novel data suggest that current nutritional strategems for preterm infants appear to promote the preferential deposition of adipose tissue in the visceral compartment. Although the long term effects of this are not known, increased visceral adipose tissue deposition is associated with increased risk of insulin-resistance and related morbidities in other age groups. These data also suggest that subcutaneous and visceral adipose tissue depositions are under different regulation during early life. Further work is necessary to understand the determinants of differential adipose tissue deposition.

0188NEO

INFECTION ON VERY LOW BIRTH WEIGHT NEWBORN INFANTS PORTUGUESE NETWORK ON VLBW NEWBORN INFANTS

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Introduction: Portuguese network on VLBW newborn babies has started on 1994. Infection has been one of the major concerning items and improvements in the database have been made with the objective of increasing our knowledge on this issue. **Aim:** To present data on epidemiology of infection in VLBW infants registered on a national network. **Methods:** Data were collected from the national registry since the year of 1998 through 2000. Systemic infection - clinical sepsis with or without positive blood culture, meningitis and pneumonia were included. **Results:** Throughout the 3 years period 2844 VLBW infants were registered in the network; 1023 (36%) had at least one episode of infection during the in hospital staying; 216 (21%) were recognized as mother-related sepsis (rate of mother-related sepsis 76/1000), with 49 (22.7%) isolates in blood culture. The most common single isolate was group B Streptococcus (n=14) followed by E. coli (n=10). The rate of early-onset proved sepsis was 15.5%. Hospital acquired sepsis affected 31% of all admitted infants surviving more than 72h; 21% had positive blood culture and the most common isolates were coagulase negative Staphylococcus (n=51) and Klebsiella (n=51). The rate of coagulase negative Staphylococcus sepsis was 11.3% of all survivors behind 72h of life. Early (<72h) or late pneumoniae affected 155 infants - 66 without sepsis; 9 infants had meningitis. One hundred eight babies died from infection. Lethality was 20.8% and 8% respectively for mother-related and hospital acquired infection. **Conclusion:** Infection is one of the most important issues in VLBW newborn infants. Knowledge of incidence of hospital acquired infection and its control is of utmost importance and is part of good practice standard. In spite of being less frequent, mother-related infection is the most lethal. *VLBW National Study Group: M Júlio Dinis (A Alegria, V Pombeiro), H M[a] Pia (F Araújo, Carmen C), H S João (A Martins, G Silva), H S° António (L Carreira, SP Frutuoso), H VN Gaia (N Miranda), H D[a] Estefânia (G.Henriques), M Bissaia Barreto (G Mimoso, C Lemos), M Daniel Matos (Eulália A, V Martins), H P Coimbra (F.Neves, L Carvalho), H Garcia de Orta (M.Primo, L Oliveira), H S. Francisco Xavier (A Nunes, M Anjos Bispo), H S[a] Maria (M Abrantes, J.Saldanha), M Alfredo Costa (T Costa, G Carvalhosa), H Fernando Fonseca (R.Abreu,C.Matos), Guimarães (A Freitas), Viana do Castelo (A Laranjeira), Vale do Sousa (Braga da Cunha), Vila da Feira (F.Fonseca) Braga (IF Cunha, A Pereira), Matosinhos (I.Martins, A Souto), Vila Real (E Gaspar), Viseu (I.Andrade), Aveiro (P Rocha, I.Damas), Leiria (L Wincler), Santarém (JM Onofre), VF Xira (CM Avelar), Setúbal (L Caturra, V.Neves), Évora (H Ornelas), Beja (F Ferreira, F.Furtado), Faro (MJ Castro), Funchal (Filomena G, O Magro), Angra do Heroísmo (F Fagundes), Ponta Delgada (F. Gomes), SAMS (D Fino, N Simões), Póvoa de Varzim(J.T. Moreira). Coordinator: JC Peixoto (SNN, SPP). Secretariat: H. Sacadura (ASIC-HPC). Epidemiologist: D Virella.

0189NEO

TWO COMMERCIAL SURFACTANT PREPARATIONS – BIOCHEMICAL & CLINICAL DIFFERENCES

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Introduction: Different surfactant preparations for therapy of the respiratory distress syndrome (RDS) are available at the moment. Plasmalogens, a minor component of pulmonary surfactant, improve surface properties [Am.J.Phys., 1998] and affect incidence of chronic lung disease [CCM, 2000]. Thus, differences in surfactant composition could be associated with differences in clinical parameters, such as surfactant response and pulmonary long term outcome. **Aim:** Comparison of lipid composition and biophysical properties of two commercial surfactant preparations (Curosurf® & Alveofact ®) and validation of clinical outcome of preterm infants treated with either surfactant. **Methods & Main results:** Composition of different lipid species was analysed after lipid extraction by means of HPLC. A significant difference was found between both surfactants with a higher concentration of plasmalogens found in Curosurf® (3.8 ±0.1 mol%) when compared with Alveofact® (0.9 ±0.3 mol%). Surface tension and viscosity was measured with the oscillating drop surfactometer. Between 01/95 and 12/99 a total of 187 infants were treated in our clinic with surfactant, randomly divided between Alveofact® (n=82) and Curosurf® (n=105). There were no differences in baseline characteristics between both groups. No significant differences were found with regard to the incidence of BPD or other secondary outcome criteria. A lower incidence for necrotizing enterocolitis (NEC) was found in Alveofact® treated patients (1 vs. 10%). **Conclusion:** The higher percentage of plasmalogens, that was described to be associated with improved surface properties and lower BPD incidence would favour the usage of Curosurf® in clinical routine. In our retrospective analysis no significant clinical differences in outcome of preterm infants treated with either Curosurf® or Alveofact® were found. The difference in NEC is likely due to the small numbers of studied infants.

0190NEO

VASCULAR FUNCTION AND BLOOD PRESSURE IN ADOLESCENT GIRLS BORN PRETERM

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Background/aims: Early perinatal modification of the vascular system has been suggested to affect the risk for cardiovascular disease in the adult population. To elucidate the role of preterm delivery we have correlated neonatal data to arterial functions and blood pressure (BP) after puberty. **Methods/design:** Case-control study of 34 preterm girls (birth weights 649 – 2684 g, gestational age 23 – 34 w) and 32 sex- and age-matched controls born at term (birth weight 3020 – 4220 g). In preterm girls, serum estradiol concentrations had been determined in the neonatal period using radioimmunoassay. At the time of vascular evaluation, all subjects were postpubertal with a mean (SD) age of 17 (2) years. Stiffness of the carotid artery and abdominal aorta were measured with ultrasonography. The pulse wave velocity (PWV) in the brachio-radial arterial segment was measured with photoplethysmography. Brachial BP and radial pulse wave analysis were used for determination of central aortic pressure profiles. A laser Doppler technique was used to measure skin microvascular perfusion before and after transdermal delivery of acetylcholine (ACh), an endothelium-dependent vasodilator. **Results:** Preterm girls had significantly higher systolic (mean 115 vs 104 mmHg, $p < 0.001$) and diastolic brachial BP (68 vs 63 mmHg, $p < 0.001$) than controls. As predicted, the derived central aortic pressures were lower than the brachial BP in all subjects, but the difference between the two groups remained unchanged. In contrast, preterm girls had lower aortic stiffness than controls ($p = 0.02$). The carotid stiffness, brachioradial PWV, endothelium dependent vasodilation and heart rate were similar in the two groups. The preterm girls were shorter ($p = 0.03$) than controls, but they had similar BMI, smoking habits (2 in each group) and use of oral contraceptives. Within the preterm group, BP and vascular functions did not show any association with birth weight, gestational age, being small or appropriate for gestational age or neonatal estradiol levels. **Conclusion:** Adolescent girls born preterm have higher blood pressure than age-matched controls born at term, in spite of a lower degree of aortic stiffness and similar endothelial function.

0191NEO

TRANSCUTANEUS MEASUREMENT OF CO_2 AND O_2 – DOES IT WORK IN CLINICAL ROUTINE?

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Introduction: PCO_2 and PO_2 are of importance in neonatal intensive care. Compared to conventional blood gas measurements that cause significant blood loss in preterms, transcutaneus (tc) measurements allow a continuous non-invasive monitoring. However, doubt is often shed upon validity of tc-values during clinical routine. **Aim:** 1) To survey the usage and subjective opinion of tc blood gas monitoring nation-wide. 2) To evaluate validity of tc-monitoring by comparing results with blood gas values obtained during clinical routine conditions. **Methods & Results:** (1) A questionnaire was sent to 56 head nurses of different neonatal intensive care units (NICU) in Germany and was completely answered by 41 (73%) NICU′s. In most (77%) NICU′s both parameters, $tcPO_2$ and $tcPCO_2$ are measured routinely. Most units change the sensors every 3 hours, however, the recommended temperature of 44°C is used in only 22%. About 90% use capillary blood gases to validate tc-values. The nursing staff in 30 NICU′s (75%) noted no difference between tc-values and blood gases. (2) To validate viability of tc-PCO_2 and -PO_2 in our NICU, routinely drawn blood gases were compared with simultaneously obtained tc values during a period of one month. In total, 662 blood gases were drawn (387 capillary, 243 arterial, 32 venous) from 35 patients (<500g: n=4, 500-1000g: n=5, 1000–1500g: n=10). In 125 samples both $tcPO_2$ and $tcPCO_2$ were available for comparison, in 263 only $tcPCO_2$ was measured. In 29% the difference between tc and arterial or capillary PO_2 was less than 6 mmHg and less than 11 mmHg in 54% of arterial and 41% of capillary values. For PCO_2 the difference between tc and blood values was lower than 6 mmHg in about 60% (difference <11mmHg in 82%). A difference less than 6 mmHg for both, PO_2 and PCO_2 was found for 26% of arterial and 16% of capillary blood gases (difference <11 mmHg in 46% and 37%, respectively). The validity of tc measurements did not correlate with the gestational age. **Conclusion:** To reduce cerebral morbidity in preterm infants a tight control of blood gases is required. Transcutaneus blood gas monitoring is widely used, however, associated with several problems in clinical routine. For PCO_2, tc measurements seem to be accurate, but the method is less valuable for monitoring PO_2.

0206NEO

USE OF POSITIVE END EXPIRATORY PRESSURE (PEEP) TO IMPROVE SYSTEMIC PERFUSION IN SINGLE VENTRICLE PHYSIOLOGY

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Background: Infants with single ventricle physiology require critical balance of pulmonary (Qp) and systemic (Qs) circulation. i.e. Qp/Qs close to 1 to decrease the work of single ventricle and prevent systemic underperfusion. Qp/Qs is determined by the vascular resistance in the respective beds. Hence, high Qp/Qs is associated with pulmonary overcirculation, with high arterial saturation (sat > 90%) and systemic underperfusion. **Objectives:** Use of non-conventional PEEP (>8 or < 4 cm H_2O) to induce pulmonary hypertension in infants with HLHS with Qp/Qs > 1 will result in decreased combined cardiac output (Qmpa), lower use of inotropes and improved systemic perfusion. **Methods:** Infants with HLHS and sat > 90% were randomized to low (< 4 cm) or high (> 8 cm) PEEP. PEEP was adjusted to achieve sat 75–85%. Vessel diameter and flow velocity integral in the main pulmonary artery and ductus arteriosus were obtained using 2D ECHO before, 1 hour and 24 hours after PEEP changes. Hence, Qmpa (flow in main pulmonary artery), Qpda (flow in Patent Ductus Arteriosus) and Qp (=Qmpa – Qdpa) were calculated. Other data collected included inotropic requirements (IN), gases, lactate (L), urine output (UO), volume expansion (Vol), $NaHCO_3$ use (Na), systolic blood pressure (BP). **Results:** Preliminary Combined Results on 11 Patients are shown in table. (low = 5, high = 6)

	Before	After	24 hours
Qmpa (ml/kg/min)	655 ± 170*	537 ± 190*	550 ± 120*
Qp/Qs	4.04 ± 2*	2.33 ± 0.8*	2.48 ± 1.0*
IN (mcg/kg)	103 ± 93*	89 ± 100	42 ± 66
UO(ml/kg/day)	2.7 ± 1.3*	4.2 ± 1.0*	4.1 ± 0.9*
L (mmol/L)	1.69 ± 0.4	1.63 ± 0.3	1.51 ± 0.4
Vol(ml/kg)	16 ± 9*	6 ± 10*	3 ± 9.4*
Na (mega/kg)	3.1 ± 3.0*	0.2 ± 0.6*	0*
BP(mmHg)	57 ± 7*	59 ± 8	62 ± 6.3*

* P<0.05 after and 24 hours compared to before

* P<0.05 after and 24 hours compared to before **Conclusion:** The use of extremes of PEEP in infants with HLHS and pulmonary overcirculation results in decreased heart workload, decreased inotropic requirements and improved systemic perfusion.

0208NEO

THE EFFECT OF MATERNAL NUTRIENT RESTRICTION ON CAROTID ARTERY VASOCONSTRICTOR RESPONSES IN THE RAT FETUS

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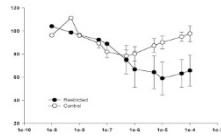
Background: Animal models of undernutrition during pregnancy have been extensively used to study the long-term effects of intrauterine growth restriction (IUGR) on cardiovascular function. Chronic substrate reduction in the fetus may induce redistribution of cardiac output and contribute to a "brain sparing" effect. Brain blood flow is dependent on carotid vascular function, however the effects of IUGR on carotid vascular responses in the rat fetus have not previously been studied. **Hypothesis:** Carotid artery responses to vasoconstrictors will be reduced in the IUGR late gestation rat fetus. **Methods:** Timed pregnant female rats were randomised on day 0 of pregnancy to a control (C, n=3) ad libitum diet or to a restricted (R, n=3) diet (50% of normal) for the duration of pregnancy. Dams were sacrificed on day 20 gestation (term = 22) and fetuses were delivered. Fetal carotid arteries were dissected and mounted on a pressurised myograph system for assessment of function. Concentration response curves were performed using the vasoconstrictor agonists phenylephrine (PE) and endothelin-1 (ET). **Results:** Fetal body weight was significantly lower in the restricted group compared to control (R=3.01 Vs C=4.17g, p=0.03). While liver (p=0.03), lung (p<0.001) and kidney (p=0.036) weights were smaller in the restricted group, there were no significant differences in heart or brain size, suggesting vascular redistribution.



Conclusion: In this model of IUGR, the differences in fetal body size and composition induced by nutrient restriction are consistent with the redistribution of fetal cardiac output. However, a more sustained α_1 adrenergic response was observed in the carotid arteries of restricted, compared to control fetuses. This is the first study to address vascular mechanisms in the rat fetus. These data demonstrate the complexity of vascular control in the fetus, improved understanding of these mechanisms are important for planning theraeutic interventions in compromised pregnancies.

0210NEO

N-IPPV VS N-CPAP FOR THE TREATMENT OF MODERATE RESPIRATORY SYNDROME IN PRETERM NEWBORN

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Background: A number of studies have evaluated nasal intermittent positive pressure ventilation (NIPPV) as a methodic of respiratory support for the treatment of apnea of prematurity or for the infant after extubation. AIMS: To compare the efficacy of NIPPV with nasal continous positive airway pressure (NCPAP) in infant with moderate respiratory distress syndrome (RDS). **Methods:** A prospective, randomized trial was performed. Infants of 28–34 gestational age (GA) with moderate RDS, defined as the presence of clinical features caractherized by need of FiO2 < 40, and a positive chest x-ray, were enrolled. Exclusion criteria from the study: patients with pneumothorax, pneumomediastinum, surgical or cardiac diseases, intraventricular hemorrage, congenital defects. The infants were assigned randomly either to NCPAP group with an end-espiration pressure varied from 2 to 8 cm H_2O or to NIPPV group, peak pressure of 14–22 cm H_2O and end-expiratory pressure of 2–8 cm H_2O, ventilatory rates of 40 breath per minutes. Arterial blood gas tension were determined at time 0 and 4 hours (hr) after the start of treatment. Statistical analyses were performed with the use of Student's t test and X2 as appropriate. $p < 0.05$ was considered statistical significant. **Results:** Between January 2001 and January 2002, 86 infants with RDS who were < 34 weeks' GA were admitted to the NICU. 44 of 86 were eligible for enrolment in this study. 22 infants were randomised to NCPAP group and 20 infants to NIPPV group. Study infants were similar in birth weight, GA, male to female rate, and other characteristics. There were no differences in the paO_2 values at time 4 hr, between the groups, but infants treated with NIPPV showed pCO_2 values lower than CPAP group at time 4 (32 + 6 vs 58 + 14). The reduction of apnoeic episodes was significantly greater in the NIPPV group (0.4 + 0.2 vs 0.9 + 0.2). The duration of need of respiratory support was longer in the NCPAP group (340+30 vs 260+20. Side effects (abdominal distension, pneumothorax) was similar for either groups. **Conclusions:** This study showed that infants with moderate RDS treated with NIPPV had a lower number of apneic episodes, needed of respirarory support shorter than those treated with CPAP, with the same side effects. We suggest that a trial of noninvasive ventilation using an alternative to initial intubation shoul be considered, so that to reducing neonatal morbidity speculating on a decreased ventilator-induced trauma and oxigen toxicity.

0213NEO

ANTIMICROBIAL PEPTIDES IN BRONCHOALVEOLAR LAVAGE IN THE NEWBORN INFANT

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Aim: Antimicrobial peptides are widespread in nature and are effectors in innate immunity. They play a critical role in host defense, however their role in innate immunity of newborn infants is not clarified. Our aim is to examine and isolate these peptides with antimicrobial activity in bronchoalveolar lavage of newborn infants. **Material and Methods:** Bronchoalveolar lavage (BAL) of nine infants, six of which were born preterm and three in term, were obtained for the duration of mechanical ventilation at day 1 to 9 except for one case, where sample was collected six weeks after birth. The supernatants of the BAL samples were adjusted with trifluoroacetic acid (TFA) to a final concentration of 0.1%. For enrichment of proteins/peptides these supernatants were passed through OASIS columns and eluted peptides/proteins were lyophilized. The samples were analyzed for antimicrobial activity against Bacillus megaterium, (strain Bm11) using an inhibition zone assay. In addition, a zone clearing on plates with cell walls from Micrococcus luteus was utilized for detection of lysozyme. Identification of the antibacterial peptide LL-37 was performed with Western blot analysis using a mouse monoclonal antibody. **Results:** Proteins/peptides in eleven BAL samples of eleven cases tested exhibited antibacterial activity against strain Bm11 (inhibition zone 10.1 ± 4.1mm) and this activity was correlated to C-reactive protein value. For the lysozyme assay all BAL samples were positive (clearing zone 12.5 ± 2.5mm). LL-37 was also detected in all samples with Western blot analysis. **Conclusion:** Antimicrobial peptides are present in BAL of preterm and term infants early after birth. Our results suggest that antimicrobial peptides have an active biological role in respiratory system of the newborn infant.

0219NEO

IBUPROFEN PDA THERAPY AND RENAL INSUFFICIENCY – A CASE REPORT

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Aim: To report our experience from ibuprofen therapy of a preterm infant with renal insufficiency and a significant patent ductus arteriosus. **Background:** A significant shunt due to a patent ductus arteriosus (PDA) is commonly associated with impaired renal function. However, renal insufficiency is often regarded as a contraindication to farmacological PDA therapy. Indomethacin decrease renal perfusion, whereas data on ibuprofen are conflicting. In clinical settings, no significant impairment of renal function has been reported during ibuprofen therapy. Results: A preterm girl was born after 26 weeks gestation by cesaeran section, due to PROM and umbilical cord prolapse. Birth weight was 1012 grams and apgar scores 8–7-9. She developed RDS, was intubated and given surfactant at four hours of postnatal age. She was extubated at 36 hours of age to nasal CPAP. On the 3rd day of life a murmur was heard and echocardiography confirmed a significant PDA, but due to an elevated serum urea of 14 mmol/l ibuprofen therapy was withheld. However, renal function deteriorated. On the 13th day of life serum urea and creatinin were 40.4 mmol/l and 165 μmol/l, respectively. Urine output was 1.5 ml/kg/h. Extensive investigations revealed no other pathology besides PDA shunting. We decided to give ibuprofen on a day-to-day basis. Clinical status, blood parameters, urine output and echocardiography were evaluated daily, before each consecutive dose of ibuprofen. The infant received a full three-dose course of ibuprofen. She remained clinically stable and responded well to treatment. Before treatment diastolic backflow was easily detected in the postductal aorta and superior mesenteric artery. Four hours after the first dose this had normalized. Ductal diameter had decreased from about 3 to 1 mm. After the third dose the ductus was closed. Over the course serum urea decreased from 40.4 to 21.2 mmol/l and serum creatinin decreased from 165 to 125 μmol/l. Urine output increased from 1.5 to 3 ml/kg/h and calculated GFR increased from 6.8 to 8.9 ml/min/1.73 m2. After treatment renal function continued to improve and had normalized on the 29th day of life. **Conclusions:** Ibuprofen therapy may be a feasible option for preterm infants with renal insufficiency but clinical studies are warranted. Infants selected for PDA treatment in spite of impaired renal function, should be closely surveilled.

0224NEO

IMPLEMENTATION OF AN EARLY DISCHARGE PROGRAMME

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Background: Traditionally, prematurely born infants have to achieve full oral feeding with weight gain before being discharged home. Increasingly they are now being discharged whilst still requiring naso-gastric (NG) feeding. The aim of this study was to investigate the effects of early discharge on infant feeding and parental confidence. **Methods:** In a 10 month period 89 families with 101 eligible infants were invited to participate; 38 families declined. Following randomisation, group 1 (n = 24 families with 27 infants; mean GA 33 weeks and BW 1909 gms) received standard care and were discharged on full oral feeding; group 2 (n = 27 families with 33 infants; mean GA 32.4 weeks and BW 1906 gms) received a program on infant behaviour, NG insertion and feeding assessment and management. Within 1 week of infants achieving full oral feeding, parents from both groups completed the Mother and Baby Scales questionnaire. **Results:** There were no differences between the 2 groups on maternal or infant characteristics. Infants in group 2 were discharged earlier than those in group 1 (mean of 4.9 days vs. 7.5 days; p= 0.01). Group 2 took significantly longer to achieve full oral feeding (mean no. of days 8.7 vs. 3.7 respectively; p=0.01) but had a greater weight gain on completion of the study (257 gms vs. 116 gms; p=0.01). Four mothers in group 1 and 2 mothers in group 2 changed from breast to formula feeding. For both groups, as parental global confidence increased so did their impressions of infant temperament as being 'easy' (p=0.001). For parents in group 2, this gave rise to a significant association with confidence in feeding (p=0.001). Parental impressions of infant 'easiness' was significantly associated with infants being more settled in-between and during feeding by parents in group 1 (p=0.021 & p=0.04) but not so by parents in group 2 (p=0.08 & p=0.18). Group 2 received planned community visits (median 2 visits/family – range 0–12). This was significantly different (p=0.002) from group 1 where no visits were anticipated and which received between 0–7 visits/family (median 1/family). **Conclusion:** The early discharge programme increased parents' awareness of and confidence in infant behaviour and feeding. This may have enabled mothers to be more successful in breastfeeding. Standard care did not always prepare families for discharge as demonstrated by the required additional community support.

0225NEO

THE NEUROPATHOLOGY RELATED TO CARDIAC ARREST IN LABOUR

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Background: Loss of the fetal heart rate during labour leading to asystole at birth can occur secondary to an acute event such as abruption or cord prolapse but may follow prolonged subacute hypoxic-ischemia. Many of those surviving the neonatal period have an excellent outcome[1]. We wished to examine the neuropathology of a population of infants who did not survive. **Methods:** Clinical data was collected prospectively on all early neonatal deaths and stillbirths occurring over 2 years as part of the Scottish Perinatal Neuropathology Study. All 22 delivery units in Scotland enrolled cases. A neuropathologist blind to the clinical details examined the brain where consent was given for extended post mortem. This involved the examination of 20 blocks collected to a standard protocol for evidence of a number of post-hypoxic histological features. Infants excluded from the original study were those with cardiac and CNS malformations and major chromosomal abnormalities. In this paper we examine the clinical features and neuropathology, where available, of cases where the fetal heart was initially present but subsequently arrested during labour. Infants who remained asystolic following delivery are classified as stillbirths(SB) whereas those who showed response to resuscitation are defined as neonatal deaths(NND). **Results:** 56 infants had cardiac arrest during labour. Specific clinical causes for cardiac arrest were placental abruption(10), cord accident(5), uterine rupture(3), shoulder dystocia(3) and others(6). In 29 there was no apparent cause. 24/56 had an extended PM. Evidence of prelabour hypoxic damage such as extensive mineralisation, established infarcts or old haemorrhage was seen in 11 (46%): Table. Neuropathology in SBs and NNDs not surviving cardiac arrest in labour.

	n	<37weeks	Extended PM	Recent damage	Prelabour damage	No damage	Age at death (med)
SB	38	21(55%)	12(32%)	2	2	7	-
NND	18	6 (33%)	12(67%)	3	9	-	21h

All 9 NNDs surviving more than 24 hours had multiorgan failure. 9 term infants had severe HIE and 2 further preterm infants had multiple seizures. There was a high incidence of pregnancy complications (77%) in general, especially antepartum haemorrhage (32%) but none of these were more common in the cases with old hypoxic damage. **Conclusions:** brain damage occurring before the onset of labour is common in infants not surviving cardiac arrest in labour. The mechanism of hypoxia-ischemia leading to intrapartum cardiac arrest in many instances is unknown. Ref 1. Casalaz DM et al. Arch Dis Child Fetal Neonatal Ed 1998;78(2):F112–5

0236NEO

DELAYED ACTIVATION OF CD8+T-CELLS IN PRETERM INFANTS TO MOTHERS WITH PROM

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Background/aims: In the newborn infant, in utero-inflammation is an important risk factor for chronic injuries, such as cerebral palsy and bronchopulmonary dysplasia. In premature rupture of membranes (PROM) inflammation of the amnion and decidual membranes play important role. Inflammation of the uterus exposes the fetus to inflammatory cytokines, but the mechanisms by which in utero-inflammation predisposes the fetus to postnatal injuries are incompletely known. In this study we aimed to compare T-lymphocyte activation in preterm infants born to mothers with and without PROM. **Methods:** The study consisted of 37 preterm infants (gestational age 27.9±2.4 weeks, birth weight 993±323 grams). PROM was present in 11 cases. Blood samples were drawn on postnatal days 1, 3, 7 and weeks 2, 4 and 6. The samples were processed for flow cytometry by double staining with fluorescent antibodies for CD4, CD8, and activation markers CD11a and CD54. A LeukoGate-antibody (CD45+CD14) was used to identify the lymphocyte population. CD4/CD8-cell ratio was calculated. The results are given as proportions of double positive -staining cells. **Results:** In infants born to mothers with PROM, when compared to the control group, the proportion of CD54-positive CD8-T-cells in the peripheral blood was higher at postnatal day 7 (7.0±5.6% vs. 3.5±3.7%; p=0.039), at 2 weeks (9.0±6.0% vs. 4.1±3.3%; p=0.011) and 4 weeks (7.9±5.2% vs. 3.7±2.2%; p=0.023) of age. No differences were found in the proportions of CD11a positive T-cells. **Conclusions:** In preterm infants born after PROM, the circulating CD8-positive-T-cells (Killer T-cells) have more active immunophenotype at the age of 1 to 4 weeks compared to preterm infants born without PROM. This delayed T-cell activation may reflect chronic immunoactivation that could play a role in the pathogenesis of chronic injuries associated with in utero-inflammation.

0237NEO

NEW NON-OCCLUSIVE BLOOD PUMP FOR ECMO

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Background: ECMO is a high-risk technique composed of a circuit, Oxygenator and a pump. One of the limitations of this technique is the difficulty to support a patient during transport. A previous prototype of non-occlusive blood pump designed for ventricular assistance by our group has been modified to support flow during ECMO. The aim of this study was to develop a portable, small, dischargeable and safe device for transport patients, especially newborns, during ECMO. **Method:** The double chamber pump consists of two parallel tubular pump heads of different sizes (5–20ml stroke volume) coupled by Y-connectors. The pump heads are fixed in a driving console that contains 4 pneumatic clip valves to control the blood flow direction. Two Venturi tubes deliver the vacuum from the pumps. The console sizes only 360*120*50 mm and is connected to a 24V power supply and a 6 bar compressed air source. A separated controlling unit manages the pumping process. The operating mode is single or double, so each pump chamber can be stopped and changed independently. The pump behaviour has been tested in a mock ECMO circuit and in a newborn piglet model of ECMO. 3 piglets (3–6 Kg) were cannulated through the right external jugular vein and right carotid arterial using standard ECMO cannula (10–12 F for venous cannula and 8 F for arterial cannula). A Quadrox® D Oxygenator was used in all experiments. Blood trauma, using osmotic resistance trauma, were compared against classical roller pump in a mock blood circuit. **Results:** In mock circulation loop experiments with water, frequencies up to 240 bpm. can be reached maintaining the stroke volume and flows up to 4 l/min were obtained against 100 mmHg after load. In the piglet model of ECMO, flows were step by step increased from 50 ml/k to a maximum of 100 ml/k. Pressure gradient across Oxygenator, flows pre and post Oxygenator and pressures from venous return and arterial limb were continuous measured. **Conclusions:** The two parallel tubular pump generates enough flow through the Oxygenator to maintain ECMO in this animal model. Hemolysis was lower compared with continuous roller pump. The low cost of the disposable part and its reduced size of the pump and its non-occlusive performance increases safety and the compact design of the console should imply a new approach for ECMO, especially during transport.

0241NEO

COMPARISON OF RECOMBINANT SP-C AND NATURAL BOVINE SURFACTANT IN PREMATURE RABBITS WITH RDS

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Background: Surfactant proteins SP-B and SP-C are important for optimal function of surfactant and have similar effects in animal studies. **Objective:** To evaluate the effect of a surfactant containing surfactant apoprotein C, dipamitoyl-phosphatidylcholine, phosphatidylglycerol (SP-C Surf) on lung function compared to a natural bovine surfactant (bSF) in a model of respiratory distress syndrome (RDS) in premature rabbits with different PEEP. **Design/Methods:** Preterm rabbits were sequentially delivered and lightly anesthetized with pentobarbitone and ketamine at 27d of gestation. Animals were tracheotomized and randomized for given either saline (control group), SP-C Surf or bSF with a treatment dose of 100 mg/kg b.w.. Rabbits were transferred to a 37° C temperature-controlled ventilator plethysmography system on initial settings of PIP = 3,5 kPa; rate = 30 breaths/min; I:E = 1:1; FiO2= 1; and PEEP 0 or 0,3 kPa. PIP was automatically adjusted for each rabbits to reach tidal volumes of 7–8 ml/kg. During ventilation for 30 minutes, dynamic compliance (Cdyn), tidal volume (Tv) and ventilation pressure (PIP-PEEP) were recorded every 5 minutes. Results are given as mean SD. Two-way analysis of variance (ANOVA) was used for comparision of differences in physiologic measurements during the ventilation period. **Results:** Cdyn, Tv and ventilatory pressure improved after administration of SP-C Surf and bSf. Administration of PEEP further improved lung function in every group. Details see table.

Treatment	Body weight	number	Cdyn (ml/kPA/kg bw)	tidal volumes(ml/kg bw)	PIP-PEEP (kPa)
control 0 PEEP	26,2±2,9	7	1,6 ±1,1	4,6 ±3,0	3,0 ±0,2
SP-C Surf 0 PEEP	28,1± 3,86	7	2,6 ±1,8*	5,6 ±2,6*	2,4 ±0,6*
bSF 0 PEEP	26,7 ±1,9	6	4,2 ±0,8*	8,0 ±0,3*	1,9 ±0,4*
control 3 PEEP	29,1 ±2,9	7	2,4 ±1,4	7,5 ±2,0§	2,5 ±0,4§
SP-C Surf 3 PEEP	26,7 ±4,6	14	4,4 ±1,0§*	8,1 ±1,1§	1,6 ±0,3*§
bSF 3 PEEP	27,7 ±4,6	11	4,9 ±1,9*§	7,3 ±2,0	1,5 ±0,8*§

p <0,05 vs 0 PEEP

Conclusions: The SP-C Surf is effective as bSF in preterm rabbits with RDS. After administration of surfactant ventilation with PEEP is mandatory in order to maintain lung function.

0242NEO

'CLICKY' HIPS: ARE THEY AT RISK FOR DEVELOPMENTAL DYSPLASIA OF HIPS?

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Background/Aim: 'Clicky' hips is not an uncommon finding during routine physical examination of newborn infants and reported to occur in 6% of infants. The prognostic significance of this finding is controversial. The aim of this study was to determine the associated risk factors, natural history, follow-up and outcome of neonates with 'clicky' hips diagnosed during newborn screening physical examination.. **Methods:** This is a retrospective study over a period of 4 years, 1996–99. The study patients included infants who had 'clicky' hips detected during newborn screening examination on the 1st or 2nd postnatal day. Those infants with limited abduction, dislocated or dislocatable hips, neuromuscular disorders and multiple malformations were excluded. In all infants the stability of hips were assessed at 6 weeks by physical examination and also by ultrasonographic study. Those with abnormal ultrasound findings or persistent 'clicky' hips on clinical examination were referred for evaluation by paediatric orthopaedic surgeons. The rest were periodically followed up until they started walking independently. **Results:** Eighty-four infants (79 full-term and 5 preterm) who had 'clicky' hips diagnosed during newborn screening physical examination were studied. Hip clicks were elicited in the right hip in 42(50%), left hip in 32(38%) and both hips in 10(12%). 44(52%) were first born, 45(54%) were females and breech presentation occurred in 12(14%). In majority 70(83%), the hip clicks resolved between 4 to 6 weeks whereas in 14(17%) the clicks persisted. The hips were stable with negative Ortolani & Barlow signs during the follow-up visits in all except one infant who had unilateral dislocatable hip. Ultrasound examination of the hips between 1 and 4 months of age revealed normal study in 57(68%), dysplasia of the hip in 11(13%), immaturity of the hip in 10(12%) and laxity of capsule in 6(7%). Orthopaedic referral was sought in those infants who had persistent hip clicks or abnormal ultrasonographic findings for further management. However no definitive therapy was required apart from the use of double diapers for about 4 to 8 weeks to keep the hips abducted. Further follow-up visits up to 12–18 months revealed stable hip examinations, normal radiological findings and normal gait. **Conclusions:** Infants with 'clicky' hips detected during routine physical examination of the newborn should be followed up because a significant proportion of them develops milder degrees hip dysplasia. However the prognosis appears to be good. Those infants in whom the click resolves with normal hip examination on reevaluation and normal ultrasonographic study between 1 to 4 months of age may not need further follow-up.

0246NEO

THE EFFECT OF PAIN ON PLASMA SUBSTANCE P & NEUROKININ A IN NEONATES

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Background: Substance P (SP) and neurokinin A (NKA) are neuropeptides involved in pain sensory signal processing[1]. They can be measured in plasma and have been associated with pain and inflammation in adults[2,3]. There is a possible role for them as markers of persistent pain in neonates, but this has not previously been investigated. The aim was to determine whether plasma SP and NKA levels varied with pain. **Methods:** This was a prospective case-controlled observational study. From July 2000 to December 2001, blood samples were collected longitudinally from 19 neonates believed to be suffering pain, e.g. due to surgery, necrotising enterocolitis, severe intraventricular haemorrhage, and meningitis. 19 controls matched for gestation and ventilatory status were recruited. Gestation ranged from 25–41 weeks. Only one sample per infant per day was taken between 0800 and 1200 hours. Neuropeptides were extracted, then measured using an in-house radioimmunoassay. Results were analysed using the Mann-Whitney U test. **Results:** Area under the curve (AUC) was calculated for three consecutive daily neuropeptide levels. There was no significant difference in median AUC for either SP (pain=3.79, control=3.03, P=0.8) or NKA (pain=10.2, control=12.3, P=0.3). One limitation of this observational study was that 15 of 19 infants believed to be suffering pain already received analgesia prior to study enrollment. Analysis of the 4 who had not received prior analgesia yielded no significant differences compared with either those who had received analgesia, or the controls. Graphs of peptide levels over time were also examined for individual infants and no consistent change noted with pain or analgesia administration. **Conclusion:** This is the first study of SP and NKA levels in neonates. Pain does not appear to have a significant effect on levels of either neuropeptide. This may be due to adequate treatment of pain with analgesia administration. It is also possible that some or all of the infants were not in pain. Only 4 did not receive analgesia. The appropriate treatment of pain should not be withheld for any study. Therefore, it may be more feasible to study SP and NKA levels in a population of infants who are not routinely receiving analgesia, but exposed to another source of possible pain or distress, such as assisted ventilation. 1. Fleetwood-Walker S. Current Opinion in Anaesthesiology 2:645–648, 1989. 2. Marshall KW. Arthritis and Rheumatism 33(1):87–90, 1990. 3. Gallai V. Cephalalgia 15(5):384–390, 1995.

0249NEO

SUBSTANCE P & NEUROKININ A IN NEONATES: EFFECT OF VENTILATION & ANALGESIA

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Background: Substance P (SP) and neurokinin A (NKA) are neuropeptides involved in transmission and modulation of pain signals[1]. They are measurable in various body fluids and have been associated with pain and inflammation in adults. They could potentially be neurochemical markers of pain in neonates. The aims of this study were to investigate the effect of ventilation on SP and NKA levels in preterm infants, and to see if analgesia affected these levels. **Methods:** From July 2000 to December 2001, blood samples were collected longitudinally from 142 neonates, gestation 23–42 weeks. Only one sample per infant per day was taken between 0800 and 1200 hours. Plasma was extracted and neuropeptides measured using an in-house radioimmunoassay. Infants with presumed painful conditions were excluded. Results were analysed using the Mann-Whitney U test. **Results:** Median neuropeptide values (pmol/L) are tabulated. Table 1a shows SP results from all neonates grouped by ventilation, and Table 1b shows corresponding NKA results. SP levels were not found to be significantly higher in ventilated infants. NKA levels were significantly lower in ventilated infants on days 1 & 2, and higher on days 7 & 14. Of 142 neonates, 33 infants ≤32 weeks' gestation were also enrolled into a randomised double-blinded controlled trial investigating the routine use of morphine infusions to sedate ventilated preterm infants. All infants on a study drug infusion (21 morphine, 12 placebo) were ventilated. Gestation, birth weight and antenatal factors were similar in both groups. Area under the curve (AUC) was calculated for neuropeptide levels on days 1 to 3. There was no significant difference in median AUC for SP (morphine=3.21, placebo=3.38, P=0.5). Median AUC for NKA was significantly lower in those ventilated infants who received morphine (morphine=11.4, placebo=13.0, P=0.05). **Conclusion:** This is the first study to investigate changes in SP and NKA levels with ventilation. SP levels do not appear to be a useful marker of persistent pain or distress. Conversely, NKA levels show significant changes with ventilation, and are further modulated by the use of analgesia. We previously reported cortisol responses in the same group of infants, demonstrating significant changes with ventilation but not with analgesia[2]. It appears that although cortisol is a useful indicator of overall stress, NKA might be more specific for pain.

Table 1a

Postnatal day	Ventilated		Not Ventilated		P value
	N	*SP*	*N*	*SP*	
1	39	1.10	31	1.47	0.7
2	40	1.63	36	1.34	0.6
3	46	2.03	96	2.00	0.2
7	30	1.89	85	1.75	0.4
14	20	1.51	62	1.33	0.5

Table 1b

Postnatal day	Ventilated		Not ventilated		P value
	N	*NKA*	*N*	*NKA*	
1	39	5.64	31	6.82	0.01
2	40	5.85	36	7.06	0.01
3	46	6.20	96	6.67	0.2
7	30	6.12	85	5.26	0.02
14	20	5.40	62	4.64	0.01

1. Fleetwood-Walker S. Current Opinion in Anaesthesiology 2:645-648, 1989.
2. Wong CM. Pediatric Research 52(5):787, 2002.

1. Fleetwood-Walker S. Current Opinion in Anaesthesiology 2:645–648, 1989. 2. Wong CM. Pediatric Research 52(5):787, 2002.

0250NEO

IN-LINE PRESSURE MEASUREMENTS IN A MODEL OF 3-COMPONENT I.V. THERAPY.

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Aim: We investigated (in-line) pressure course during and after occlusion of different pumps in a simulation model in order to choose an appropriate pump system for our (pre)term infants. **Methods:** 5 different (syringe) pumps were tested in the study. The model simulated i.v. therapy of 3 components, comparable to T.P.N. administration used in a 1-kg preterm infant. The pumps were positioned vertically: Upper pump (UP) with a flow rate of 2,5 ml/h, middle pump (MP) with a flow rate of 1,6 ml/h and the lower pump (LP) with a flow rate of 0,3 ml/h. In-line pressure was measured using a DTX^{TM} Plus Transducer (sampling rate of 1 Hz) at UP, MP, LP and just before the location of the IV administration. Measurements per model in triplicate: △t1 time delay between start of infusion therapy and first droplet was used as an estimate of "being on pressure" of the system, △t2 time delay between occlusion and first alarm, △t3 time delay between discontinuing the occluding pump and second alarm, △P automatic pressure decline after attaining the pressure limit was used as an estimate for in-line mixing of components. Data expressed as mean (SD).

Results:

Pump	△t1 (s)	△t2 (min)	△t3 (min)	△P (mmHg)
Terumo, Terefusion	443 (49)	17 (3)	-	-
Fresenius, Orchestra	23 (3)	21 (3)	8 (2)	97 (19)
Braun, Perfusor FM	36 (2)	9 (0)	3 (0)	36 (3)
Graseby, Omnifuse	32 (4)	22 (1)	14 (0)	114 (1)
Alaris, Asena CC	38 (5)	17 (1)	1 (1)	35 (7)

Conclusion: Considerable differences exist in (in-line) pressure course and alarm function between the pumps. 4 out of 5 are on pressure within 1 min. Braun and Alaris react quicker after occlusion. In-line mixing between the different components was remarkably less with Braun and Alaris.

0254NEO

LEVELS OF IGF-I VEGF IN RHUEPO TREATED PREMATURES FOR ANEMIA OF PREMATURITY (AOP): ASSOCIATION WITH RETINOPATHY OF PREMATURITY (ROP), (PILOT STUDY).

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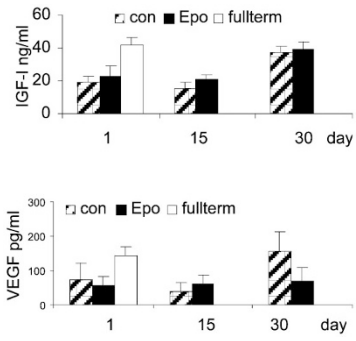
Background: Based on experimental data on adult murine retinas, systemic application of rHuEpo crosses the blood-retina barrier. Also, when it was administered before or immediately after retinal ischemia, not only reduced histopathological damage but promoted functional recovery (Grimm et al Nat Med 2002). Besides, VEGF is instrumental in the development of abnormal retinal vasculature and IGF -1 is necessary at minimal levels to promote maximum function of VEGF. When IGF-I is persistently low, vessels cease to grow and VEGF accumulates in the vitreous, leading subsequently in neovascularization and ROP. Erythropoietin (Epo) interacts with VEGF to potentiate its vascular activity. Epo and VEGF often co-distribute and are regulated by hypoxia inducible factor (HIF-I).OBJECTIVE: The aim of this prospective controlled study was to assess, if early rHuEPO treatment for AOP would have a preventive effect in ROP through optimizing both VEGF and IGF-I. **Methods:** 15 premature neonates (GA<30 wks, BW<1250g) were entered in a randomized controlled study of rHuEPO treatment. The neonates assigned to receive either rHuEPO (250 units/g/every other day) or not, early after birth. Levels of VEGF and IGF-I were measured in both serum and plasma at 1st ,12–16th and 30–35th day after birth using enzyme immunoassay and immunoradiometric assay respectively. Clinical and ROP data were recorded. VEGF and IGF-I levels were also measured in 12 fullterm neonates the 1st day of life.



0255NEO

RESPONSES TO ISOPROSTANES IN NEONATAL PORCINE PULMONARY AND MESENTERIC VASCULAR SMOOTH MUSCLE.

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Background/aims: Isoprostanes are prostaglandin (PG)-like compounds that are produced independently of the cyclooxygenase enzyme by free radical catalyzed peroxidation of arachidonic acid. We aimed to study the effects of several E-ring and F-ring isoprostanes on mechanical activity in pulmonary arteries (PA), pulmonary veins (PV) and in mesenteric arteries (MA) from newborn and 2-wk-old piglets. **Methods:** The responses to 8-iso-PGE_1, 8-iso-PGE_2, 8-iso-$PGF_{1\alpha}$, 8-iso-$PGF_{1\beta}$, 8-iso-$PGF_{2\alpha}$, 8-iso-$PGF_{2\beta}$, and the thromboxane A_2 mimetic U46619 were studied using organ bath techniques. **Results:** Isoprostanes produced concentration-dependent contraction of PA, PV and MA. In PA and PV, 8-iso-$PGF_{2\alpha}$ was the most potent and efficacious of the isoprostanes with a log EC_{50} of -5.34 ± 0.3 in the newborn and 7.03 ± 0.3 in the 2-wk-old PA. However, isoprostanes were markedly less potent vasoconstrictors than U46619 (log EC_{50} of - 8 ± 0.2 in the newborn and - 8.18 ± 0.2 in the 2-wk-old PA). In MA, 8-iso-PGE_2 (in the newborn) and 8-iso-$PGF_{2\beta}$ (in the 2-wk-old) were the most potent vasoconstrictors. The contractile responses to all the isoprostanes were reverted by the thromboxane A_2 receptor (TP) antagonist SQ 29,548, indicating that isoprostane-evoked responses involved primarily TP receptors. After precontraction of the vessels with U46619 or endothelin-1 (in the presence or in the absence of SQ 29,548), no relaxant responses to isoprostanes were observed. **Conclusions:** Isoprostanes are potent vasoconstrictors of neonatal porcine pulmonary and mesenteric vascular smooth muscle, primarily through TP receptors. Our findings support a role for the isoprostanes in the regulation of neonatal pulmonary and systemic vascular tone.

0260NEO

ONTOGENY OF CYCLIC GMP REGULATION OF ADENYLATE CYCLASE RELAXANT EFFECTS IN PIGLET INTRAPULMONARY AND CORONARY ARTERIES.

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Background/aims: Aim: Cyclic GMP and cyclic AMP are major second messengers that play a key role in eliciting vascular relaxation after stimulation of the corresponding upstream receptors. Our aim was to determine the ontogeny of the contribution of the nitric oxide (NO)/cyclicGMP pathway to pulmonary vascular relaxation in response to cyclic AMP elevation with the adenylate cyclase activator forskolin. **Methods:** Isolated rings from third generation pulmonary and coronary arteries (left anterior descending) from 1-day-old, and 2-week-old piglets were mounted in organ chambers for isometric tension recording. **Results:** In pulmonary and coronary arteries, preconstricted with the thromboxane A_2 mimetic U46619, forskolin induced a concentration-dependent relaxation which increased with age in pulmonary arteries (log EC_{50} of -6.45 ± 0.1 in the newborn and -7.13 ± 0.1 in the 2-wk-old; $P<0.05$) but not in coronary arteries (log EC_{50} of -6.64 ± 0.2 in the newborn and -7.07 ± 0.2 in the 2-wk-old). Forskolin-induced relaxation was reduced by removal of the endothelium, blockade of NO synthase with L-NAME (0.1 mM), and blockade of soluble guanylate cyclase with ODQ (10 μM). The NO substrate L-arginine (0.1 mM) did not affect forskolin-induced relaxation. Increase in cyclic GMP with the NO donor sodium nitroprusside (30 nM) or the specific inhibitor of the phosphodiesterase isoform 5 sildenafil (10 nM) did not affect forskolin-induced relaxation of pulmonary or coronary arteries. **Conclusions:** These results strongly suggest that endogenous NO is critically important for cyclic AMP-induced relaxation in neonatal pulmonary and coronary arteries.

0261NEO

CARDIORESPIRATORY EFFECTS OF RED CELL TRANSFUSION IN PRETERM INFANTS

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Background: Early in the neonatal period, red cell and other volume transfusions are frequently given to preterm infants as an attempt to maintain adequate tissue perfusion. However, few data have been reported on the cardiorespiratory effects of such transfusions. **Aim:** To assess the short-term cardiorespiratory effects of a standard erythrocyte transfusion in very low birth weight (<1500 g) infants. **Methods:** Thirty-seven infants (birth weight 920±230 g, gestational age 27.8±2.1 wks, age at study 6.1±3.9 days) with indwelling arterial lines were studied when 10 ml/kg of packed donor red cells were transfused based on clinical judgement. Infants with persistent ductus arteriosus and/or inotropic treatment were excluded from the study. Oxygen saturation, ultrasonographically measured left ventricular output (LVO) and stroke volume (SV), arterial systolic, diastolic, and mean arterial pressure, heart rate (HR), and capillary refill time (CRT) were assessed immediately prior to the transfusion and within an hour after the transfusion was completed. **Results:** CRT was significantly shorter after the transfusion than prior to it (2.1±0.9 versus 2.4±1.0 s, $p<0.05$). LVO, SV and arterial pressures remained unaltered. Oxygen saturation after the transfusion was lower than before the transfusion (94.0±3.8 versus 95.3±2.5%) despite unaltered oxygen supply. **Conclusions:** The data suggest that although a volume transfusion of 10 ml/kg may marginally improve peripheral perfusion, it does not influence cardiac output and arterial blood pressure in normotensive preterm infants. It may, however, cause a transient decrease in oxygenation, which could be due to volume overload resulting in impairment of pulmonary mechanics, or to a change in blood oxygen affinity caused by the adult haemoglobin of the transfused red cells.

0264NEO

MECHANISM OF FETAL DEATH BY TRANSPLACENTAL BACTERIAL LIPOPOLYSACCHARIDE (LPS).

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Background: Maternal infection is a significant cause of spontaneous abortion and fetal death in humans. However its pathophysiology remains unclear. We have previously shown that intra-amniotic lipopolysaccharide (LPS) can cause fetal inflammatory response and cardiac dysfunction. We hypothesized that in maternal infection the fetal abortion is a cause of fetal death by the same mechanism. **Methods:** At 14 days of gestation LPS or vehicle was administered intraperitoneally to pregnant mice of the DBA-strain. Various cardiac and circulatory parameters were obtained from fetuses by Doppler echocardiography before LPS and six hours later. After the last ultrasound, fetal tissues, placenta, fetal membranes and amniotic fluid were collected. The expression of cytokines and other inflammatory mediators were determined using ribonuclease protection assay (RPA) and cytometric bead array (CBA). Histopathology of placenta was carried out using hematoxylin-eosin staining. **Results:** Six hours after LPS injection placenta showed severe vascular dilatation and micronecrosis, whereas in vehicle treated mice these signs were absent. In LPS group fetal cardiac out flow mean velocity (OFVmean) was lower ($p<0.005$) than in vehicle group. There was no difference in proportions of isovolumetric relaxation and contractions times between groups. Pulsatility indices (PI) of umbilical artery and descending aorta and PI for veins (PIV) from ductus venosus were higher after LPS. In addition, 53% of LPS treated fetuses had atrioventricular valve regurgitation (AVVR) compared to vehicle group where only one fetus had AVVR. Intraperitoneal LPS to the doe acutely induced the expression of tumor necrosis factor-alpha (TNF-α), interleukins 1-aplha (IL-1α) and 6 (IL-6) ($p<0.05$) in placenta. However, there was no detectable induction of inflammatory mediators neither in fetal tissues nor in fetal membranes. There was increase of TNF-α and IL-6 in maternal serum ($p<0.05$) after LPS. In contrast, intraperitoneal LPS did not increase cytokines in amniotic fluid. **Conclusions:** According to present results we propose a mechanism of fetal death by LPS in maternal compartment. Intraperitoneal LPS given to mother did not acutely induce fetal inflammatory response. However the placental inflammatory response was evident. Placental congestion caused by LPS increased cardiac afterload and led to heart failure in fetus. We propose that placenta acutely responds to inflammatory stimuli from maternal compartment.

0266NEO

ION TRANSPORT AND LUNG COMPLIANCE IN HEALTHY TERM INFANTS

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Background: Fetal lung liquid removal is critical for successful adaptation of the perinatal lung to air-breathing. Active transport of Na from lung lumen through apical Na-channels like ENaC, and basolateral NaK-ATPase establishes an osmotic gradient for the movement of lung liquid across airway epithelium. **Objective:** To characterize whether ion transport correlates with change in lung compliance in healthy term newborn infants after vaginal delivery (VD-infants) and cesarean section without labor (CS-infants). **Design/Methods:** The study subjects consisted of 28 healthy newborn infants, of whom 15 were VD-infants (gestational age range 37–42 wks), and 13 were CS-infants (gest age 36–42 wks). The first measurements were performed at < 4 h, and compared to measurements done during 24–48 h of age. Airway ion transport was measured by recording the maximum basal transepithelial nasal potential difference (N-PD). Na-channel activity was quantified by following inhibition of N-PD after topical application of 100 μM amiloride. Lung compliance (LC) was measured at polysomnography-controlled quiet nREM sleep using the double-occlusion method. **Results:** Basal N-PD measured at < 4 h and at 24–48 h remained at -11±6 (m±SD) mV in VD-infants, whereas in CS-infants basal N-PD remained at -22±12 mV ($p<0.05$ for difference). During the follow-up neither group showed change in N-PD. In VD-infants amiloride-induced inhibition of the basal N-PD at <4 h was 51±16 and 48±20 % during 24–48 h, whereas CS-infants amiloride-sensitivity was 38±22 and 30±20 %, respectively. In VD-infants, LC measured at <4 h increased from 11±3 to 19±7 ml/kPa/kg during 24–48 h ($p<0.05$). In CS-infants, LC did not change (at <4 h LC = 17±6 and at 24–48 h 20±7 ml/kPa/kg). Inhibition % of the initial N-PD after amiloride at <4 h had a significant positive correlation with LC at 24–48 h ($r=0.60$, $p<0.05$, $n=13$). **Conclusions:** In healthy newborn infants N-PD remains constant over the first three postnatal days. The more negative nasal potential difference in CS-infants is in harmony with the previous observations. Activation of Na transport may precede postnatal improvement of lung compliance.

0269NEO

VASCULAR TONE OF HUMAN UMBILICAL VEIN: OXYGEN, NO, AND ENDOTHELIN

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Background: The contribution of umbilical vein vascular tone to the regulation of umbilical blood flow had been regarded as negligible, since the umbilical vein was thought to operate at maximal vasodilatation already at resting conditions. However, we were able to demonstrate an oxygen-dependent regulation of the vascular tone of human umbilical vein. In particular, we found an endothelium-dependent vasodilatation at hypoxia. We now intended to characterize the contribution of the locally released vasoactive compounds nitric oxide (NO) and endothelin (ET) to this oxygen-dependent regulation of vascular tone. An increase in the basal release of NO is known to mediate vasodilatation in response to various stimuli. The release of ET from the vessel wall is affected by the local pO_2. ET is known to mediate vasoconstriction via ET_A receptors and ET_{B2} receptors on vascular smooth muscle cells, whereas vasodilatation is mediated via ET_{B1} receptors on endothelial cells. It is unclear if ET_{B2} receptors are present on vascular smooth muscle cells of the human umbilical vein or not. **Aims:** We hypothesized that NO mediates the endothelium-dependent vasorelaxation of human umbilical vein at hypoxia. In addition we tested if the human umbilical vein has ET_{B2} receptors and investigated which ET receptors are activated when ET is released in response to variation of the local pO_2. **Methods:** Simultaneous registration of intracellular membrane potential and isometric tension of intact and endothelium-denuded vessel strips with and without NO synthase inhibition (L-NAME, 10^{-4} M, n = 7), ET_A receptor blockade (BQ-123, 10^{-5}, 10^{-6}, and 10^{-7} M, n = 5 to 7 at each respective concentration of BQ-123 used), or ET_B receptor blockade (BQ-788, 10^{-7} M, n = 5) during variation of the pO_2 in the bath solution between 5 and 104 mm Hg. Registration of isometric tension of intact and endothelium-denuded preparations during selective stimulation of ET_B receptors by sarafotoxin c (Sfc, 10^{-11}, 10^{-10}, 10^{-9}, and 10^{-8} M, n = 5 to 7 at each of the respective Sfc-concentration used) at 39 mm Hg pO_2 in an additional series of experiments. **Results:** Increasing pO_2 from 5 to 104 mm Hg resulted in depolarization from –58.6 ± 1.1 to –53.3 ± 1.0 mV ($p < 0.001$) and in increase of isometric tension from 0.673 ± 0.037 to 0.825 ± 0.044 g ($p < 0.02$). In relation to the physiological intrauterine pO_2 range (22 – 35 mm Hg) these results imply hyperpolarization and vasodilatation at hypoxia. Removal of the endothelium reversed the hypoxic hyperpolarization and vasodilatation, which were restored by treatment of endothelium-denuded preparations with BQ-788. At pO_2 values below 39 mm Hg intact preparations treated with either L-NAME or BQ-123 were more depolarized than controls ($p < 0.05$) and revealed an increase in isometric tension. The effects of BQ-123 were independent of the dose of BQ-123 used. Sfc exerted a dose-dependent vasoconstricting effect which was more pronounced in endothelium-denuded than in intact preparations. **Conclusions:** NO mediates the endothelium-dependent hypoxic hyperpolarization and vasodilatation of human umbilical vein. NO thereby offsets a vasoconstricting effect of endothelin via activation of ET_{B2} receptors which are present on vascular smooth muscle cells of the human umbilical vein. Our finding that treatment of intact preparations with the blocker of vasoconstricting ET_A receptors BQ-123 resulted in vasoconstriction suggests a cross-over of BQ-123 to vasodilating ET_{B1} receptors on endothelial cells in the human umbilical vein.

0274NEO

MEAN CEREBRAL SATURATION IS AN INDEX OF NEONATAL CEREBRAL BLOOD FLOW

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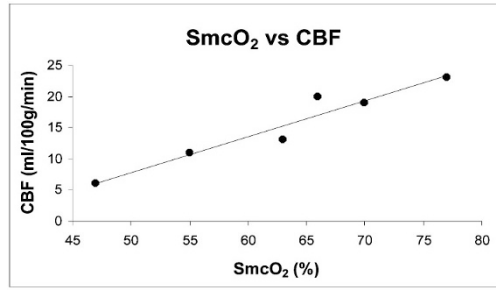
Background: Continuous monitoring of cerebral blood flow (CBF) can facilitate brain orientated care of extremely sick term and preterm neonates. Existing methods, however, are invasive and can only provide intermittent measurements. Several surrogates for CBF have been suggested[1]. Spatially resolved near infrared spectroscopy is able to provide continuous quantitative measurements of mean cerebral oxygen saturation ($SmcO_2$) at the cotside[2]. $SmcO_2$ is a composite measure dependent on cerebral oxygen delivery and extraction (which is low in the newborn infant). **Aim:** By comparing paired measurements of $SmcO_2$ and CBF we aimed to determine whether $SmcO_2$ is a reliable index of CBF in preterm infants. **Methods:** Six preterm infants born at a median gestational age of 24 (23–31) weeks were studied. The median age at study was 6 (2–43) days post delivery. All infants received ventilatory support. Two infants had evidence of intracranial haemorrhage on cranial ultrasound. A NIRO300 (Hamamatsu Photonics K.K., Tokyo, Japan) was used with the optodes placed over the right parietal region. Continuous baseline $SmcO_2$ data was averaged for 20 minutes prior to flow measurements. CBF was measured using the oxygen bolus technique[2]. A total of 5 flow measurements were attempted in each infant. Flow was calculated over 6 seconds. The data were analysed using linear regression. **Results:** The median $SmcO_2$ was 65 (47–77)% and CBF was 16 (6–23) ml $100g^{-1}$ min^{-}. There was a significant correlation between $SmcO_2$ and CBF ($r^2=0.92$).



Conclusion: $SmcO_2$ is able to provide a continuous index of cerebral blood flow in preterm infants undergoing intensive care. This could be of value in the management of infants at risk of cerebral injury. 1. Tsuji M. et al. Pediatrics 2000;106:625–632. 2. Matcher S.J. et al Proc SPIE 1995;2389:486–495. 3. Edwards A.D. et al. The Lancet 1988;8614:770–771.

0276NEO

LEPTIN AND GROWTH IN PRETERM INFANTS

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Aims: To study the longitudinal profile of leptin in preterm infants during the first year of postnatal life and to analyse whether this profile of leptin was associated with the corresponding changes in body composition estimated by bioelectrical impedance (BI) analysis. **Methods:** 36 healthy preterm infants (32.0±2.1 weeks GA, 1704±364 g BW) were prospectively enrolled. Serum leptin levels (RIA), anthropometric variables and BI (Maltron BF/905) were measured and a 3-day dietary record was collected when the preterm infants were 36 w postconceptional age and 3, 6 and 12 mo corrected postnatal age (CA). **Results:** The increase in weight, length, head circumference, braquial perimeter and total body water (estimated by BI) through the study period, was significant higher in the male than in the female preterm infants. However, we did not find significant differences among sexes in energy and protein intake, sum of 4 skinfolds, total body fat (TBF) and serum leptin levels. Skinfold measurement and % of TBF showed a significant increase from baseline to 3 mo CA (Sum of 4 skinfold: 16.5±2.6 mm vs 31.4±5.8 mm; TBF: 4.3±5.3% vs 26.2±5.0%) , decreasing slowly from 6 to 12 mo CA (Sum of 4 skinfold: 30.0±5.5 mm vs 27.3±6.2 mm, TBF: 28.6±5.1% vs 23.1±6.6%). Similar changes occurred with regard to serum leptin levels (baseline: 1.5±0.8 ng/mL, 3mo CA: 5.0±2.6 ng/mL, 6 mo CA: 3.9±1.7 ng/mL, 12 mo CA: 3.3±1.7 ng/mL), which exhibited a strong correlation with these variables and with body mass index (BMI) at 6 mo CA (leptin vs sum of 4 skinfolds $r=0.767$, $p=0.0001$; leoptin vs TBF: $r=0.533$, $p=0.001$; leptin vs BMI: $r=0.695$, $p=0.0001$). **Conclusions:** The rapid increment of adiposity during the first months of life, which is associated with a increase in leptin levels, suggest that the "adipoinsular axis" is active at this stage of development in premature infants.

0277NEO

FETAL CONCENTRATIONS OF DIMETHYLARGININES IN PREECLAMPSIA

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Background: During normal pregnancy, nitric oxide (NO) induced vasodilation is part of cardiovascular changes mandatory for adequate oxygen and nutrient delivery to the fetus. Elevated levels of asymmetric dimethylarginine (ADMA), an endogenous inhibitor of NO synthase, and symmetric dimethylarginine (SDMA), which competes with arginine for cellular transport across the y+ pump, have been reported in plasma of women with preeclampsia. However, plasma concentrations of dimethylarginines in preterm infants born to women with preeclampsia are currently unknown. Therefore, we measured venous cord plasma concentrations of ADMA, SDMA and arginine in preterm infants born to women with preeclampsia (preeclampsia) and born to women without preeclampsia (no preeclampsia). **Methods:** Plasma concentrations of ADMA, SDMA and arginine were measured with high performance liquid chromatography in venous cord blood samples of preterm infants (gestational age (GA) <32 weeks and/or birth weight (BW) <1500 gram). Statistical comparisons were performed by Mann Whitney U test. Data are expressed as median (range), except for GA and BW (mean ± SD).

Results:

	Preeclampsia (n=6)	No preeclampsia (n=11)
Arginine (_mol/L)	92.1 (65.0-117.2)*	67.4 (25.4-102.2)
ADMA (_mol/L)	1.38 (1.17-1.68)	1.34 (0.49-1.67)
SDMA (_mol/L)	2.01 (1.52-2.75)†	1.40 (1.06-2.02)

* p= 0.06, † p= 0.02 GA (214 ± 4.4 days vs. 207 ± 9.3) and BW (1302 ± 351 vs. 1282 ± 503) were not different in the preeclampsia and the no preeclampsia group. **Conclusion:** SDMA is significantly higher whereas arginine tends to be higher in fetuses of women with preeclampsia than in women without preeclampsia. We suggest that SDMA may play a role in the circulation of the fetus of women with preeclampsia.

0280NEO

TRANSIENT TACHYPNEA OF THE NEWBORN (TTN) AND POLYMORPHISMS OF SURFACTANT PROTEIN B (SP-B)

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Background: TTN is usually a benign self-limiting respiratory disorder in the immediate neonatal period. The lipophilic surfactant-associated protein B (SP-B) was demonstrated to be the most relevant structural component of the surfactant system for immediate postnatal pulmonary adaptation. Deficiency of SP-B results in fatal congenital alveolar proteinosis. Polymorphisms within the intron 4 of the SP-B gene were shown to be related to the course of respiratory distress syndrome. **Objective:** We therefore aimed at investigating whether genetic variations of SP-B may be associated with TTN. **Methods:** In order to identify SP-B heterocygous 121ins2 mutation and intron 4 polymorphisms, we analyzed genomic DNA by means of PCR-amplification, fragment length and sequence analysis in 83 healthy term infants (group 1) and 76 term neonates presenting with TTN (group 2). Newborns with any infection, pulmonary or cardiac congenital malformations, postnatal asphyxia and infants of diabetic mothers were excluded. **Results:** Both groups showed no statistical difference in gestational age (median: 39 wk versus 38 wk), birth weight (median: 3325 g versus 3015 g) , Apgar-score(5min) < 7 (0% each) and umbilical artery pH < 7.10 (0% versus 1.3%). The frequency of male infants and caeserian section were significantly higher in group 2 compared to group 1 (68.4% versus 44.6%, p<0,05 ; 68.4% versus 30%, p<0,05). None of the neonates were heterocygous for the 121ins2 SP-B mutation. The frequency of intron 4 variations did not differ between healthy and TTN newborns (8.4% versus 7.9%). **Conclusion:** We conclude polymorphisms of intron 4 not to affect the frequency of TTN. Further investigation is needed to understand underlying mechanisms of TTN.

0282NEO

NEONATAL JAUNDICE: A(TA)7TAA POLYMORPHISM, BREAST MILK BGLUCURONIDASE

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Background: TA repeat promoter polymorphism in the gene for bilirubin uridine diphosphate-glucuronosyltransferase (UGT1A1) has been associated with Gilbert syndrome and incidence of neonatal hyperbilirubinemia. Increased βglucuronidase activity in breast milk was also pointed as another contributory factor for prolonged jaundice in breast-fed babies. However, the role of these "icterogenic" factors in neonatal jaundice is still controversial. **Objective:** To determine whether A(TA)7TAA polymorphism and/or βglucuronidase increase in breast milk correlate with unconjugated hyperbilirubinemia triggered by breast-feeding. **Design/Methods:** Twenty three exclusively breast-fed, jaundiced, caucasian neonates, both males and females, with indications for phototherapy were enrolled in the study group (SG). Thirty-four neonates with same characteristics but not jaundiced were enrolled as control group (CG). All of them were full-term with birth weights greater than 2500 g and with a normal gestational history. Blood and milk samples were collected from day 3 to 12 (5.2±1, 9 days) in SG.In the CG, cord blood was used and milk samples were collected during the second week of life. DNA was isolated and amplified by PCR using selected primers and [α-^{35}S]dATP. The products were resolved on denaturing polyacrylamide gels. The βglucuronidase assay was performed using phenolphthalein-mono-beta-glucuronic acid substrate (Sigma kit). Statistical analysis used: chi-square for categorical variables and Mann-Whitney test for continue variables. **Results:** Total and unconjugated bilirubin concentrations ranged from 15,2 to 28,7 mg/dl (18,8±3 mg/dl) and from 0,17 to 0,8 mg/dl (0,33±0, 16 mg/dl), respectively. In SG one 7/7 genotype was found and 9 (39%) newborns presented the heterozygous 6/7 genotype. All the other infants were homozygous for the normal 6/6 genotype. Enzyme activities were low in 15 milk samples (<1 USM/mg protein), moderately increased in 5 (1 to 2 USM/mg protein) and highly elevated in the last 3 (>2 USM/mg protein). In CG two7/7genotype was found (5,8%), 12(35%) newborns presented the heterozygous 6/7 genotype, one 7/8 genotype, one 5/6 genotype and the others 18 were 6/6 genotype. Enzyme activities were determinate in 12 milks and were low in 11 and moderately increased only in one (p<0,01). **Conclusions:** TA insertion in the promoter of UGT1A1 and increased βglucuronidase activity may be "icterogenic" factors, but are neither the main nor the only causes of severe neonatal jaundice. Funded by Ministério da Saúde (Proj n°42/01).

0283NEO

DISORDERED ORAL VASCULAR NETWORKS IN BRONCHOPULMONARY DYSPLASIA

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Background/aims: A decreased production of angiogenic factors in premature newborns who develop bronchopulmonary dysplasia (BPD) has been previously reported. Injury to the developing lung, whether due to hyperoxia or mechanical ventilation, results in disordered vascular development, ranging from an apparent arrest of microvascular development to extensive microvascular derangement. Here, we tested the hypothesis that an abnormal vascular network pattern is present on extra-pulmonary sites of infants with BPD. **Methods:** Fifteen consecutive infants with BPD (M: 9, F:6 ; gestational age: 27.5 ± 2.0 wk, birth weight: 850 ± 125 gr) and 15 sex and gestational age-matched control infants without BPD (M: 9, F: 6; gestational age: 27.6 ± 2.6 wk, birth weight: 865 ± 135 gr) were examined. The lower gingival and vestibular oral mucosa was chosen as the extra-pulmonary study area due to high vasculature pattern visibility and easy accessibility. Blood vessel area (BVA%) and fractal dimension (D) at two scales (D 1–46, and D 1–15) of the vascular networks were determined. **Results:** The oral vascular networks of BPD patients showed significantly lower BVA% (35.05 ± 8.86% vs. 65.31 ± 12.43%, P<0.0001), and higher complexity (D 1–46: 1.92 ± 0.036 vs. 1.75 ± 0.091, P<0.0001; D 1–15: 1.29 ± 0.072 vs. 1.17± 0.032, P<0.0001) than controls. An inverse correlations between BVA% and fractal dimension was observed (BVA% vs. D 1–46: r= -0.60, P=0.01; BVA% vs. D 1–15: r= -0.61, P=0.0088). The receiver-operating characteristic curve analysis results indicated BVA% ≤ 49.17% as correctly discriminating between BPD patients and controls (100% sensitivity and 100% specificity). **Conclusions:** Our findings indicate that BPD is associated with a significantly disordered oral mucosa vascularization and support the hypothesis that alterations in vascular growth factors may participate in the pathophysiology of the injury leading to BPD.

0284NEO

TOLL-LIKE RECEPTOR 4 IS VARIABLY EXPRESSED ON MONOCYTES FROM PREMATURE AND MATURE INFANTS OR ADULTS

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Background: Premature newborns are highly susceptible to severe infections with gram-negative bacteria. The reasons for this susceptibility are partially explained by immature innate immune responses, such as decreased neutrophil and monocyte activity and decreased concentrations of complement factors. However, additional mechanisms might be important and are still matter of debate. The importance of pattern recognition domains, such as Toll like receptors (TLR), in immunostimulation was clearly accepted within the last years. **Methods:** We investigated the presence of TLR4, the receptor for LPS from the cell-wall of gram-negative bacteria on monocytes. We compared TLR4 cell surface expression by flow-cytometry on monocytes from preterm and term newborns to adult levels. Additionally, TLR4-mRNA was quantified by RT-PCR. **Results:** The surface expression of TLR4 on monocytes from very low birth weight premature infants was reduced in comparison to that of mature infants and was significantly lower than in adults (2–18% versus 60–80%). Furthermore, monocytes from very low birth weight premature infants showed a clear reduction of specific mRNA in comparison to adult levels. **Conclusion:** We thus assume from our data that the development and maturity of TLR4 might be one of the factors contributing to the susceptibility of premature infants to infections with gram-negative bacteria.

0285NEO

THE LEIDEN DEVELOPMENTAL CARE STUDY: THE EFFECT OF DEVELOPMENTAL CARE ON THE VENTILATION OF PRETERM INFANTS <32 WEEKS GESTATIONAL AGE

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Background: Previous studies have suggested that the NIDCAP (Newborn Individualized Developmental Care and Assessment Program) may have a positive effect on the need for ventilatory support. This study is part of a 2- phase RCT in which first basic elements of developmental care (DC) (phase 1) and then NIDCAP (phase 2), are implemented in a stepwise fashion. The effect of basic elements of DC (covering of incubators, use of positioning aids and facilitation of self-soothing/ regulatory behavior) on the requirement for ventilatory support was examined. **Aim:** To investigate the effect of basic elements of developmental care (DC) on duration of ventilatory support in preterm infants < 32 wks. **Methods:** Phase 1: Comparing developmental care (DC) with standard nursing care (C) in infants born < 32 wks. Infants were randomized within 48 hours of birth to the DC group or the C group. The total number of days of ventilatory support was defined as total days of SIMV, HFOV and CPAP. **Results:** 178 infants were included (DC=91; C=87). There was no significant difference in the number of days of ventilatory support between DC (13.8 days) and C (15.3 days) in the total study group, p=0.49. 56 infants were born with a birthweight <1000 gr (DC= 26; C=30). The DC group required 7.2 days less ventilatory support (18.3 days) compared to the C group (25.5 days), p= 0.11. In a subgroup of 42 surviving infants <1000 gr (DC=19; C=23), the DC required 8.3 days less ventilatory support (21.4 days) compared to the C group (29.7), p=0.11. Correcting for SGA (<P10) did not alter the results. **Conclusions:** Basic developmental care may have a positive effect on the number of days of ventilatory support required for infants with a birthweight <1000 gr. Although the difference is not statistically significant, the reduction in days of ventilatory support is of clinical relevance.

0286NEO

THE EXPRESSION OF MURINE HOX GENES DURING LUNG MATURATION

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Background: The structural development and functional maturation of the lungs are dependent upon a number of transcription factors including homeobox genes. The Hox homeobox genes are located within 4 clusters (A to D) and arranged into 13 paralogous groups (1 to 13) in the mammalian genome. Hox proteins are regarded as master regulators of gene expression and the mRNAs of Hoxa-5, Hoxb-5 and Hoxb-6 have been shown to be high in early fetal lung decreasing with advancing age as measured by semi-quantitative techniques. The advanced technology of real time PCR (RQ-PCR) permits the measurement of gene expression more quantitatively. Full expression profiling of all 39 Hox genes during lung development has not previously been reported. **Aims:** To design and validate a RQ-PCR system for measurement of murine Hox expression during lung maturation. **Methods:** Specific TaqMan® primers and probes for the 39 murine Hox genes and 2 markers of lung maturation (surfactant protein B and fatty acid synthase) were validated by cloning and sequencing of the amplified products. Total RNA was obtained from the lungs of C57BL mice at intervals between 14.5 days post-conception (e14.5) to 20 days postnatal age (d20) and reverse transcribed to cDNA. The ABI7700 Sequence Detection System was used to measure gene expression standardised to 18S ribosomal RNA. **Results:** The expression profile of all 39 Hox genes was measured for each of 6 time points. Hox genes in clusters A and B and those between paralog groups 3 and 7 had the highest level of expression in the lungs with Hoxa-5 and Hoxa-3 the most highly expressed at all time points. A wave of reduced expression in 32 Hox genes during the final days of intrauterine life was observed. Surfactant protein B expression increased up to 200-fold from e14.5 to d1. Fatty acid synthase showed peak expression at e18.5 which declined after birth. The expression levels of these control genes followed that of previous reports. **Conclusion:** The application of a RQ-PCR platform has identified the changes of Hox gene expression during lung maturation in the mouse.

0288NEO

THE LEIDEN DEVELOPMENTAL CARE STUDY: THE EFFECT OF DEVELOPMENTAL CARE ON GROWTH OF PRETERM INFANTS <32 WEEKS GESTATIONAL AGE

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Background Previous studies suggest that the NIDCAP (Newborn Developmental Care and Assessment Program) may have a positive effect on growth. This study is a part of a two phase RCT in which first basic elements of developmental care (DC) (Phase 1) and then NIDCAP (Phase 2) are implemented in a stepwise fashion. Previous studies have only used the standard measurements of growth (grams and centimeters). In this study of basic developmental care we used both the standard measures and the standard deviation scores (SDS) from the growth curves based on Usher and McLean. We then examined if there is any effect using basic elements of developmental care (covering of incubators, use of positioning aids and facilitation of self-soothing/ regulatory behavior) on the growth expressed in standard measures (grams and cm) and in SDS. **Aim** To investigate the effect of basic elements of developmental care (DC) on growth from birth until term age (weight gain, head circumference en length) expressed in grams and cm and standard deviation scores (SDS) of preterm infants born < 32 weeks. **Methods** RCT comparing developmental care (DC) with standard care (C) in infants born GA < 32 weeks. Infants were randomized within 48 hours of birth to the DC group or C group. Growth (weight measured daily; head circumference and length measured weekly) expressed as grams and cm and SDS between birth and term age was measured. **Results** The total study population included 178 infants (DC=91, C=87): 20 infants died (DC=12, C=8), 11 infants were lost to follow-up, 6 infants were not measured at term age, 3 babies were excluded because of hydrocephalus. SGA (P<10) (DC=20, C=16) infants were excluded from this analysis. The growth data from 102 infants (DC=49, C=53) were analyzed. There was no significant difference in growth parameters between DC and C infants at birth. The DC group showed a significant larger mean head circumference at term age of 36.3 cm (p=0.019) and significant growth in SDS of 1.21 (p=0.040). The C group had a mean head circumference of 35.6 cm and growth SDS of 0.62. There was no significant difference in weight gain and a trend (p=0.067) towards improved linear growth in the DC group. **Conclusions** Basic developmental care has a significant positive effect on the head circumference growth from birth until term age in AGA preterm infants born <32 weeks gestational age.

0291NEO

EXPRESSION OF HEAT SHOCK PROTEIN 70 IS INCREASED BUT VASCULAR ENDOTHELIAL GROWTH FACTOR RECEPTOR 1 IS DECREASED IN FETAL CAPILLARIES IN PLACENTAS FROM PRETERM DELIVERIES WITH CHORIOAMNIONITIS

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Background: Chorioamnionitis and systemic inflammatory response syndrome are associated with neonatal morbidity and mortality. Aim: We hypothesized that chorioamnionitis injures the fetal endothelium, activates proinflammatory gene transcription via NF-kappaB and may affect growth factors for fetal capillaries in the placenta. **Methods:** Paraffin embedded placenta tissue from preterm babies were stained for Heat Shock Protein (HSP) 70, an unspecific marker for cell injury, nuclear factor kappa B (NF-kappaB) and Vascular Endothelial Growth Factor (VEGF) Receptor 1. Immunohistochemistry was analysed in a four-step semi-quantitative scale. The patients were divided into 3 groups according to histology: chorioamnionitis with funisitis (n=11; birth weight (BW) median 860g, 95% confidence interval (CI) 588-1516g; gestational age (GA) median 26 wks, CI 22–31 wks), chorioamnionitis without funisitis (n=9; BW median 950g, CI 632-1704g; GA median 28 wks, CI 24–31 wks) and a control group without infection (n=12; BW median 865g, CI 581-1596g; GA median 26 wks, CI 23–31 wks). **Results:** In patients with chorioamnionitis plus funisitis or chorioamnionitis alone HSP 70 expression was increased (median 3.5; CI 2.4–3.8; respectively median 3.4, CI 1.9–3.8) over control group (median 0.7; CI 0.1–1.4; $p<0.05$). NF-kappaB was detected in the nucleus of endothelial cells in both patients with chorioamnionitis plus funisitis or chorioamnionitis alone. VEGF-R1 staining was reduced in patients with chorioamnionitis plus funisitis or chorioamnionitis alone (median 1.5; CI 0.4–2.2; respectively median 1.4, CI 0.3–1.9) in comparison to control group (median 2.4; CI 1.7–2.9; $p<0.05$). **Conclusion:** There was no difference between patients with chorioamnionitis plus funisitis or chorioamnionitis alone. Chorioamnionitis injured the fetal capillaries and activated NF-kappaB in fetal endothelial cells. The expression of VEGF-R1 was decreased in patients with chorioamnionitis. The injury and proinflammatory activation of fetal endothelium and reduction of VEGF-R1 in chorioamnionitis may not be limited to the placenta but may also involve various organs of the preterm baby and may play a role in neonatal morbidity.

0292NEO

INHALED NITRIC OXIDE (INO) IN NEWBORNS WITH PERSISTENT PULMONARY HYPERTENSION (PPHN): EFFECTS ON PULMONARY AND SISTEMIC CYTOKINES

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Background: Use of INO is increasing in Neonatal Intensive Care Units as elective treatment of PPHN but the impact of this drug on an already inflamed and developing lung is largely unknown. **Aims:** to determine whether INO administered to term or near-term infants with PPHN improves oxygenation with corresponding changes in concentration of some pro- and anti-inflammatory cytokines in bronchoalveolar lavage fluid (BALF) and plasma. **Methods:** 4 near-term babies (GA: 35 ± 1.2 wks. BW: 3158 ± 656 g.) on sIMV, with severe hypoxaemia (oxygenation index (OI) > 25 and/or echocardiographic evidence of PPHN), received a single dose of surfactant and INO at 40 ppm for the first 24 h, 20 ppm in the following 24 hours and then the concentration was decreased until stop after a mean duration of 70 ± 24 hours. Plasma and BALF determinations of IL-6, IL-8, MCP-1, IL-10, VEGF, TGFβ-1 (ELISA) were obtained at day "0", before treatment, 24 h, 48 h during INO therapy, and 24 h after stopping it. **Results:** All babies had a positive response to INO, survived and were extubated during the first week of life; none needed to be treated with oxygen at 28 days and 36 wks pca. No IVH were recorded. ELF (BALF determinations corrected by the urea method): no significant differences were found in concentrations of IL-6, IL-8 or MCP-1 when their values were compared between baseline and during INO or after INO therapy, even if there was a trend toward a reduction of these cytokines over time, with corresponding improvement of the respiratory status of the newborns. There was a four-fold increase of IL-10 over time ($p<0.05$). VEGF increased from very low levels pre-treatment: 806 ± 408 pg/ml to higher levels post therapy: 39440 ± 21860 pg/ml ($p<0.05$). Plasma: a significant reduction of IL-6 was found between baseline and last determination ($p<0.05$). Similar trend was observed for IL-8. **Conclusions:** The alteration of pulmonary microvasculature, a hallmark of PPHN, is reflected by the very low initials levels of VEGF, which significantly increased during INO therapy. INO could exert anti-inflammatory effects by increasing IL-10 and VEGF concentrations in BALF and reducing IL-6 and IL-8 in plasma.

0294NEO

WEB-BASED PREDICTIVE MODELING OF EXTUBATION OUTCOME IN PRETERM INFANTS

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Background: Even though ventilator management of premature infants has greatly benefited from advancements in monitoring technology, no standards have yet been established for determining optimal extubation time. Approximately 30% of preterm infants will fail extubation, requiring reintubation and continued mechanical ventilation. Another group of infants actually ready for extubation is overlooked in the busy NICU and subjected to unnecessary risks of developing barotrauma, ROP and BPD. This research provides neonatologists in the NICU with a reliable tool for optimal ventilator weaning strategies for each patient while at the same time providing clues about underlying physiological processes.**Objective:** To develop a tool for clinicians to predict extubation outcome in mechanically ventilated premature infants that would integrate the most advanced modeling approaches available with the simplicity and wide availability of a web-based deployment. **Methods:** Relevant parameters for prediction of extubation outcome were identified. Data on 183 premature infants were collected by review of medical charts and used to develop, train and test state of the art artificial intelligence and multiparametric predictive models, respectively artificial neural networks (ANN) and multi-logistic regression (MLR). The modeling tools were compared among themselves and with the clinician's own predictive insight using sensitivity analysis and Receiver Operating Characteristic (ROC) curves. ANN models outperformed MLR, which outlines the non-linear nature of the problem (see results), and a web-based interface was deployed to access them from any system connected to the internet and equipped with a web-browser. Code implementation is entirely on the server side, under UNIX operating system, Apache web-server and MATLAB scientific computing programming environment. **Results:** 51 parameters were identified for use in the development of the prediction model. The optimal ANN model used 13 parameters, 7 hidden nodes and had a ROC area of 0.81 for the training set and 0.87 for the validation set. The optimal MLR model contained 4 variables and had ROC areas of 0.81 and 0.75 The ANN model selected was deployed with a web-interface requiring the clinician to enter 13 relevant parameters for a given infant to return a prediction regarding the extubation outcome.**Conclusions:** The web-based implementation enables the integration of advanced modeling approaches with easy-usage, no maintenance requirements and wide availability. Accordingly, ANN predictive tool developed provides decision-support to clinicians in NICUs anywhere with access to the Internet in determining whether to extubate a premature infant. Along with the prediction for extubation outcome, reliability measures are provided to enable the clinician to categorize the prediction into success or failure by applying the most appropriate sensitivity/specificity threshold. A novelty index is provided to allow the clinician to assess the confidence level of the prediction. Furthermore, the potential is created for further integration with broader clinical management systems such that the predicted outcomes once observed are reported back to the ANN tool for fine-tuning of its predictive capabilities.

0295NEO

ROLE OF ALVEOLAR MACROPHAGE (AM) IN CHRONIC LUNG DISEASE OF PREMATURITY (CLD)

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Background: The role of AM in CLD has not been well investigated. AM play a key role in the resolution of the acute inflammatory response but also significantly contribute to chronic inflammation, remodeling, and fibrosis as a consequence of the production of growth factors that support the proliferation of mesenchimal and epithelial cells. **Aims:** To evaluate the number and distribution of inflammatory cells in bronchoalveolar lavage fluid (BALF) from mechanically ventilated preterm infants with RDS during the first week of life in relation to the subsequent development of CLD(O_2-dependence at 36 post-conceptional weeks). **Methods:** 35 neonates with GA < 30 wks [median 27 (24–29)] and BW < 1250 gr [median 940 (440–1130)] were studied. All babies received natural surfactant (Curosurf, Chiesi Farmaceutici, Parma, Italy), none corticosteroids. Patients with connatal pneumonia or with lung colonization during the study period were excluded. BALF was obtained at 1, 3, 5 and 7 days after birth, unless early extubation. The absolute cell count was obtained by automatic analyzer (Bayer H*3) and differential cell count was calculated from 1000 cells, on centrifuge preparations (Cytospin 2, Shandon Products Ltd). Data were analyzed using non parametric tests with significance of $p<0.05$. **Results:** 8 neonates (23%) developed CLD (CLD Group) [GA median 27 wks (26–29)] ;BW median 825 g (440–1040)] whereas 27 did not (Control Group)) [GA median 27 wks (24–29)] ;BW median 940 g (630–1130)]. There were no significant differences in total leukocytes and in neutrophils (PMN) count between the two groups; absolute values of AM count increased in the CLD group as early as 5 days respect to the Control group and reached a statistically significant difference on day 7 [2.9 (0.4–5.2) cells $x10^9$/L and 0.2 (0.1–1) $x10^9$/L respectively] ($p< 0,05$). **Conclusions:** Babies who developed CLD had more AM on days 5 and 7 than those who recovered from acute lung injury. Further studies are required to establish the effective role of AM in the balance of lung injury and its resolution.

0297NEO

PLACENTAL LEPTIN & RESISTIN METABOLISM IS RELATED TO GESTATION & PATHOLOGY

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Background: Leptin and resistin are adipose tissue derived hormones, which are possibly involved in weight regulation (leptin) and insulin resistance (resistin). Both hormones are also produced by the placenta. Leptin is a growth factor for the fetus, the role of resistin in gestation is not clear, but resistin is possibly involved in gestational diabetes. There are only few data about placental hormone production and metabolism in preterm and pathological pregnancies. **Material & Methods:** 93 placentas; measurement of leptin and resistin tissue mRNA content; dual in vitro perfusion of isolated cotyledons (n=37) for determination of glucose consumption, lactate production, creatinine transfer, release of hCG, leptin, and resistin. Tissue samples/perfusion experiments: <22 weeks (w) n=11/0; 22–35w, n=16/12; >35w n=66/25, diabetic n=6/1, preeclampsia n=7/2, infection (proven by histology) n=9/4, intrauterine growth restriction (IUGR) n=5/2. **Results:** No significant influence of gestational age or placental pathology on glucose consumption, lactate production and substrate transfer (p=0,6). Leptin and resistin mRNA content decreased during gestation (p<0,05). HCG release is higher in preterm than in term placentas (221±40 vs 61±47 IU/g/min, p<0,05), leptin release seems also to be higher in preterm placentas (349±84 vs 237±94 ng/g/min, n.s.). Term placentas released only few amounts of resistin (2,2±1,7 ng/g/min, 70% maternal, 30% fetal). Resistin mRNA content in placentas with infection is increased compared to normal placentas (p<0,05), whereas leptin mRNA content is increased in preeclampsia and IUGR (p<0,05). **Conclusion:** The dual in vitro placenta perfusion model can be safely expanded to preterm and pathological placentas. These data provide important information about placental function in terms of hormonal release in normal, and pathological pregnancies.

0300NEO

THE EFFECT OF HYPOXIA ON PLACENTAL LEPTIN RELEASE IN THE PERFUSED PLACENTA

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Background: Placental leptin (L) expression is markedly increased in pregnancies complicated by severe preeclamsia, possibly caused by placental hypoxia. In vitro L secretion was shown to be significantly increased in chorioncarcinoma cell lines under hypoxic conditions. In the present study we investigated the effects of hypoxia on placental L production and mRNA expression in the placenta using two different approaches: true and chemical induced hypoxia. **Methods:** Dual in vitro perfusion of isolated cotyledons from normal term placentas (n=30). Three groups, normoxic control perfusion (1h) was followed by the experimental phase. 1) Normoxia (pO2 > 110mmHg, 6h, n=10); 2) Hypoxia: a) perfusion using low pO2 (pO2 < 35mmHg, 6h, n=10); b) chemically induced (CoCl 1mM, 6h, n=10). Perfusion volume, glucose consumption and lactate production as well as hCG and L release were measured in control perfusion and experimental phase. Erythropoetin (EPO) mRNA, known as a hypoxia regulated transcript and L mRNA were quantified before and after perfusion using Taq-man real time PCR. **Results:** No significant differences for glucose consumption and lactate production.

	Hypoxia before	after	CoCl before	after	Normoxia before	after
Leptin release ng/ml/min	194±72	*73±56	237±102	*21±10	237±76	202±71
hCG release mIU/ml/min	104±34	*26±9	71±12	*51±10	62±11	66±10
L/18S mRNA	0.3±0.1	0.2±0.1	0.3±0.2	0.1±0.02	0.2±0.1	0.2±0.1
EPO/ -Actin mRNA	0.9±0.4	*1.3±0.6	0.9±0.3	*4.6±1.1	0.1±0.02	0.5±0.24

*p<0.05

Conclusion: EPO increase was as expected. Surprisingly L-mRNA expression seemed to be uneffected by hypoxia, indicating either no regulation of L-mRNA or a too short observation period. The data suggest that there is a short term decrease of hormonal release rates under hypoxia.

0306NEO

UTILITY OF TWO CHANNEL CONTINUOUS EEG (EEGC-2C) IN THE NICU

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Background: Our aim was to assess if new technologies such as EEGc-2C with frequency analysis by Compressed Spectral Disposition (DEC), integrated with standard monitoring, could be useful in extreme sick newborn with difficult clinical neurological evaluation. **Methods:** From June 2000 to March 2003, 106 high-risk neurological newborn were prospectively studied using Continuous EEG Monitoring (EEG monitoring systems, Hewlett Packard, Germany). Standard nine channels analogical EEG (sEEG) was obtained as control at least one time in all patients. Data were correlated with clinical exam and neuro-image findings. **Results:** Five pathologic categories were studied. Group I: Preterm babies (n=12). Absence of normal patterns of maturation with extremely low voltage or seizures, correlated with adverse outcome. Group II: Term babies with severe HIE (n=7), 3 with serial record pattern (extremely low voltage-Burst/Suppression-improvement), 2 with maintained low voltage and 2 with seizures. Group III: Neonatal seizures (n=14), 6 had vascular pathology, 3 metabolic disease, 2 brain abnormalities and 3 idiopathic. Group IV: ECMO support (n=27): 9 with seizures (more than 50% subclinical seizures), 9 transient inter-hemispheric asymmetry to postural oedema, 9 persistent depression of background activity and poor outcome. Group V: Control newborns with high neurological risk (n=16) during cardiovascular surgery (pre and post surgery). **Conclusions:** EEGc-2C with DEC, integrated with overall neonatal monitoring, is suitable for cerebral activity monitoring in a noninvasive and real time manner, is useful to evaluate background activity assuring normal maturation in preterm babies. EEGc-2C with DEC provides early diagnosis of seizures and drug response. Newborns with subtle or subclinical seizures and patients with motor or behavioural phenomena resembling seizures could be misdiagnosed without continuous monitoring.

0307NEO

INTRAPERITONEAL PFC AFFECT LPS INDUCED PULMONARY VEGF EXPRESSION

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Background: VEGF (Vascular endothelial growth factor) regulates among others vascular permeability. The initial phase of an acute pulmonary damage with lung edema, as it occurs i. e. in systemic inflammatory reactions (SIRS), is associated with an altered pulmonary VEGF expression. The creation of a lung edema is suppressed by perfluorocarbones (PFC). Intraperitoneal applied PFC are resorbed and eliminated by the lung. **Hypothesis:** LPS-induced alterations of the pulmonary VEGF expression are suppressed by intraperitoneal PFC application. **Methods:** Male Wistar rats with an age of 2 months obtained 1 mg/kg LPS (E.coli) i.v. First of all temporal kinetics of VEGF expression in the lungs were examined after LPS injection. In a 2nd trial the intraperitoneal PFC (PF 5080) application (10 ml/kg) was studied: I) at the same time, II) 24 h and III) 96 h before LPS administration. These animals were killed 6 hours after LPS-administration and the lungs were prepared for PCR (VEGFmRNA) as well as VEGF-immunohistochemistry. **Results:** Intravenous LPS injection influences the VEGF-synthesis on mRNA level as well as on the protein level. This influence could be suppressed by the PFC administration; with the most clear effect when applied at the same time, but also when PFC was applied 96 h before LPS administration. **Conclusion:** LPS induced effects in the lung can be suppressed by intraperitoneal PFC application. Thus, the intraperitoneal PFC application could be an interesting therapeutic first step for prevention, respectively therapy in a systemic inflammatory reaction of peritoneal origin.

0309NEO

PERINATAL NICOTINE AFFECTS BRAINSTEM SUBSTANCE P LEVELS IN NEWBORN RAT

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Background/aims: Prenatal nicotine exposure has been shown to have profound effects on neuronal development and affects several neurotransmitter systems. Substance P (SP) is known to be involved in the central control of respiration in the newborn mammal. Maternal cigarette smoking increases the risk of sudden infant death syndrome (SIDS). Human infant victims of SIDS have increased SP concentrations in medulla oblongata. We therefore hypothesised that nicotine would affect SP levels in the brain in newborn rat. **Methods:** We investigated the effect of perinatal exposure to nicotine, at a daily dose of 3 mg/kg, on early postnatal levels of substance P-like immunoreactivity (SP-LI) in brain and adrenals. SP-LI was determined by radioimmunoassay. **Results and conclusions:** We found that perinatal exposure to nicotine increased levels of SP-LI in the brainstem without changing levels in other parts of the brain or in the adrenals. These results indicate the possibility of the involvement of the substance P system in the detrimental effects of perinatal nicotine exposure.

0311NEO

COMPARISON OF TWO COHORTS OF ELBWI BORN IN 1999–2000 AND 1996–97

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Background: During the 1990's improved outcome of extremely low birthweight infants (ELBWI) has been reported in several studies based on neonatal intensive care unit (NICU) patients. However, few population-based reports still exist on the changing outcome. **Aims:** To compare the short-term outcome of ELBWI born in 1999–2000 to that of ELBWI born in 1996–97. **Subjects and methods:** The study population included all stillborn and live-born infants with a birth weight of below 1000 g born in Finland during the two two-year study periods. Data including 101 variables concerning the perinatal and neonatal outcome were collected from all maternity hospitals with uniform prospectively designed forms up to the post-conceptional age of 40 weeks. Pearsons Chi-square-test was used in comparisons. **Results:** A total of 502 and 529 ELBWI were born in 1999–2000 and 1996–97, respectively. The proportions of stillborn ELBWI, of infants who died perinatally, neonatally, and post-neonatally were similar in the two cohorts (34%, 55%, 36%, and 2% in 1999–2000 vs. 34%, 55%, 38%, and 2% in 1996–1997, respectively). Of all infants who died before the post-conceptional age of 40 weeks 76% vs. 79%, respectively, died during the first 3 days. Rates of neonatal diseases in ELBWI admitted to NICUs (n=281 and n=309 in 1999–2000 and 1996–97, respectively), retinopathy of prematurity and need for supplementary oxygen in infants alive at the post-conceptional age of 36 weeks (n= 202 and n=211 and in 1999–2000 and 1996–97, respectively) are presented in the table

Disease	Birth years		p
	1996-1997	1999-2000	
Respiratory distress	66 %	84 %	0.005
Intraventricular haemorrhage (gr II-IV)	21 %	26 %	0.164
Septicaemia (blood culture positive)	23 %	32 %	0.009
NEC (requiring operation)	8 %	5 %	0.151
ROP (stages I-II)	34 %	31 %	0.638
ROP (stages III-V)	9 %	6 %	0.144
Supplementary oxygen at the post-conceptional age of 36 weeks	39 %	49 %	0.060

Conclusion: No improvement in survival was found in ELBWI born in Finland during the late 1990's. Most deaths occurred soon after the birth in both cohorts and the pot-neonatal mortality remained low. Morbidity rates were high. The increasing trends detected in several neonatal disease rates are alarming and warrant instant evaluation of possible reasons.

0315NEO

ERYTHROPOIETIN PROMOTES HUMAN FETAL LUNG DEVELOPMENT IN VITRO

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Background: Recent studies have demonstrated that erythropoietin (Epo) has effects on cells other than those involved in erythropoiesis. These findings have been supported by the localization of Epo receptor (EpoR) to a variety of fetal organs including the brain and lung (Juul et al, 1998). Additionally, a prior study (Griffiths et al, 1997) found that ill very low birthweight infants treated with exogenous Epo required fewer days of oxygen compared to randomized control patients suggestive of effects of exogenous Epo on the developing human lung. **Objective:** To determine if Epo modulates epithelial and/or endothelial cell differentiation or proliferation in the developing human lung. **Design/Methods:** Midtrimester human fetal lung (HFL) maintained in explant culture was utilized. Immunohistochemistry for EpoR and for endogenous Epo was performed. As a marker for the effect of Epo on type II pneumonocyte function, surfactant associated protein A (SP-A) levels in HFL explants maintained in the absence or presence of Epo was determined by immunoblot analysis of total protein. Morphometric analysis of HFL explants was performed to determine the proportion of epithelial cells present in control vs EPO treated tissues. Bromodeoxyuridine (BrdU) uptake into the DNA of proliferating epithelial cells was determined by immunostaining for BrdU. Capillary endothelial precursor cells (CEPC) were isolated from HFL tissue and the presence of EpoR mRNA in these cells was determined by RT-PCR. The effect of Epo on CEPC proliferation was determined by the incorporation of labeled thymidine into DNA to assess the possible role of Epo on vascular development in the human lung. **Results:** Immunoreactivity for EpoR in HFL localized to epithelial cells and to a population of mesenchymal cells. Endogenous Epo protein was not detectable in HFL or HFL explants cultured in 2% or 20% oxygen. Immunoblot analysis of total tissue protein from HFL tissues incubated for 4 days in the absence or presence of Epo (5 IU/ml, 10 IU/ml, 50 IU/ml) revealed dose dependent increased levels of SP-A of 30%, 110% and 130%, respectively, compared to control explants. Morphometric analysis of the HFL explants revealed no differences in epithelial cell volume densities in control compared to EPO treated tissues. BrdU uptake was decreased in the epithelium of EPO (10 IU/ml) treated tissues vs control and EPO (5 IU/ml) treated tissues. EpoR mRNA was detected by RT-PCR in HFL CEPC. CEPC incubated in the absence or presence of Epo (5 IU/ml, 10 IU/ml, 50 IU/ml) demonstrated dose dependent increases in the incorporation of labeled thymidine into DNA with Epo dose (137%, 637%, 1153%, respectively, compared to control). **Conclusions:** Exogenous Epo increases SP-A levels in HFL explants in association with a decrease in the proliferation of distal airway epithelial cells. Data suggestive that EPO stimulates the differentiation of distal airway epithelial cells into type II pneumonocytes in HFL in vitro. EPO stimulates the proliferation of capillary endothelial precursor cells derived from HFL. These data demonstrate a likely role for Epo in epithelial cell differentiation and capillary endothelial cell proliferation in the developing human lung.

0317NEO

SURVIVAL OF ELBW AND VLBW INFANTS BORN IN AL AIN REGION, UAE

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Background: Preterm delivery and subsequent neonatal intensive care continue to be major health care burdens. Preterm birth accounts for 75% of all perinatal mortality. The UAE has undergone an unprecedented improvement in healthcare delivery over the past 20 years with perinatal mortality rates now approaching those of western nations. Survival rates for preterm infants, while extensively reported in other countries, have not been reported for a regional UAE population. **Aims:** The aim of this study was to establish survival to discharge statistics for extremely low birthweight (ELBW) and very low birthweight (VLBW) infants born in the Al Ain Medical District as a baseline to measure future improvement in healthcare delivery for this patient population. **Methods:** This retrospective study reviewed delivery and nursery records for all infants born in the region's three hospitals over an 18-month period from January 1, 2000 until June 30, 2001. Outcomes were classified as early neonatal death, late neonatal death, and survival to discharge from hospital. Infants with lethal anomalies were excluded from the analysis. Information from Labour Ward and Nursery databases were examined independently and data were entered into SPSS for Windows for analysis. **Results:** The total number of livebirths over the study period was 12,283. Over 98% of births in the region occur in hospital and the majority of those occurring outside hospital present promptly to the Labour Ward. Hospital A had 2895 livebirths and 5 E-VLBW infants, hospital B had 6028 livebirths and 63 E-VLBW infants and hospital C had 3360 livebirths and 56 E-VLBW infants. The E-VLBW rates for each hospital were: A – 1.7 per 1000, B – 10.4 per 1000 and C – 16.7 per 1000 livebirths. During the study there were 52 ELBW livebirths and 72 VLBW livebirths, representing 0.4% and 0.6% of the total deliveries respectively. Survival to discharge was 29% (15/52) for ELBW infants and 85% (61/72) for VLBW infants. For infants weighing 700g or less the survival rate was 4% (1/23). The group weighing 701–900g had a survival rate of 43% (9/21) while the group weighing 901-1100g had a survival rate of 68% (15/22). Survival of the group weighing greater than 1100g was 88% (51/58). There was a clear improvement in survival with increasing birthweight. ($p<0.001$) Neonatal intensive care within the region is semi-regionalized to hospitals B and C. There was a minor trend to decreased survival in hospital B: total E-VLBW survival O.R. 1.85 (0.89–3.87), ELBW survival O.R.3.26 (0.91–11.86) and VLBW survival O.R. 1.68 (0.45–6.27). However, this trend was almost entirely accounted for by an excess of infants weighing less than 701g being delivered in hospital B. The higher E-VLBW rate at hospital C was largely due to an increase in multiple gestation pregnancies seen at that hospital compared with hospital B with an O.R. of 5.05 (1.52–16.7). Hospital C has the regional Fertility Unit. There were no ethnic differences seen in E-VLBW delivery rates. **Conclusions:** Survival to discharge rates for the ELBW and VLBW populations in the Al Ain health district, UAE have been reported. These rates are below those reported by investigators in western countries in all birthweight groupings. Further study is needed to explore the possible reasons for these findings and to determine the incidence of neurodevelopmental sequalae in ELBW and VLBW survivors in the region.

0323NEO

INCREASED PLASMA 8-ISOPROSTANE IN INFANTS DEVELOPING BRONCHOPULMONARY DYSPLASIA

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Background/aims: Oxidative stress contributes to the pathogenesis of BPD and other complications in preterm newborn infants. F2-isoprostanes, prostaglandin F2-like compounds produced non-enzymatically via lipid peroxidation, are markers of oxidative stress in vivo. N-acetylcysteine (NAC) is a free radical scavenger and a precursor of cysteine, which is the rate-limiting substrate of glutathione synthesis but deficient in preterm infants. **Objective:** To assess 1) the plasma 8-isoprostane as a risk indicator for oxidative damage in extremely low birth weight infants (ELBWI), and 2) the effect of NAC infusion on this marker. **Design/Methods:** In a randomized controlled trial IV NAC (16–32 mg/kg/day) or placebo was administered to ELBWI with the aim of preventing BPD. Plasma free 8-isoprostane (NAC n= 41, placebo n=42) concentrations were measured on day 3 and 7 of life. The mean (SD) gestational age was 26.6 (1.7) weeks, and birth weight 765 (124) grams in the NAC group, and 26.7 (2.0) weeks and 752 (142) grams in the placebo group. Plasma 8-isoprostane was analyzed by an EIA Kit (Cayman Chemical). **Results:** The median free 8-isoprostane concentrations (interquartile range, IQR) on day 3 and on day 7 were 37.0 (32.5) pg/ml and 44.0 (36.5) pg/ml in the NAC group, and 42.5 (46.3) pg/ml and 44.5 (52.0) pg/ml in the placebo group, respectively. The concentration increased in both groups from day 3 to day 7, but there was no difference between the groups. In infants who died or developed BPD (n=29), the median (IQR) free 8-isoprostane concentration was significantly higher, 50.0 (56.5) pg/ml on day 3, and 57.0 (89.0) pg/ml on day 7, when compared to survivors without BPD (n=54), 34.5 (26.8) pg/ml on day 3, and 39.5 (28.0) pg/ml on day 7 (p=0.005). **Conclusions:** Plasma free 8-isoprostane may be an early marker of BPD. NAC did not have any significant effect on the level of 8-isoprostane.

0327NEO

VALUE OF TROPONIN I AND CORTISOL AS EARLY MARKERS OF HEMODYNAMIC INSTABILITY IN PRETERM INFANTS

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Background: The pathophysiology of cardiovascular instability in preterm infants during the immediate postnatal period is not well understood. Recent data support the important role not only of adrenergic-receptor downregulation and adrenal insufficiency in pressor-resistant hypotension, but also of myocardial dysfunction in hypotensive preterm infants. Cardiac troponin I (cTnI) has been identified as a sensitive and specific marker of myocardial damage. **Aims:** To evaluate if cTnI and basal cortisol levels have any effect on the development of hemodynamic instability and/or its response to vasopressor treatment in low birth weight infants (LBWI). **Design:** As part of a blinded controlled trial to explore the effects on brain hemodynamics of two different inotropic agents, newborns < 1501 g or < 31wk gestational age (GA) with hypotension (HP) (mean arterial pressure < GA in wk) during the first 24 h of life, were randomized to dopamine (maximum 10μg/k/min) (n=20) or epinephrine (maximum 0.5μg/kg/min) (n=18). In case of failure of the first drug, the other was added. Those patients with pressor-resistant hypotension received hydrocortisone. Eighteen infants who did not suffer hypotension served as controls (C). Perinatal and postnatal data were prospectively recorded. **Main outcome measures:** cTnI and cortisol plasma levels at baseline after enrollement (BL) and at 3rd day. **Results:** Patient's birth weight and GA were 1003±282 g (HP) vs 1170±310 g (C) (NS) and 28.1±2 wk (HP) vs 30.4±2(C) (p<0.01). No differences were observed in antenatal steroids, maternal pre-eclampsia, type of delivery and small for date. Chorioamnionitis was more frequent in HP (29% vs 0%; p< 0.01). BL cTnI values were significantly higher in HP (0.16±0.15 ng/ml vs.0.06±0.13 ng/ml, p<0.05). BL cTnI was significantly higher in patients who needed 2 inotropic agents (0.23±0.16 ng/ml vs 0.12 ±0.14 ng/ml , p<0.05). However, no differences were found in BL cTnI among HP patients that received steroid therapy. Third day cTnI values did no differ between the groups (HP: 0.03±0.0038 ng/ml vs C: 0.033±0.004 ng/ml). BL cortisol values were similar (HP 16.7±13μg/dl vs. C 16.6±12μg/dl). No differences were found in patients who needed 2 inotropes (20±18 μg/dl) or steroid treatment (17.5±12.7μg/dl). Heart rate was significantly higher in HP with no differences in mean arterial pressure after onset of inotropic support. No differences were found in incidence of ductus arteriosus, respiratory distress syndrome and chronic lung disease, although the duration of mechanical ventilation and oxygen supply, and need of high frequency ventilation were significantly higher in HP. **Conclusions:** In these preliminary results, cTnI seems to be a better early marker for need of cardiovascular support than basal cortisol in LBWI. Myocardial dysfunction, as indicated by higher cTnI levels, must play a key-role in such hemodynamic instability.

0328NEO

SYSTEMIC EFFECTS OF DOPAMINE (DP) VS EPINEPHRINE (EP) FOR INOTROPIC SUPPORT IN PRETERM INFANTS. PRELIMINARY RESULTS

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Background: DP is the most used inotropic drug to treat hemodynamic instability in preterm infants; however, new strategies, such as low-dose EP have shown a better effect on cardiac contractility, probably due to a predominant β-effect. We conducted a randomized blinded controlled trial to explore the effects on brain hemodynamics of these inotropes in low birth weight (LBW) infants with cardiovascular support. **Objective:** To compare the effectiveness of both agents in increasing systemic arterial blood pressure and to evaluate the frequency of adverse events related to treatment with DP vs EP. **Design/Methods:** Newborns <1501g birth weight or <31 wk gestational age (GA), with mean blood pressure (MBP, mmHg)<GA in wk during the first 24 h of life, received DP (2.5, 5, 7.5, 10 μg/K/min) (n=20) or EP (0.125, 0.250, 0.375, 0.5 μg/K/min)(n=18). The dose was increased until the optimal MBP (15% increase) was achieved and maintained. In the case of treatment failure the other drug was added. Types of outcome measures: A) Short-term changes (first 96 h) in heart rate (HR), MBP (indwelling arterial line or oscillometry), acid-base status, lactate, glycemia, urine output and fluids-carbohydrate debit. B) Medium-term morbidity: enteral nutrition tolerance and severity of lung disease and cerebral ultrasound diagnosis (CUS). **Results:** The study populations did not differ respect to use of antenatal steroids, chorioamnionitis, premature rupture of membranes, Apgar score, birth weight, GA, intrauterine growth restriction, sex or CRIB score. No differences were found in the rate of treatment failure (DP 30% and EP 39%) or need of other rescue treatment (volume expansion, other inotropes or hydrocortisone). EP showed a trend towards higher HR (p<.05 at 6 and 12 h), MBP (p<.05 at 6 and 78h), plasma lactate (p<.05 during first 48 h) and glycemia(p<.05 at 6 and 12 h), and lower pH (p<.05 at 6 and 12h), base-excess and bicarbonate (p<.05 at 6h). However, groups did not differ respect to urine output, fluids and carbohydrate supply or insuline requirements. No differences were found regarding incidence of RDS, days on mechanical ventilation or oxygen supply, days to reach full enteral nutrition or severity of CUS diagnosis, either pre or post-vasopressor treatment. Considering only patients successfully treated, EP was stopped earlier than DP (41 vs 73 hs, p<.05). **Conclusions:** Low-dose EP is as effective as low-moderate dose DP to treat hemodynamic instability in LBW infants, although with higher rate of transient side-effects. Speculation: Prolonging low-DP infusion rate does not seem to have any further beneficial effect on splacnic circulation, and should be reconsidered.

0340NEO

EFFECT OF PRENATAL DEXAMETHASONE ON LUNG IN NEONATAL RATS EXPOSED TO HIPOXIA AND RECOVERED IN OXYGEN OR AIR.

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Aims: To evaluate postnatal effect of dexamethasone prenatal treatment on newborn rats and to test the hypothesis that treated with DEX prenatal would to manifest protections against hypoxia and its recovery with 0_2 or air ambient. **Material and Methods:** Wistar rats with timed on 20 day pregnancy were used. DEX (doses 0,4 mgr /kg body weight/d) or equivalent saline solution was administered i.v to mothers at 20 th and 21 th day of gestation. All rats delivery their pups naturally within 48h after last injection. Both groups of pups rats were randomly assigned to either. At 4–6h of life pups rats were exposed in sequential way during 2h in hypoxia, and recovery in >95% 02 or air ambient. Lung and body weight were measured. Lungs were homogenized and were assayed for DNA and SOD,CAT and GP activity. Morphometric study: after lung fixation by intratracheal instillation of formol at a pressure of 20 cmh20. Light level quantitative morphometric assessment was done on coded slides with x 400 magnification and a eye piece with a simple square grid pattern (model CPLW 1018, Zeiss Optical, Hanover Md) Statistical Analyses. ANOVA test was done followed by Bonferroni test. P<0.05 was considered. **Results:** Lung antioxidant enzyme activities in control group for SOD,CAT,GP were similar after hypoxia and air recovery, and increased in response to hyperoxic recovery in control group. In the DEX group lung activity of SOD, CAT increased in response to hypoxia and recovery with hyperoxia or air . Morphometric changes are showed in table I. Table I.- Comparative quantitative morphometry of newborn rats after hypoxia and recovery.

GROUP	TREAT.	Wet lung W /Dry lung W	MORPHOMETRY Sa (cm^2)	Sv (cm^{-1})	N.v ($/mm^3$)	rv (μ)	
Air	SALINE	4,71±0.97	40.91±10.51		118.6±64	190±115	22.25–2.5
	DEX	5,14±1,4	59.77±21.58		309±21	85±12*	54.1±12*
Hypoxia	SALINE	4,92±1,09	75.60±10.0		410.6±53	130±2	50.0±1
	DEX	4,87±0.9	101.17±21.41		359±21	100±24*	54.8±4.4
Hypoxia+ Hyperoxia	SALINE	3,82±0.54	120.92±32.41		466±32	206±30	43.14–5.3
	DLX	3,73±0,72	85.90±14.91		354,9±14	91±15*	56.2±2.5*
Hypoxia + Air	SALINE	4,61±1,23	119,48±24.568		388±24	133±10	50.8±1.7
	DEX	5,56±0,9	86,7±10.58		346,4±1	103.6±9*	51.6±2.8

W.(weight), Sa (alveolar surface), SV (surface density of alveolar walls), Nv (numerical density of alveoli), * significant differences (P<0,05) with control group . **Conclusion:** In newborn rats prenatal DEX show some of hypothesized effects against oxidative stress Increased cellular concentrations of oxygen radicals under hypoxic conditions could stimulate antioxidant enzyme rises. Hyperoxia exposure and prenatal DEX increase AOE response. However prenatal DEX to rats causes a reduction in alveolar number and alveolar surface.

0350NEO

BILIRUBIN IS A MODULATOR OF INTESTINAL PERMEABILITY IN VIVO AND IN VITRO: PRELIMINARY DATA.

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Background: The intestinal epithelial barrier (IEB) provides a first-line defence against "non-self" molecules and bacterial products in the intestinal lumen. Permeability of the IEB during the neonatal period is increased, but factors modulating such permeability have not been well established yet. It has been previously hypothesized that unconjugated bilirubin (uBb) may regulate intestinal permeability in the neonate. Aim In the current study, the effects of hyperbilirubinemia on intestinal permeability were investigated both in vivo and in vitro. **Methods** Fecal α_1-antitrypsin (fA1AT) concentrations were measured to study intestinal permeability in vivo. Stool samples were collected from six-days old, at term, AGA, jaundiced (n=8; Bt12mg/dl) and non-jaundiced (n=5; Bt<8mg/dl) newborns. fA1AT concentrations were determined by radial immunodiffusion on LC-partigen plates containing an anti-A1AT monoclonal antibody. Monolayers of the human intestinal cell line CaCo-2 were used as in vitro model of the IEB. Cells were challenged with increasing concentrations of uBb (50–400 μM); transepithelial electrical resistance (TEER) and paracellular fluxes of the non-absorbable marker Lucifer Yellow (LY) were measured to study the monolayers' permeability. Cell viability was assessed using the MTT test. Enterocyte cytoskeletal actin organization was investigated with optic microscopy after phalloidin staining. **Results In vivo:** higher levels of fA1AT were found in the jaundiced group (0.45 mg/gr of feces ±0.09) compared to the non-jaundiced group (0.28 mg/gr of feces ± 0.07). In vitro: uBb induced a dose-dependent decrease of TEER (reduction of basal value: 15% at 50 □ M, 20% at 200 □ M and 25% at 400 □ M) and a dose-dependent increase of LY paracellular passage. uBb did not affect cell viability over the studied concentration range, while it was responsible for a significant intracellular actin reorganization. **Conclusions** Intestinal permeability in six-days old jaundiced neonates is higher than in non-jaundiced controls. uBb increases intestinal permeability in vitro modulating the paracellular pathway, probably via cytoskeletal actin reorganization. These results may guide further studies concerning neonatal hyperbilirubinemia as a promoting factor of food allergies and/or intestinal inflammation.

0353NEO

PERINATAL CHANGES OF BDNF IN PRE-AND FULLTERM NEONATES

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Background/Aims: Brain derived neurotrophic factor (BDNF), a member of the neurotrophic family, is abundant in brain and peripheral nerves, where it affects normal development, growth, survival, maintenance and repair after injury. Furthermore, BDNF is implicated in the immune response. This study aimed at exploring perinatal changes of BDNF in single preterm (P) and fullterm (F) neonates, characteristic of early or at term transition form intrauterine to extrauterine life. **Methods:** Twenty-one healthy, appropriate for gestational age (AGA) fullterm neonates (mean gestational age 39±0.5-range 38–40 weeks) and 9 healthy AGA preterm neonates (mean gestational age 29±0.3-range 28–30 weeks), as well as their mothers participated in the study. Blood was drawn from the mothers at the first stage of labor (MS), from the doubly clamped umbilical cord-representing fetal state (UC) and from the neonates on the first (N1) and fourth (N4) day of life. BDNF was measured in the serum by enzyme immunoassay methods. **Results:** Levels of BDNF (mean±SE) in: a) FMS (6221±694)did not differ from PMS (6921±642) (p: NS), but both were significantly higher than respective UC, N1 and N4 (in all cases $p<0.05$) b) FUC (3735±685), FN1(3698±369) and FN4 (3714±354) were significantly higher than PUC (1723±332), PN1 (2632±598) and PN4 (2182±268) respectively ($p<0.05$ respectively) c) PN1 showed a significant increase as compared to PUC ($p<0.05$); moreover FN1 were significantly higher than PN1 ($p<0.05$) d) PN4 showed a significant decrease as compared to PN1, but remained significantly higher than PUC e) FN4 were significantly higher than PN4. **Conclusion:** Higher BDNF MS levels may reflect placental involvement as well as mature neurologic and immune systems. Respective higher BDNF levels in F than P may also reflect advanced maturity in the former. PN1 increase of BDNF levels as compared to PUC may indicate stimulation of immune response (monocytes and macrophages) with exposure to extrauterine environment. Nevertheless, this stimulation is insufficient in P, who by decreasing N4 levels are by far less protected than F neonates.

0358NEO

IL-8 INCREASES IN THE LUNGS OF PIGLETS WITH MAS

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Background/Aims: Meconium aspiration syndrome (MAS) is associated with inflammation. IL-8 may be present in meconium and stimulate chemotactic activity of neutrophils. We have not found significant levels of IL-8 in meconium and hypothesized production of IL-8 in MAS as in acute inflammation. **Methods:** Meconium aspiration syndrome was induced in newborn pigs by instilling intratracheally meconium following a hypoxic episode. Hypoxia was induced by 8% oxygen in nitrogen and maintained until BE was ≤ –20 mmol/l. Then meconium (dissolved in saline to 135 mg/ml) was instilled to the lungs (675 mg/kg piglet = 5ml/kg, n=14 or 540 mg/kg= 4ml/kg, n=12). Five minutes later each group was randomised to lung instillation of either 30% bovine albumin (essentially fatty free acid) 1.4ml/kg as rescue therapy or isotonic saline 1.4 ml/kg. In controls the lungs were instilled with isotonic saline (5 ml/kg) followed by 1.4ml/kg albumin after five minutes (n=4). Lung-mechanics, hemodynamics and IL-8 (ELISA Kit Swine, KCS 0081 Med Probe) in tracheal aspirate were followed for the next eight hours. **Results:** IL-8 increased ($p<0.001$, ANOVA) in all MAS-animals (fig 2 and 3). In MAS-animals with the lowest dose of meconium (540mg/kg) a five-fold increase was observed from baseline (1876±704 pg/ml) to maximum (9542±1340 pg/ml) at eight hours after instillation of meconium (fig 2). In MAS-animals receiving the highest dose of meconium (675mg/kg) a ten-fold increase was observed from baseline (1038 ±446 pg/ml) to maximum (10038± 1764 pg/ml) at four hours after instillation of meconium (fig 3). The increase in IL-8 paralleled increase in oxygenation (fig 8 and 9) and ventilation indices (fig 5 and 6). In the control animals a two fold increase (non-significant) of IL-8 was observed from baseline (3551±1602 pg/ml) to culmination (6721±3690 pg/ml)(fig 1) two hours after instillation of meconium. We observed no difference in MAS-animals receiving saline vs albumin as rescue therapy (data not shown). **Conclusion:** We observed a statistically significant increase of IL-8 in the lungs of MAS animals as opposed to control animals. The increase of IL-8 paralleled deterioration of oxygenation index (OI) and ventilation index (VI).

0378NEO

NON-INVASIVE CARBON DIOXIDE MONITORING IN NEONATAL TRANSPORT

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Background: Assessing the efficacy of ventilation during neonatal transport is difficult. Non-invasive carbon dioxide (CO_2) monitoring increases the likelihood of having a normal pH and P_aCO_2. Transcutaneous ($TcCO_2$) monitors are frequently used but bulky and heavy, whilst the small, more easily used end tidal CO_2 ($EtCO_2$) monitors are inaccurate in severe lung disease and V/Q mismatching. New advances have attempted to overcome these limitations. **Aims:** To assess the relationship between $EtCO_2$ and $TcCO_2$ during neonatal transport. **Methods:** Ventilated infants transported by road to a tertiary neonatal unit were enrolled. Infants were excluded if >28 days, had a capillary refill time >2 seconds or either $TcCO_2$ or $EtCO_2$ readings were lost during transport. After calibrating $TcCO_2$ (Microgas 7650, Linde) and side-stream $EtCO_2$ (Microstream system, Agilent) monitors, paired CO_2 (mmHg) measurements were recorded every 20 minutes, starting at stabilisation with an arterial blood gas and continuing for the whole transport. Ventilation changes were at the discretion of the transport team. The differences between P_a CO_2, $TcCO_2$ and $EtCO_2$ ($P_{(a-Tc)}CO_2$, $P_{(a-Et)}CO_2$ and $P_{(Tc-Et)}CO_2$) were analysed using a paired t test. The Bland-Altman method was used to assess bias and repeatability. **Results:** 21 infants were enrolled (median birth weight 2260gm, median gestational age 35 weeks, median age at enrolment 4.8 hours, mean pH 7.32, mean F_iO_2 0.52 and mean alveolar-arterial oxygen gradient 0.85). 103 $P_{(Tc-Et)}CO_2$, 21 $P_{(a-Tc)}CO_2$ and 21 $P_{(a-Et)}CO_2$ samples were recorded. $TcCO_2$ correlated strongly (r=0.92) and accurately reflected P_aCO_2. $EtCO_2$ also correlated strongly with P_aCO_2 and $TcCO_2$ (r=0.82 and 0.92 respectively). However $EtCO_2$ underestimated CO_2 at a clinically unacceptable level and the bias if the $EtCO_2$ was independent of the CO_2 and severity of lung disease. Table: Paired CO_2 differences (mmHg)

	n	Mean [SD]	95% CI	p
$P_{(a-Tc)}CO_2$	21	-1.0 [5.3]	-3.4,1.4	0.4
$P_{(a-Et)}CO_2$	21	7.8 [7.4]	4.4,11.2	<0.001
$P_{(Tc-Et)}CO_2$	103	8.1 [5.4]	7.0,9.2	<0.001

Conclusions: $TcCO_2$ generally agreed with P_aCO_2. $EtCO_2$ had a clinically unacceptable bias of –8 mmHg. As such $TcCO_2$ should, currently, be considered the preferred method of non-invasive CO_2 monitoring for neonatal transport. $EtCO_2$ may have an adjunctive role, especially to confirm the position of the endotracheal tube.

0383NEO

URINARY EPIDERMAL GROWTH FACTOR IN PRETERM INFANTS DURING THE FIRST WEEKS OF LIFE

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Background/Aim: Amniotic fluid is rich in many biologically active substances including epidermal growth factor (EGF). Experimentally EGF has been shown to be important for normal intestinal differentiation and postnatal adaptation. Human milk is a good source of EGF suggesting a role for EGF also in human intestinal development. After a preterm delivery, the neonates supply of EGF is abruptly diminished especially if enteral feeds are delayed. **Objective:** To characterize factors associated with urinary EGF (U-EGF) concentrations in very low birth weight infants during the first weeks of life and to find evidence for its possible use as a therapeutic agent in neonatology. **Methods:** 81 infants with a mean gest.age of 27wk (range 23–32) and a birthweight of 0.92kg (0.39–1.5) were enrolled in the study.41% were SGA, 41% of the mothers received antibiotics and 90% antenatal steroids. U-EGF was measured by immunofluorometry weekly until the child was transferred to another unit or to a max of 6 wk. The concentrations were normalized to urinary creatinine levels (U-Crea). Adrenal function was tested by ACTH test at d1 or d2. Multivariate linear regression was used to characterize possible background variables affecting the U-EGF. **Results:** The mean (SD) U-EGF/U-Crea concentration increased from 1949 (928) g/mol at 0wk to 4515 (1485) at 6wk ($p<0.01$, ANOVA). In linear regression, pre-eclampsia, maternal antibiotics, plasma cortisol level in ACTH test and steroid treatment during the first wk of life explained 25% of the variation in U-EGF/U-Crea at 0 wk. At 1–2 wk, maternal antibiotics and later need of steroids for severe bronchopulmonary dysplasia (BPD) together explained 20% of U-EGF/U-Crea. From 2 to 4 wk, gestational age and the use of steroids during the first wk of life explained one third of the variation. The type of enteral feeding, length of parenteral nutrition, presence of abdominal symptoms or surgical necrotizing enterocolitis were not correlated with U-EGF/U-Crea concentrations. **Conclusions:** U-EGF/U-Crea increases in preterm infants after birth. Maternal antibiotics and poor adrenal function are associated with low levels of U-EGF/U-Crea during the first 2 wk of life. After 2 wk the development of severe BPD and low gestational age at birth are associated with low U-EGF/U-Crea concentrations. The results suggest that low EGF levels are associated with immaturity and its complications related to pulmonary problems.

0396NEO

HOW GOOD ARE WE AT PREDICTING VERY LOW RISK OF POOR LONG-TERM OUTCOME IN VERY LOW BIRTH WEIGHT INFANTS?

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Background: Very low birth weight infants (VLBW) are at high risk for neurodevelopmental disabilities. Most follow-up studies of VLBW infants report the strength of the association between neonatal determinants and outcomes, or overall prognostic information aimed at identifying children with poor long term outcomes. However, for a great number of VLBW infants risk of disabilities is in reality very low and often the medical information received by the parents about the future of their child is tainted with excessive doubts and uncertainty. **Aims.** To describe the probabilities distribution of poor long-term outcome for different prognostic models, with special emphasis on the lower end of the distribution. **Method:** Follow-up study of 553 VLBW infants born in a third level Hospital between 1991 and 2000, who survived to a postmenstrual age of 36 weeks and were assessed at two years of corrected age. The main outcome was survival without neurodevelopmental disabilities at two years of corrected age. Neurodevelopmental disabilities were considered present when 1 or more of the following conditions were present: disabling cerebral palsy, cognitive delay (mental development score below 70), severe hearing loss, bilateral blindness and other disabling conditions (supplemental oxygen at two years, parenteral nutrition). The ultrasonographic scans were read according to the presence of peri/intraventricular haemorrhage, white matter damage (echodense and echolucent intraparenquimal lesion) and ventriculomegaly. Other neonatal determinants such as chronic lung disease or threshold retinopathy of prematurity were introduced in the logistic models to estimate the predicted probabilities and their 95%CI. The overall discriminant performance of the different models were compared with ROC curves. A probability below 5% was considered a very low risk of disability. **Results:** 54 of the 553 infants (9.8 %; 7.5–12.5) had neurodevelopmental handicap at two years of corrected age. A simple model with gestational age, birth weight and ultrasound findings classify correctly 79% of the patients in the cohort; 37% get a probability of poor long-term outcome under 5%. A less parsimonious model increases significantly the correct classification to 86%; 62% get a probability under 5%.. **Conclusions:** Prognostic information derived from statistical models may have limitations of precision and generalizability. Nevertheless it seems that prognostic models may identify a large proportion of VLBW infants with a very low risk (less than 5%) of poor long-term outcome.

0395NEO

VERY LOW BIRTH WEIGHT INFANTS. ALWAYS STUDYING THE WORST OUTCOMES?

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Background: Very low birth weight infants (VLBW) are at high risk for neurodevelopmental disabilities. Most follow-up studies of VLBW infants report prognostic information aimed at identifying children with poor long term outcomes. Infants with high risk of neurosensory impairment require changes in management plans during NICU admission and after discharge. Parents of these high risk infants should be informed about the different problems which may occur in the following months or years. However, for a great number of VLBW infants risk of disabilities is in reality very low and often the medical information received by the parents about the future of their child is tainted with excessive doubts and uncertainty. The emotional, mental, and physical health of the parents may affect the child's development, health and quality of life. Therefore, clinicians should try to identify VLBW infants with good outcome and deliver more optimistic information to these parents in order to decrease suffering and uncertainty. **Aims:** To identify VLBW infants with a very low risk of disabilities at two years of corrected age, according to birth weight, gestational age and ultrasonographic signs of brain injury. **Method:** Follow-up study of 553 VLBW infants born in a third level Hospital between 1991 and 2000, who survived to a postmenstrual age of 36 weeks and were assessed at two years of corrected age. The main outcome was survival without neurodevelopmental disabilities at two years of corrected age. Neurodevelopmental disabilities were considered present when 1 or more of the following conditions were present: disabling cerebral palsy, cognitive delay (mental development score below 70), severe hearing loss, bilateral blindness and other disabling conditions (supplemental oxygen at two years, parenteral nutrition). The ultrasonographic scans were read according to the presence of peri/intraventricular haemorrhage, white matter damage (echodense and echolucent intraparenquimal lesion) and ventriculomegaly. Observed probabilities and 95%CI of death or neurodevelopmental disabilities are presented for the different categories of children. We considered a very low risk of disability a probability below 5%. **Results:** 54 of the 553 infants (9.8 %; 7.5–12.5) had neurodevelopmental handicap at two years of corrected age. 205 infants (37%) were equal or more than 30 weeks of gestational age, more than 1000 g of birth weight, without peri/intraventricular haemorrhage, without white matter damage and without or with light ventriculomegaly. In this group of infants, the proportion of neurodevelopmental disabilities at two years of corrected age was 1.5% (0.4–4). 225 infants (40%) were equal or less than 29 weeks or less 1000g, and without peri/intraventricular haemorrhage, without white matter damage and without or with light ventriculomegaly. The proportion of neurodevelopmental disabilities in this last group was 7.1% (4.2–11). **Conclusions:** In VLBW infants who survive to a postmenstrual age of 36 weeks, simple data about birth weight, gestational age and ultrasongraphic scans allows to identify a group of VLBW with a very low observed probability of disabilities (below 5%) and parents of these low risk infants should be informed according to it.

0398NEO

GASTRIC EMPTYING AFTER CESAREAN DELIVERY: ITS RELATIONSHIP WITH NUTRITIONAL AND RESPIRATORY OUTCOMES.

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Background: Gastric suction for emptying the stomach of newborns after caesarean section is performed systematically in some institutions. It is thought that it can prevent infants from aspirating and improve some aspects of their nutritional and respiratory behaviour. The objective of this prospective, randomised clinical trial was to evaluate in caesarean-delivered full-term newborns the effect on short-term outcomes of gastric emptying after delivery. **Methods:** Fifty-six full-term newborns were randomly assigned to two groups. Gastric-suction was performed on one group (32) and the rest (24) acted as control. Those with history of obstetrical problems (including meconium-stained amniotic fluid) or with Apgar scores < 7 at 5 minutes were excluded. Perinatal information was recorded and after gastric emptying some respiratory and nutritional outcomes (including retching, vomiting, regurgitation and choking) and some metabolic parameters, such as glycaemia and bilirubin, were monitored. **Results:** None of the infants included in the trial showed significant respiratory distress or symptoms of aspiration. The most frequent symptom noted was regurgitation, which affected 51% of all the newborns, irrespective of which group they were assigned to. No significant differences (p0.05), were detected in vomiting (22% vs. 29%), retching (29% vs. 20%) and choking (18.75% vs. 12.5%) between suctioned and non-suctioned groups respectively. None of these episodes required oxygen or medical resuscitation techniques. The characteristics of the gastric contents were not related to any perinatal factors recorded. The alimentary patterns (breast-feeding or formula) and such metabolic variables, such as glycaemia and bilirubin, were the same in both groups. None of the infants in the suctioned group experienced any complications either during or after the procedure. **Conclusions:** We did not detect any effect in short-term nutritional and respiratory behaviour related to gastric suction. We found no justification for routine gastric suction of otherwise healthy full-term newborns delivered by caesarean section.

0406NEO

SERUM LEVELS OF SURFACTANT PROTEIN D DEPENDANT ON PREMATURITY ?

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Background: Immaturity of lung function and immune response remain major problems in preterm infants. The surfactant protein (SP-) D, member of the C-type lectin family, plays a role in innate host defense and therefore reveales a special function in the surfactant system. Intrapulmonary concentrations of surfactant proteins are known to be dependent on gestational age (GA). Serum levels may either depend on pulmonary local concentrations or on impaired alveolo-capillary membrane function. **Aim of the study:** We thus aimed at investigating SP-D serum concentrations in preterm newborns compared to term infants. **Patients and methods.** 30 preterm infants from 24 to 32 weeks of GA and 15 full term newborn babies were included prospectively in the study. Umbilical cord blood was obtained immediately after birth. Levels of SP-D were determined using a sandwich type enzyme immunoassay system with two monoclonal antibodies that lead to photometric determined extinction rate after reaction with a chromogenic substrate. Assays were performed in duplicate for each sample. **Results:** The SP-D levels of full term newborn infants were 2.2 ± 0.6 ng/mL, and tended to be lower in preterm babies < 32 weeks GA (1.9 ± 1.4 ng/mL). SP-D levels were significantly lower in preterms of 28 to 32 weeks GA compared to term infants (1.7 ± 1.4 ng/mL; n=24; p<0,05). In contrast preterms below 28 weeks GA had higher concentrations than the above mentioned group (2.2 ± 1.5 ng/mL; n=16). **Conclusion:** SP-D serum concentrations in newborns have not been studied yet and may give insight into lung maturation. Extremely immature infants had higher SP-D serum levels than those of 28 to 32 weeks GA, indicating a leakage concerning the alveolo-capillary membrane. Further analyses need to reveal correlations between SP-D serum concentrations to clinical course and pulmonary outcome of these infants.

0411NEO

VOLUME-CONTROLLED INTERMITTENT MANDATORY VENTILATION IN PRETERM INFANTS WITH HYPOXEMIC EPISODES.

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Background: Preterm infants undergoing mechanical ventilation often present with episodes of hypoxemia caused by active exhalation resulting in loss of functional residual capacity (FRC) and impaired lung mechanics (Bolivar et al. 1995). **Aims:** To compare the effects of volume-controlled (VC) synchronized intermittent mandatory ventilation (SIMV) with pressure-controlled (PC) SIMV on gas exchange in very low birth weight infants (VLBWI) recovering from respiratory failure. **Methods:** 15 VLBWI with a GA of 25±2 wks, BW 612±149 g with a postnatal age of 33±13 d and at least 2 episodes of desaturation/h (defined as oxygen saturation < 75 % as measured by pulse oximetry [SpO_2]) for at least 8 h were ventilated with the following settings: FiO_2: 0.35±0.12, PIP: 20.0±1.3 cmH_2O, PEEP: 5–6 cmH_2O, rate of 39±13 breaths/min. Infants were exposed in random order to VC-SIMV and PC-SIMV for 4 h each. During VC-SIMV the tidal volume (Vt) was set to the Vt measured immediately before this study during PC-SIMV (7.8±1.4 ml/kg). The upper safety pressure limit during VC was set to 40 cmH_2O. The primary outcome measure was time with a SpO_2 < 80 %, secondary outcome measures were time with hyperoxemia (defined as SpO_2 > 97 %) and FiO_2 exposure. Data is presented as mean±SD or median(min-max). **Results:** There was no significant difference in time with a SpO_2 < 80 % (expressed as percentage of total experimental time: VC: 10.4±4.0 % vs. PC: 10.9±4.2 %). There was no difference in time of hyperoxemia (VC: 0.2(0–10.0) % vs. PC: 0.5 (0–12.7) %) and FiO_2 exposure:

FiO_2	0.21	0.22-0.29	0.30-0.39	0.40-0.49	0.50-0.69	0.70-1.0
VC	0(0-67)	2(0-59)	3(0-93)	7(0-50)	0(0-67)	0(0-18)
PC	0(0-61)	2(0-61)	2(0-61)	9(1-99)	2(0-60)	0(0-64)

Conclusions: VC-SIMV did not reduce desaturations in VLBWI recovering from respiratory failure. We speculate that the leak around the endotracheal tube prevents the effectiveness of volume-controlled SIMV to maintain FRC in VLBWI with desaturations during mechanical ventilation.

0414NEO

QUANTITATIVE EEG ANALYSIS IN NEONATES TREATED WITH EXTRACORPOREAL MEMBRANE OXYGENATION (ECMO)

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Background: Neurological impairment remains a harassing problem for children surviving ECMO. Quantitative EEG analysis provides reproducible data of cortical function even in paralysed children. Aim of the study was to test whether children on ECMO show differences in quantitative EEG compared to controls. **Method:** In 10 critically ill neonates, 5 of them on ECMO, 50 digital 18-leads EEG samples were performed. Absolute and relative power of alpha and delta frequency bands calculated separately for each hemisphere were evaluated using frontocentral leads. Values were compared by Kruskal-Wallis test and Dunns comparisons. Sedoanalgesia, pH, pCO2, lactate, body temperature and mean arterial pressure were recorded additionally. **Results:** Absolute power of alpha and delta frequency band differed significantly between study groups. Relative power differed only in delta frequency band. **Conclusion:** These preliminary data support the hypothesis that neonates treated with ECMO experience changes of cortical function as shown by quantitative EEG analysis.

0424NEO

CARBON DIOXIDE REMOVAL MAY BE AN INDICATOR OF LUNG OVERDISTENSION DURING HFOV

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Background: The safe and effective application of HFOV is dependent upon ventilation at the correct lung volume. Clinicians have traditionally relied upon oxygenation and chest radiography as indicators of lung volume when determining optimum mean airway pressure (P_{aw}), but each of these parameters has major limitations. **Aims:** To investigate whether CO_2 removal might be related to P_{aw} during HFOV, and might thus have utility in indicating lung volume. **Methods:** Preterm lambs were delivered by caesarean section at either 125 (Group PL_{125}; n=6) or 132 (Group PL_{132}; n=7) days gestation (total gestation: 150 days). The fetal head was delivered and intubated with a 3.5 mm cuffed endotracheal tube, and the lambs were then ventilated with a SensorMedics 3100A oscillator in 100% O_2, at a frequency of 8 Hz and at an amplitude of 40 cm H_2O; oscillatory amplitude was subsequently kept constant. Catheters were inserted into the umbilical artery and vein. On initiation of HFOV, alveolar recruitment was ensured by increasing P_{aw} to 30 cm H_2O for five minutes, and then P_{aw} was decreased to 24 and 20 cm H_2O in groups PL_{125} and PL_{132} respectively. In a derecruitment series of measurements, P_{aw} was reduced in steps of 2 cm H_2O and an arterial blood gas sample was taken for measurement of $P_{a,O2}$ and $P_{a,CO2}$ at each setting. A 15-minute period was allowed between measurements for equilibration of lung volume. When O_2 saturation deteriorated below 80%, the lungs were considered derecruited and a recruitment series of measurements were taken with as P_{aw} was increased in steps of 2 cm H_2O. **Results:** As expected, $P_{a,O2}$ deteriorated as P_{aw} was reduced in both groups, with derecruitment at 14 and 10 cm H_2O in groups PL_{125} and PL_{132} respectively. There was, however, no associated change in CO_2 removal. In the recruitment series, as P_{aw} was increased, there was little improvement in oxygenation in group PL_{125} and a trend to improvement in group PL_{132}. There was however, a 50% increase in $P_{a,CO2}$ in both groups at the highest P_{aw} setting used (24 and 20 cm H_2O in the groups PL_{125} and PL_{132} respectively). **Conclusions:** During recruitment in the preterm lamb at a fixed frequency and amplitude, there is a proportional relationship between $P_{a,CO2}$ and P_{aw} during HFOV. This suggests that CO_2 clearance may become progressively impaired as the lung is overdistended. Real-time monitoring of $P_{a,CO2}$ may have some utility as an indicator of lung overdistension during HFOV.

0427NEO

NEONATAL SEIZURES ASSESSED BY NEAR INFRARED SPECTROSCOPY

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Background: Neonatal seizures are a main problem in the NICU, particularly in infants who have suffered from perinatal asphyxia. Available methods to detect their onset and course such as EEG, CT and MR are mostly performed when seizures have already occurred. Near infrared Spectroscopy, NIRS is a non-invasive tool by which it is possible to irradiate tissues with near infrared light at multiple wavelengths and determine concentration changes of natural chomphopres (oxy and deoxy haemoglobin) from the measured light attenuation. When applied to the brain, NIRS has been shown to give reliable data that correlates neuronal activation in the illuminated cortical area to changes in haemoglobin concentration. The question is if it possible to detect hemoglobin concentration changes during endogenous pathological stimulation (i.e. seizures). There is a lack of research on NIRS and neonatal epilepsy in the present literature. **Objective:** To assess the viability of NIRS in monitoring cerebral haemodynamics during neonatal seizures. **Design/Methods:** We have monitored 10 newborns who showed clinical and EEGraphic seizures. In 5 cases seizures occurred in infants who previously suffered from perinatal asphyxia, whereas the other 5 had different etiology. NIRS recordings were performed together with 1-channel continuous EEG (CFM). EEG and CT were also performed. Two couples of NIRS optodes were used. They were placed symmetrically above the fornto-parietal lobe on both hemispheres. **Results:** Our preliminary results showed a good correlation between the NIRS trace and the type of neuronal activity recorded by the CFM. Moreover, infants who showed a decreasing [Hb tot] pattern during the seizure showed the poorest outcome. **Conclusions:** These data suggest that NIRS might be a simple, cost-effective and non-invasive additional tool to be used in NICU to monitor newborns who are at risk of or have already shown neonatal seizures.

0428NEO

WHICH IS THE PREFERRED SUBSTRATE FOR PULMONARY SURFACTANT DISATURATED PHOSPHATIDYLCHOLINE (DSPC) SYNTHESIS IN NEWBORN INFANTS?

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Backgroud: Surfactant is a complex mixture of lipids and proteins that reduces the surface tension at the alveolar surface. Surfactant deficiency is the hallmark of neonatal respiratory distress syndrome (NRDS) The most abundant surfactant component is disaturated-phosphatidylcholine (DSPC). From animal studies glucose and palmitic acid are reported to be the most important DSPC synthetic metabolic precursors. No such information is available in humans. Moreover it not known which is the most prominent (glucose vs. palmitate) DSPC precursor. **Objective:** To study the feasibility of a new, stable isotope tracer approach, using the simultaneous administration of two metabolic precursors (glucose and palmitate), to measure DSPC synthesis and kinetics in vivo in pre term infants with respiratory failure. **Methods:** We studied 8 pre term infants intubated because of respiratory failure (birth weight (BW) 1.15±0.20 kg, gestational age (GA) 28±1 weeks) all admitted to the Neonatal Intensive Care Unit, Padova, Italy. DSPC secretion time (ST), fractional synthesis rate (FSR), and peak time (PK) were measured by a 24 h simultaneous intravenous administration of U13C-glucose and of 16,16,16 2H-palmitate. DSPC was extracted from sequential tracheal aspirates and isolated by thin layer chromatography. Isotopic enrichment curves of DSPC were obtained determining the 13C/12C and 2H/1H ratios of DSPC palmitate methyl esters (13C-PA and 2H-PA) using gas-chromatography isotope ratio mass spectrometry (GC-IRMS) and plasma precursors enrichment by chemical ionisation mass spectrometry. **Results:** Significant isotopic enrichment of both tracers in DSPC was measurable from tracheal aspirates of all study patients. ST was 19.9±6.9 vs. 25.0±9.1 hours (ns), PK 64±24 vs. 62±19 h (ns) and FSR was 26±28 % vs. 22±15 % per day (ns) for 13C-PA and 2H-PA respectively. **Conclusion:** We successfully measured DSPC synthesis and kinetics from plasma glucose and plasma palmitate in the same infant. In our patient population the contribution of plasma glucose and of plasma palmitate to surfactant DSPC synthesis were rather similar. This method is suited for the study of dietary and hormonal interventions on surfactant synthesis in humans.

0429NEO

OUTCOME VARIABILITY IN VERY LOW BIRTH WEIGHT INFANTS. A STUDY IN 30 SPANISH NEONATAL UNITS.

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Introduction: Standardised comparisons of mortality and morbidity data of Very Low Birth Weight (VLBW) infants are the best quality-control (Q-C) indicators of Perinatal Care. **Aim:** To describe and analyze outcomes variability of VLBW infants cared in 30 Spanish NICUs, using the standardised methodology developed by the Vermont-Oxford Neonatal Network (VON) . **Patients and Methods:** A cohort of 1.008 VLBW infants born on 2001, and cared in 30 NICUS were included. Perinatal risk factors, frequent interventions (e.g. CPR, respiratory care, major surgery), outcomes (e.g. death, BPD, IVH, infection), and mortality were analysed. Results were also compared with data reported by VON for 2000. Statistical analysis. Adjusted, weight-specific, rates, trends and inter-quartile ranges were calculated. Comparisons of means, $\chi 2$ was used to evaluate the outcomes. Significance was $p<0.05$. **Results:** Mean birth weight and GA were 1131 g, 29.6 wks, respectively. Incidence of prenatal steroid exposure and multiple birth were 63.8%, and 35.8%. A total of 359 (35.6%) infants were intubated and 185 (18.4%) received prophylactic surfactant at birth. Some 504 infants needed conventional ventilation, and 400 (40.7%) were given surfactant at the NICU. Mortality rate prior to discharge was 13%. Infants receiving surfactant at birth had a lower BW and GA and had higher rates of mortality and morbility. The rates of grade 3–4 IVH and O_2 at 28 days and 36 wks were 9, 26.1 and 16.3%, respectively. A large Center-to-Center variability of both, interventions and outcomes was observed. **Conclusion:** This Q-C methodology could be applied at European level, to set a Network of NICUs for the detection of opportunities for improving care, outcome research and performance of non-industry promoted randomised clinical trials in this very high-risk population.

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0430NEO

EFFECTS OF SURFAXIN® VS. PORCINE SURFACTANT IN PREMATURE LAMBS

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Background: Animal-derived, protein-containing surfactants (SF) appear to be superior to protein-free surfactants. Lucinactant (Surfaxin®), a synthetic, humanised SF containing a SP-B peptide analog has been shown effective in animal models and phase II clinical trials. To date, Surfaxin® has not been compared to an animal-derived SF in a premature animal model. **Aim:** To compare the acute and sustained effects (12 hrs) of Surfaxin® vs. a porcine SF (Poractant alfa; Curosurf®) on gas exchange, lung mechanics, and cardiovascular function in premature lambs with RDS. **Methods:** Twin premature lambs were obtained by C-section from date-mated ewes with multiple pregnancies (GA:135 d; term:145d). The fetal head was exteriorized. A tracheotomy was performed, catheters placed in a jugular vein and carotid artery, animals were anesthetized, paralyzed and the umbilical cord cut. After 5 min of CMV, twins were randomly assigned to one of two groups: Group I (n=6), treated with Surfaxin® (30 mg/mL; 5.8 mL/Kg), and Group II (n=6), received Curosurf® (80 mg/mL; 2.5 mL/Kg); both SF were instilled as a bolus. Heart rate, SAP, pH and arterial blood gases and lung mechanics were registered for 12 h. ANOVA was performed, $p<0.05$. **Results:** Baseline fetal pH was equal in both groups (7.27). After 5-min of CMV a severe RDS develop ($pH<7.08$, $PaCO_2$80mmHg, PaO_2<40mmHg, and Cdyn<0.08 mL/cmH_2O/Kg). After SF was instilled, a similar improvement in gas exchange and lung mechanics was observed in both groups (pH: 7.3±0.1 vs 7.4±0.1; $PaCO_2$: 48±18 vs 40±19 mmHg; PaO_2: 167±120 vs 259±125 mmHg; Cdyn: 0.3±0.1 vs 0.3±0.1 mL/cmH_2O/Kg; at 1 h in group I vs group II). The improvement in lung functions was sustained for the 12-h experimental period, with no statistical differences seen between groups in all registered parameters. Cardiovascular profile remained stable in both groups throughout the experiment. **Conclusion:** In preterm lambs with RDS, bolus tracheal Surfaxin® instillation produced similar improvements in gas exchange and lung mechanics as that observed with a porcine-derived SF. Partially supported by grants FIS 01/1461 and 01/0110–01, GV 200112024 and 200112026 and Esteve Labs and Discovery Labs Inc.

0431NEO

HYPERVENTILATON DOES NOT IMPROVE OUTCOME IN ASPHYXIATED NEONATES.

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Background: Hyperventilation causing vasodilatation of the pulmonary arteries may reduce right ventricle afterload, thus improving myocardial performance and outcome during asphyxia in newborn infants. **Methods:** 118 infants were randomly assigned to become blindly resuscitated with room air (RAR) or 100% oxygen (OxR). Blood gases were extracted from umbilical cord at birth, and from umbilical or radial artery at the end of resuscitation and at clinical stabilization. Clinical parameters, blood gases, RCP, myocardial troponina 1, GSH, GSSG, MDA and SOD activity were determined. Control infants were healthy non-asphyxiated infants.

Results:

	Room – air (n=63)			100% Oxygen (n=55)		
	Low pCO2	Normal pCO2	High pCO2	Low pCO2	Normal pCO2	High pCO2
Clinical Recovery (min)	7,4±1,4**	4,7±0,6	7,3±0,7**	8,7±1,4**	7,3±0,7**	8,5±1,5**
GSSG µmol	85,3±19,3	80,4±15,4	88,4±12,7	119,7±23,8*	112,4±9,8*	120,7±18,3*
SOD IU/g Hb	3,5±0,5	2,8±0,3	3,0±0,8	4,3±0,9*	4,0±0,5*	4,5±1,1*
MDA nmol/mL)	5,5	4,9	6,1*	7,6**	6,8*	8,5**

* p<0.05 ** p<0,001 versus normal pCO2 room air resuscitated

* p<0.05 ** p<0,001 versus normal pCO2 room air resuscitated

Conclusions: Asphyxiated newly born infants ventilated with room air and within normoxia and normocarbia, have an improved outcome and less oxidative stress.

0439NEO

A NOVEL ANTI-APOPTOTIC PATHWAY IN THE DEVELOPING CNS

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Background/Aims: The cortical brain undergoes rapid development and remodeling during the last trimester, which coincides with the onset of viability for premature infants. A large body of data has demonstrated apoptotic neurodegeneration resulting from hypoxia, excitotoxcicity, excess nitric oxide, reactive oxygen species derived from hyperoxygenation, as well as exposure to ethanol. A more complete understanding of the molecular mechanisms by which developing neurons are protected from pro-apoptotic signaling may lead to a refinement of current treatment modalities in the NICU that mitigate cellular loss in the developing CNS. We present data implicating a transcriptional repressor previously thought to be involved in the regulation of neurogenic differentiation programs, in the regulation of neuronal survival. We hypothesize that survival pathways such as the one that includes this repressor, called ZEB (for Zinc-finger E-box Binding transcriptional repressor), have evolved to protect these differentiating blast cells. Our aim is to build a foundation to understand the molecular mechanisms by which this can occur. **Methods:** We have used a variety of techniques, including immunostaining of paraffin-embedded sections of mouse embryos, transfection of ZEB expression constructs into neuronal cells in culture, and a standard yeast two-hybrid screen, to obtain the results outlined below. **Results:** First, in cells from primary neuronal cultures derived from late-stage rat fetuses, the expression of ZEB mRNA is up-regulated (as measured via semi-quantitaive Rt-PCR relative to the expresion of GAPDH mRNA) in response to adminstration of the neuroprotective agent EPO, and, converssely, is down-regulated in response to pro-apoptotic stimuli (such as excitotoxic agents or conditions of hypoxia/glucose depletion). Second, over-expressed ZEB protein in neuronal cell lines protects them from apoptosis-inducing agents. Last, several proteins which physically interact with ZEB are either directly or indirectly involved in apoptotic/cell survival pathways. **Conclusions:** We have accumulated compelling evidence that ZEB plays a role in neuronal cell survival. We present a schematic highlighting the known elements of this pathway, as well as the some of the factors from pathways we believe intersect with this one. Such an understanding may provide the foundation for the modification of therapies administered to premature infants to mitigate potential CNS injury.

0444NEO

INTRAPERITONEAL PERFLUORCARBONS (PFC) INFLUENCES LPS INDUCED PULMONARY TNF-ALPHA EXPRESSION

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Background: Anti-inflammatory properties of intraperitoneal (i.p.) delivered PFC could be a new interesting therapeutical approach. After resorption from the i.p.compartment and transport via blood, the PFC is eliminated by pulmonary exhalation. So a reduction of systemic as well as pulmonary inflammation can be expected. To use the potential of i.p. PFC, it is necessary to know about the time course of elimination. **Hypothesis:** a) The elimination of PFC can be estimated indirectly by measuring the loss of body weight of rats after i.p. application. b) The resorption of anti-inflammatory i.p. PFC should reduce LPS induced expression of proinflammatory TNF-alpha. **Methods:** a) Crossover-study,3 male wistar rats, during 4 days measuring of weight every 4 hours after application of 10 ml PFC vs. Sodium vs. Control; b) 37 male wistar rats, in 6 groups, received i.v. LPS (1mg/kg) and were treated as follows: I. control – no PFC, II. PFC + LPS simultaneously, III. Sodium + LPS simultaneously, IV. PFC 24 hrs prior to LPS, V. PFC 24 hrs prior to Sodium, VI. PFC 96 hrs prior to LPS; doses: PFC (PF 5080) / Sodium 10 ml i.p., LPS (serotype 0111:b4) in 1 ml; animals were killed after 6 hrs of treatment with LPS; measurements: TNF-alpha mRNA+ immunhistochemistry of lung. **Results:** a) After application of i.p. PFC in rats we found instead of the physiological weight gain (5.9 +1.3 g/d) a period of constant body weight. b) The LPS application increased the TNF-alpha expression. This can be influenced by i.p. PFC to a certain extent. A simultaneous application of LPS and PFC showed the strongest suppression of TNF-alpha expression. **Discussion:** a) An elimination of intraperitoneal PFC is likely to occur within 60 hrs after application (that means a probably rate of 3.5 ml PFC/d). b) The reduction of pulmonary TNF-alpha expression by resorption of i.p.PFC opens therapeutical options for systemic inflammations.

0445NEO

KL4-PEPTIDE SURFACTANT (SURFAXIN®) VS. CUROSURF® FOR PREVENTION OF RDS IN VERY PRETERM BABIES

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Background/Aims: To compare the safety and efficacy of the prophylactic administration of a novel surfactant (Surfaxin®; lucinactant), a peptide-mimic of human surfactant protein B (SP-B), versus the predominately used natural surfactant in Europe (Curosurf®). **Method** A masked, international, multi-centre, randomised-controlled, non-inferiority trial with 27 participating centres. Inclusion criteria – gestational age < 29 weeks and birth weight < 1250 g. Key endpoints – incidence of being both alive and not having Bronchopulmonary Dysplasia (BPD) at day 28 and 36 weeks post-conceptional age (PCA). Other efficacy/safety variables included mortality, incidence of RDS at 24 hours of age, incidence of concurrent diagnoses (air leaks, NEC, IVH, ROP and pulmonary haemorrhage) through 36 weeks PCA, and neurodevelopmental outcome at 6 and 12 months of age. The study was approved by individual institutional ethics committees and monitored by a Data Safety Monitoring Board. **Results** A total of 252 preterm newborns were enrolled in the study. Their mean gestational age and birth weight were 26.4 weeks and 926 g respectively. Mortality through 36 weeks PCA was 18.3% and 61.9% of neonates were alive and without BPD at that timepoint. The incidence of RDS at 24 hours among babies in the study population was 10.4%. The incidence of other complications, reported as Serious Adverse Events, were as follows:

N	PIE N (%)	PTX N (%)	Pulm Hem N (%)	IVH[#] N (%)	NEC N (%)	ROP N (%)
252	7 (3)	13 (5)	9 (4)	22 (9)	15 (6)	16 (6)

[#] Grades III/IV

[#] Grades III/IV

Summary This is the first report of a prophylactic trial of a non-animal derived, SP-B analogue, peptide-based surfactant against prevention of RDS. The detailed analysis of results comparing the two groups of study population will be presented at this meeting.

0448NEO

SURVIVAL AND OUTCOMES IMPROVEMENT OF VLBW INFANTS BORN AT A TERTIARY NICU IN CHILE. ASSOCIATED FACTORS AND RESOURCE UTILIZATION IN LAST YEARS.

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Background: VLBW infants survival has dramatically increased in recent years. Important morbidity and mortality variations have been reported among NICUs, related to the type of population and resource utilization. **Objective:** To describe morbidity and survival of VLBW inborn infants in a tertiary NICU and to analyze factors that may influence outcomes, including resource utilization. **Design/Methods:** Biodemographic data of all VLBW inborn infants including: survival, morbidity, and used resources were collected between 1991 and 2001. Outcomes were compared among 3 consecutive periods of time divided according to resource utilization and changes in the NICU guidelines. **Results:** 410 VLBW infants were analyzed. There were no differences in birth weight, gestational age and gender among periods. As shown in table 1, there was a significant improvement in survival and decrease in asphyxia, PDA,ROP and BDP, although there was an increase in IVH.

	1991-1994 (144)	1995-1997 (98)	1998-2001 (168)	p value
BW (g)	1070±276	1087±274	1073±224	NS
Survival (%)	71*	83	90*	p<0,01
5 min Apgar <3(%)	11	4,1*	1,2*	p<0,01
PDA (%)	29	24	21*	p<0,05
IVH/ IVH III-IV (%)	12/ 6	20/ 8*	19/ 12*	p<0,05
ROP (%)	53	40	38*	p<0,05
BPD 36w (%)	27	32	14*	p<0,05

	1991-1994 (144)	1995-1997 (98)	1998-2001 (168)	p value
Antenatal steroids (%)	31	74*	66*	P<0,01
Surfactant (%)	34	50*	59*	p<0,05
IMV duration: days-median(p25-75)	5(2-16)	2(1-6)*	3(2-10)*	p<0,05
NICU daily census	13,6	14,4	16,2	
VLBW Patient/ year (inborn)	30(29)	40(33)	48(42)	
Daily Neonatologist hours/patient	1,1	1,75*	1,65*	p<0,05
Daily RNurse hours/patient	7,7	7,5	7,7	NS

Conclusions: There was a significant improvement in survival over time and reduction in most VLBW infants morbidities. This improvement was associated with better resource utilization and acquired experience. Of concern is the increase in IVH, but these could be related to a better diagnosis and survival of these infants.

0459NEO

INCIDENCE OF MARASMUS AMONG THE VERY LOW BIRTH WEIGHT INFANTS DURING THEIR NICU STAY.

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Background: It is well recognised that postnatal growth failure occurs in low birth weight neonates who undergo intensive care in neonatal units. Whether the degree of acquired growth failure meets the criteria suggested by WHO for marasmus has not been studied. An effort to quantify the degree of growth failure among premature neonates weighing less than 1250 grams during their NICU stay was attempted. **Aims:** 1.To compare postnatal weight pattern of neonates weighing less than 1250 grams with their intrauterine peers of similar post-conceptual age. 2.To measure any gross deviation from AAP recommendation of keeping postnatal growth that approximates inutero growth of normal preterm at the same post conceptional age. **Methods:** All live born infants with birth weight less than 1250 grams, irrespective of gestational age, born between 1st January1997 and June 2002 at Regional Maternity Hospital Limerick, were selected. Those with gross congenital anomaly were excluded from the study. Weekly weight measurements were tabulated for each baby. Using this data, growth curves were plotted according to gestational ages at birth. Such growth curves were individually compared with estimated fetal weight (eFW) curves, as were the mean growth curves for different gestational age. **Results:** 104 neonates qualified for the above study. 29(26.85%) infants were between 24 and 26 weeks gestational age at birth, while 50(46.29%) between 27 to 29 weeks and 15(13.89%) at 30 weeks of gestation. Mean postnatal growth charts showed that an average infant in the study, less than or equal to 28 weeks gestation, was appropriate for gestation age, whereas infants of 29 or more gestational age were on an average small for gestational age. Five (4.8 %) infants were less than 60% of expected weight at birth (between 30 – 33 gestation). 47 (45.2%) babies fulfilled the criteria for marasmus at some phase of NICU stay and 10 (9.6%) had marasmus at the time of discharge. Once marasmic, they remained so for an average of 4.7 weeks (in case of 26 –29 weekers) or for 7.6 weeks (in case of less than 26 weekers or more than 29 weekers). All infants however, irrespective of gestational age, reached below 3rd centile for age for most of their NICU stay. **Conclusion:** In comparison to their intrauterine fetal growth pattern, significant number (45.2 %) of infants less than 1250 grams at birth became marasmic during their NICU stay. Only 4.8% had weight less than 60% of expected at birth, and 12.25% were discharged home with Marasmus, taking intrauterine fetal growth as a standard of expected extrauterine growth. Analysing the trend of appearance of marasmus, majority of the infants, however, were able to recover from the severe malnourishment while being an inpatient at NICU.

0060BRA

ANTICARDIOLIPIN, GLUTAMIC ACID DECARBOXYLASE, AND ANTINUCLEAR ANTIBODIES IN EPILEPTIC CHILDREN

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Background: In the last few years, aberrations of the immunological system have been reported to be associated with epilepsy. The aim of this study was to explore the hypothesis that raised anticardiolipin antibodies, glutamic acid decarboxylase and antinuclear antibodies may be associated with epilepsy and/or pharmacoresistance. **Methods:** The prevalence of anticardiolipin and antinuclear antibodies as well as serum glutamic acid decarboxylase antibodies in epileptic children and controls were tested. Titres were detected in 74 epileptic patients and 50 controls. Epileptic patients were divided into two Groups according to their response to anticonvulsant therapy: Group 1 included 52 children (30 females and 22 males with a mean age ±SD of 7.0 ± 2.4 years) suffering from different types of epilepsy who were treated with various anticonvulsants; Group II included 22 children (10 females and 12 males with a mean age of 6.2 ± 3.6 years) suffering from therapy-resistant epilepsy. **Results:** The prevalence of anticardiolipin antibodies was significantly higher in epileptic patients than in controls, while there was no significant difference between patients who were seizure-free and those with uncontrolled epilepsy. No significant difference was found in glutamic acid decarboxylase antibodies between epileptic children and controls, and between patients who were seizure free and those with uncontrolled epilepsy; a significant difference in the percentage of antinuclear antibodies was found between epileptic children and controls while no difference was found between well-controlled and drug-resistent epilepsy. **Conclusion:** The prevalence of anticardiolipin and antinuclear antibodies is higher in patients with epilepsy than in controls. There is no significant difference in serum glutamic acid decarboxylase antibodies between epileptic children and controls, and between patients who were seizure free and those with uncontrolled epilepsy.

0073BRA

TIME COURSE OF IGFBP1 FOLLOWING PERINATAL ASPHYXIA

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Background: Studies of the molecular biology of the response to hypoxia have suggested that Insulin Like Growth Factor Binding Proteins (IGFBPs) may be more directly related to ischaemic injury than factors such as pH and lactate, which relate to hypoxia and anaerobic metabolism. Data support the hypothesis that hypoxia regulation of IGFBP-1 gene expression may be a mechanism operating in the human fetus, in utero, under conditions of severe hypoxia. Measurement of IGFBP-1 levels in cord blood of term infants with hypoxia have demonstrated a marked increase when compared with controls. We sought to establish a timeline of the increase of IGFBP1 after perinatal asphyxia to evaluate its possible role as a predictor of outcome. **Methods:** Near-term infants (≥35 weeks gestational age) less than 12 hours of age with the following signs of perinatal asphyxia were admitted to the study: non reassuring fetal status (indicated by signs such as late decelerations on cardiotocographic monitoring, fetal bradycardia or meconium staining of the amniotic fluid) and Apgar score ≤ 6 at 5 minutes or first arterial pH ≤ 7.15 and signs of encephalopathy Grade 2–3 (Sarnat&Sarnat). Measurement of IGFBP1 was done every 6 hours for the first 24 hours, then daily until day 3 from indwelling arterial catheters. Measurements of insulin, cortisol and blood sugar were performed simultaneously. Control infants consisted of healthy term infants. Neonates with congenital infection, metabolic disorders, congenital cerebral abnormalities and dysmorphic infants were excluded. **Results:** 20 neonates were included in the study group, 20 infants in the control group. The mean GA was 39.4 weeks, the mean bw 3730g and 3520g,respectively, and there were no differences in the mode of delivery. There were no differences of cortisol or insulin levels between control group and hypoxia group. The IGFBP1 concentrations between the asphyxia group and control group was significantly different up to 72 hours of age (18.5±11 vs 6.5±7.3 nmol/L). **Conclusions:** IGFBP1 after birth is markedly increased in infants with perinatal asphyxia when compared with controls. As the t1/2 of IGFBP-1 is only a few minutes, this persistent elevation denotes the need for on-going metabolic regulation and possible injury as the event resolves.

0092BRA

PSYCHIATRIC SYMPTOMS IN LOW BIRTH WEIGHT CHILDREN AT 14 YEARS OF AGE

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Background/Aims: High prevalence of behavioral problems has been reported in low birth weight children. Few studies have included psychiatric assessment in adolescence. Aims of the study was to evaluate the risk of psychiatric disorders associated with low birth weight. **Methods:** 56 very low birth weight children (VLBW: birth weight (bw) <1500g), 60 small for gestational age (SGA: bw 10 th percentile at term) and 83 controls (bw ≥10th percentile at term) were examined at the age of 14 in a population based study. Psychiatric diagnoses and symptoms were assessed by using the semi-structured interview: Schedule for Affective Disorders and Schizophrenia for School Aged Children (KSADS), Autism Spectrum Screening Questionnaire (ASSQ) and ADHD-Rating Scale IV. **Results:** There were no differences in age, gender or socio-economic status between the groups. VLBW teenagers had higher prevalence of psychiatric disorders (25%) than controls (7%) (OR 4.3, 95CI 1.5–12). When including adolescents with symptoms ≥75% of full diagnostic criteria, 46% of VLBW and 13% of controls had emotional problems (OR 5.7, 95CI 2.5–13). Anxiety disorders were the most common diagnoses: 14% of VLBW, 4% of controls (OR 4.4, 95CI 1.1–17.6). Four VLBW males had ADHD (7%) and one of the controls. When including individuals with symptoms ≥75% of diagnostic criteria, 25% of VLBW had attention problems, 5% of controls (OR=6.6, 95CI: 2–21.3). The ADHD-Rating Scale showed attention problems in the VLBW group vs. controls ($p < 0.01$), without gender differences. Four VLBW-children had symptoms resembling Asperger's Disorder, and ASSQ sum scores suggested problems in the autistic spectrum for the VLBW-group compared to controls ($p < 0.001$). Although the SGA teenagers seemed to have more emotional and behavioral symptoms than controls, there were no significant differences. **Conclusions:** VLBW teenagers are at risk of developing psychiatric symptoms and disorders at the age of 14, especially anxiety disorders and attention deficit. Autistic spectrum characteristics of VLBW-teenagers warrant further research.

0128BRA

HYPEROXIA INDUCES MICROGLIAL EXPRESSION OF INOS IN THE IMMATURE RAT BRAIN

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Background: Relative hyperoxia is a condition frequently encountered in premature infants, either spontaneously or during treatment in the Neonatal Intensive Care Unit. The effects of high inspiratory oxygen concentrations on immature brain cells and their signalling cascades are largely unknown. **Aim:** To investigate the effect of hyperoxia on the amount and topographic distribution of iNOS-expression (inducible nitric oxide synthase) in the immature rat brain. Furthermore to localize hyperoxia-induced formation of peroxynitrite as a potential marker of cellular damage to immature cerebral structures. **Methods:** 7 day old Wistar rat pups were exposed to >80% oxygen for 24 hours and were then transcardially perfused. Following paraformaldehyde fixation, brains were paraffin-embedded and immunohistochemically stained for iNOS and nitrotyrosine. iNOS protein was quantified by Western blot, iNOS mRNA expression was studied by RT-PCR. **Results:** Total brain iNOS mRNA was upregulated, demonstrating a peak at 6 hours following the onset of hyperoxia. There was a threefold increase in iNOS protein in retrosplenial cortex and hippocampus when compared to control animals. Immunohistochemical staining was predominantly observed in microglial cells of hippocampus and frontal cortex with some iNOS reactivity in endothelial and perivascular cells. Nitrotyrosine staining was positive in apical dendrites of neurons in the frontal cortex. There was no positive staining for iNOS or nitrotyrosine in control animals. **Conclusions:** Hyperoxia causes iNOS mRNA and protein upregulation in microglial cells of the immature rat brain. Positive neuronal nitrotyrosine staining indicates formation of peroxynitrite with potential deleterious effects for immature cellular structures in the neonatal brain.

0147BRA

MICE LACKING P66^{SHC} SHOW DECREASED NEOVASCULARIZATION IN A MODEL OF RETINOPATHY OF PREMATURITY

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Background: Hyperoxia, vascular oxidative damage and subsequent retinal ischemia all play a significant role in the genesis of retinal neovascularization typical of retinopathy of prematurity (ROP). Newborn mice exposed to hyperoxia exhibit retinal vascular proliferation and represent an accepted model of ROP. The signalling protein p66^{shc}, present in the retina, mediates intracytoplasmic free radical formation and apoptosis in response to cellular stress. **Aim:** In this study we tried to investigate the role of protein p66^{shc} in the abnormal angiogenic process in the mouse model of ROP. **Methods:** The experiments were performed in 12 mice where the p66shc gene was inactivated (p66^{shc}-/-) and in 12 wild type control animals (wt). Six animals in each group (p66^{shc}-/- and wt) were exposed to either 75% oxygen or room air from postnatal day 7 (P7) to 12 (P12). The animals were then sacrificed at P12 or P17 (n=3 per group) and perfused through the left ventricle with fluorescein isothiocyanate-dextran (2 x 10^6 molecular weight), 50 mg/ml in PBS. The severity of neovascularization was quantified in flat-mounted retinas dividing each retinal quadrant into three equal parts (clock hours) and each clock hour was scored for the presence of neovascular growth, as tufts, ridges or capillary clumps. Thus, each retina could have a neovascularization score from 0 to 12. Endothelial proliferation towards the vitreous was also assessed by the average number of endothelial cell nuclei beneath the retinal internal limiting membrane in 4 eye sections per animal. **Results:** No significant differences were noted between p66^{shc}-/- and wt mice exposed to room air. In the oxygen-treated groups at P12, the posterior avascular area of p66^{shc}-/- mice was reduced compared to the wt controls and, at P17, the retinal neovascular score of p66^{shc}-/- mice was significantly lower than that of wt (7.3+/-1.2 vs 11.3+/-0.5; $p<0.001$). At the same timepoint, the average number of nuclei beneath the internal membrane was dramatically reduced in p66^{shc}-/- mice compared to wt (0.7+/-0.5 vs 20.3+/-5.7; $p<0.0001$). **Conclusions:** These preliminary results indicate that the retinal neovascularization response to hyperoxia is partially inhibited in mice lacking p66^{shc}, suggesting that this protein could mediate in part the endothelial proliferative response. It is unclear whether p66^{shc} plays an initial role in hyperoxia signalling or in the subsequent angiogenic stage secondary to focal retinal ischemia. Further experiments are required to address this issue. (Supported by grants of the Italian Ministry of Health n. 196/2001 and n.ICS120.RC2001

0164BRA

TITLE: HYPOXIC RESPONSE IN NEWBORN RAT IS ATTENUATED BY NEUROKININ 1 RECEPTOR BLOCKADE

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Background and Aim: Substance P (SP) is considered to be involved in the regulation of respiration, in particular when respiratory demands are increased, such as during hypoxic stress. In the present study we have investigated the effects of intracerebroventricular pre-treatment with the selective NK-1 receptor antagonist RP67580 on the respiratory response to hypoxia in 5-day old rat pups. We have also used in situ hybridisation to investigate possible activation of areas known to be involved in respiratory control. **Results:** Basal respiration was not altered by RP67580. When subjected to hypoxia (10% O_2), rat pups pre-treated with RP67580 were unable to sustain the increased respiratory frequency at 10 min. In situ hybridisation demonstrated increased expression of c-fos mRNA in several brainstem areas following hypoxia. This activation was blocked by the antagonist in the retrotrapezoid nucleus and the rostral ventrolateral medulla, areas known to be involved in the hypoxic ventilatory response. **Conclusions:** This study corroborates a role of endogenously released SP, mediated via NK-1 receptors, in the response to hypoxia and suggests that neurons in the rostral ventrolateral medulla are important in this function. It also represents a further example that neuropeptides are released under stressful conditions.

0171BRA

LONGITUDINAL MR STUDIES AND OUTCOME IN NEONATAL ENCEPHALOPATHY

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Background: Data from conventional MR imaging and ^{31}P and ^{1}H MR spectroscopy obtained in the first 10 days after birth are predictive of outcome in infants with neonatal encephalopathy. During the chronic phase, lactic alkalosis in the basal ganglia has been shown to persist for months in infants with severe neurodevelopmental outcome. Further characterisation of localised cerebral metabolism during the chronic phase will provide information on the long-term response of the brain to an insult and subsequent diaschisis. This may be useful in developing neuroprotective strategies. **Aim:** To compare metabolism in both the basal ganglia (BG) and white matter (WM) during the chronic phase after NE according to outcome groups. **Methods:** 32 term infants with NE were included. 22 were studied at 3 monthly intervals during the first 15 months using MRI, ^{1}H MRS (BG, WM) and whole brain ^{31}P MRS. Neurodevelopmental outcome was assessed at 2 years as normal, moderate and severe. MR images obtained in the first 2 weeks were graded as normal, moderate and severely abnormal. ^{31}P and ^{1}H MRS data were compared between MRI and outcome groups. **Results:** A total of 80 studies were obtained. MR images were normal in 10, moderately abnormal in 10 and severely abnormal in 12 infants (10 died in the first 2 weeks). Confirming previous findings, there was a direct correlation between the extent of BG involvement on MRI and neurodevelopmental outcome. At <2 weeks, BG lactate/Cr was higher in the severe group (2.0 ± 1.68) compared to the normal (0.30 ± 0.17) /moderate (0.37 ± 0.14) groups ($p< 0.05$). Lactate/Cr remained elevated in the severe outcome group compared to the normal and moderate groups up to 15 and 4 months respectively. At <2 weeks, BG and WM NAA/Cr were lower in the severe group (BG 1.0 ± 0.18; WM 1.16 ± 0.26) compared to the normal (BG 1.49 ± 0.33; WM 1.70 ± 0.49) and moderate groups (BG 1.26 ± 0.26; WM 1.54 ± 0.38) ($p< 0.05$). BG NAA/Cr remained lower in the severe outcome group compared to the normal and moderate groups up to 15 and 4 months respectively. There was no difference in WM NAA/Cr between the groups after 2 weeks. Choline-containing compounds (Cho)/Cr in the BG was lower in the severe group (1.46 ± 0.14) compared to the normal group (1.97 ± 0.2) from 1 month ($p< 0.05$). BG and WM myo-inositol/Cr was higher in the severe group (BG 0.91 ± 0.14; WM 1.16 ± 0.06) compared to the normal group (BG 0.48 ± 0.1; WM 0.71 ± 0.21) from 4 months ($p< 0.05$, $p<0.05$). Brain pH_i was more alkaline in the severe group compared to the normal group for up to 15 months. There was no difference between normal and moderate groups in the first 2 weeks, however, there were differences at 4 months (pH_i) and 15 months (BG lactate/Cr, WM NAA/Cr) ($p<0.05$). **Conclusions:** During the first 2 weeks, conventional MR images, BG lactate/Cr, BG and WM NAA/Cr and whole brain pH_i correlated with neurodevelopmental outcome. In the chronic period, the severe group showed persistent brain alkalosis, elevated lactate/Cr, reduced BG Cho/Cr and NAA/Cr; and elevated myo-inositol/Cr in both BG and WM. Differences between normal and moderate groups for whole brain pH_i, BG lactate/Cr and WM NAA/Cr were only noted in the chronic phase.

0177BRA

DDT AND DDE CONCENTRATIONS IN HUMAN MILK AT COLOSTRUM AND INFANT'S VISUAL FUNCTION AT 12 MONTHS OF LIFE.

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Background: Exposure to dichlorodiphenyl-Trichloroethane (DDT) and Dichlorodiphenyl- Dichloroethane (DDE) may negatively influence infants' neurodevelopment. **Aim:** To examine the relationships between DDT and DDE concentrations in human milk at colostrum and visual function of infants through the first 12 months of life. **Methods:** Twenty-five consecutive women (mean age 33 y, range 23–42) who delivered healthy, at term singleton infants in our maternity ward and living for at least 20 y in the metropolitan area of or just out of Milan were recruited. Mothers exclusively breast fed for at least 4 months and then up to 6 months while introducing solids in their infants' diet. Mothers had blood and milk samples collected at colostrum, while their infants had blood sampled just before discharge. Milk DDT and DDE concentrations were determined. Serum fatty acids were determined in mothers and in infants with capillary gas-chromatography. Visual function was evaluated at 12 months of life by evaluating P100 wave latency with visual evoked potentials. **Results:** Median DDT and DDE concentrations in milk in the first stages of lactation (colostrum) were, respectively, 13.7 ng/g lipid weight (range 5.4–61.0) and 455 ng/g lipid weight (range 69–1116). Older mothers exhibited higher concentrations of both DDT ($r=0.51$, $p=0.05$) and DDE ($r=0.712$, $p<0.0001$). At 12 months of life, median P100 wave latencies at 15 and 60 minutes of arc (') were, respectively 115 ms (range 97–160) and 123 ms (105–163). At univariate analysis P100 wave latency length at 15' was associated with DDT ($r=0.53$, $p=0.02$) and alpha-linolenic acid in infant ($r=0.52$,$p=0.03$). P100 wave latency at 60' was associated with DDT ($r=0.48$, $p=0.04$). After adjusting for confounders P100 wave latency at 15' and 60' remained associated with DDT ($p<0.05$). **Conclusion:** Within this study population, the concentrations of DDT and DDE in colostrum are associated with an increased length of P100 wave latency in infants at 12 months of life. These data, while confirming that human milk may be a marker of the degree of environmental contamination, suggest that the early exposure to these pollutants might have long-term effects even in babies fed at the breast according to current indications.

0185BRA

INFLUENCE OF EXTRAUTERINE LIFE ON CEREBRAL ACTIVITY IN PRETERM INFANTS < 30 WEEKS OF GESTATION

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Background: In contrast to preterm infants with a gestational age > 30 weeks of gestation no reference values for amplitude-integrated EEG registrations are known for preterm infants with a lower gestational age (< 30 weeks). Also less is known about the influence of extrauterine life on cerebral activity in these infants. Therefore the aim of this study was to assess longitudinally the development of cerebral activity measured by amplitude-integrated EEG for creating reference values and for evaluation of possible differences in longitudinal values as support for an influence of extrauterine life on cerebral activity. **Methods:** Consecutively 250 preterm infants > 30 weeks of gestation were evaluated weekly until discharge. Cerebral activity was registered by aEEG (Cerebral Function Monitor, Lectromed, UK). For creating reference values only neurologically normal preterms (n=97) were taken into account. Evaluation of aEEG-tracing was done descriptively by pattern recognition (continuous and discontinuous patterns (discontiniuous high voltage and discontinuous low voltage pattern) and percentage of each pattern of total registration was calculated in each registration. **Results:** With increasing gestational age percentage of continuous pattern was increasing and percentage of discontinuous patterns were decreasing. The same change in percentages of pattern distribution was seen with increasing gestational age without an influence of original former gestational age. In longitudinal view over several weeks influence of chronological life on cerebral activity (percentage of aEEG patterns) was bigger than original gestational age in statistical analysis. **Conclusion:** In healthy preterm infants with a gestational age < 30 weeks of gestation a major influence of extrauterine life with increasing „more mature“ patterns with increasing chronological life with less influence of original former gestational age can be observed.

0192BRA

CEREBRAL MRI FINDINGS AT 14 YEARS OF AGE IN VLBW AND SGA CHILDREN

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Background/Aims: High prevalence of abnormal cerebral MRI findings has been reported in low birth weight children at different ages. Few studies have compared the MRI findings in very low birth weight (VLBW: birth weight (bw) <1500grams) prematures and small for gestational age (GA: bw <10th percentile at term) children with non-SGA (bw >10th percentile at term) controls. **Methods:** 25 VLBW children, 29 SGA children and 41 controls were examined with cerebral MRI at 14 years of age in a population based study. MR images were qualitatively assessed by radiologists who were blinded to the neonatal histories. Size of ventricles, white and grey matter abnormalities was reported. **Results:** VLBW teenagers had significantly higher prevalence of different types of MRI abnormalities compared with SGA and controls. SGA children did not differ from the controls with regard to MRI findings. Dilation of the ventricular system was found in 76% of the VLBW children, in 20.7% of the SGA children (OR 3.7, 95CI 1.7–7.7) and in 19.5% of controls (OR 3.9, 95CI 2.0–7.5). Dilation was mostly seen as focal enlargement of the occipital horns in VLBW children. White matter reduction was found in 60% of the VLBW children and in 10.3% of the SGA children (OR 5.8, 95CI 1.9–18). None of the controls had this finding. Corpus callosum pathology was found in 44% of the VLBW children, in 3.4% of the SGA children (OR 12.8, 95CI 1.8–92) and in 2.4% of controls (OR 18.0, 95CI 2.5–131). 28% of the VLBW children and 2.4% of controls had periventricular gliosis (OR 11.5, 95CI 1.5–88). Gliosis was located in the occipital and parietal white matter. Excluding five children with cerebral palsy (4 VLBW and 1 SGA) did not alter the significant differences in MRI findings in VLBW children compared with children born at term. **Conclusions:** Cerebral MRI pathology especially in white matter is a common finding in VLBW teenagers. The findings may indicate minor perinatal PVL. The findings in term SGA children did not differ from that in controls. Dilation of the ventricular system is a common finding also in SGA children and in controls. The clinical implication of this warrants further study.

0194BRA

DOSE-DEPENDENT NEUROPROTECTIVE EFFECT OF WIN-55212 IN AN IN VITRO NEWBORN RAT MODEL OF BRAIN HYPOXIC-ISCHEMIC INSULT

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Background: oxygen-glucose deprivation (OGD) of brain slices is an in vitro model of hypoxic-ischemic brain insult allowing the characterization of the neuroprotective effect of new agents, as cannabinoid agonists, in a controlled situation close similar to in vivo conditions. **Aim:** to in vitro study the neuroprotecive effect of the cannabinoid agonist WIN-55212 in newborn brain using an OGD model. **Methods:** seven-day-old newborn Wistar rats were killed by decapitation, obtaining 600 μm-thick brain slices, containing hippocampus, which were placed in a warmed bath at 37°C and incubated in a modified Krebs-Henseleit solution bubbled with 95%O2–5%CO2 for 45 min. Then, OGD slices were incubated in a glucose-free solution equilibrated with 95%N2/5%CO2 for 10, 15 or 20 min, whereas control slices remained in basal conditions. After these periods, slices medium was replaced with normal incubation solution. Medium samples were obtained every 30 min for 2 hours, to measure LDH activity (in mOD/min) by spectrophotometry to quantify necrotic tissue damage. The experiment was repeated in the presence of WIN-55212 (10 nM, 100 nM, or 1 μM). **Results:** OGD induced a time-dependent damage in brain tissue (LDH activity at 30 min, [mean±SEM]: 24.1±2.2, 67.91±3.6, 82.1±4.1, and 137.8±9.2 mOD/min, for control, OGD 10 min, OGD 15 min, and OGD 20 min, respectively, ANOVA $p<0.05$). Giving these results, OGD 15 min was selected for further experiments. In these conditions, WIN-55212 showed a strong neuroprotective effect at 100 nM, whereas neither 10 nM nor 1 μM concentrations induced neuroprotection (LDH activity at 30 min, [mean±SEM]: 32.2±3.2, 97.9±5.1, 108.8±8.8, 48.2±3.1, and 96.9±4.3 mOD/min, for control, OGD 15 min, and OGD 15 min plus WIN-55212 10 nM, 100 nM, or 1 μM, respectively, ANOVA $p<0.05$). **Conclusions:** 1) OGD successfully induced neuronal damage in newborn rat brain slices, time-dependently; 15 min of OGD appears as the optimal procedure. 2) In these conditions, 100 nM WIN-55212 induced a robust neuroprotective effect; lower doses appear as ineffective, whereas higher doses might be toxic. (Supported by a grant FISs PI021540/02)

0253BRA

EFFECTS OF POSTNATAL DEXAMETHASONE ON CRANIAL ULTRASOUND AND NEUROMOTOR MATURATION

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Background: Recent follow up studies have raised the possibility that postnatal dexamethasone treatment may be associated with an adverse effect on subsequent neuromotor function. However, there are hardly any studies reporting the effect of postnatal dexamethasone on cranial ultrasound. **Aim:** To examine any possible effects of postnatal dexamethasone on cranial ultrasound and its association with neurodevelopmental outcome. **Method:** We studied 46 neonates that were enrolled in the OSECT trial. All neonates have a gestational age of <30 weeks, required mechanical ventilation and $FiO_2$0.30, during the first 72 hours of life. Twenty eight neonates (group A) received early or late dexamethasone (0.5mg/kg/day for 3 days, followed by 0.25, 0.1 and 0.05mg/kg/day, for 3 days each dosage regimen) and 18 (group B) inhaled budesonide or nothing. An ultrasound was performed exactly at 6 weeks of age in all infants and it was reviewed by the same radiologist. All children had a detailed neurological examination by the same neurologist between the ages of 2 to 6 years. **Results:** Severe abnormalities on cranial ultrasound at 6 weeks of age were observed in 8(29%) of the 28 babies in group A and in 8 (44%) of the 18 in group B ($p=0.29$). Severe neurodevelopmental disabilities were found in 15(54%) of the 28 babies in group A compared to only 5 (28%) of those 18 in group B ($p=0.08$). A great difference was observed between the two groups in the incidence of cerebral palsy which was found in 54% in group A and in only 28% in group B. No difference was found in the incidence of psychomotor disabilities and neurosensory defects between the two groups. **Conclusion:** Postnatal dexamethasone is probably associated with abnormal neurological outcome and therefore should be used with caution during the neonatal period. It is possible that dexamethasone and/or its preservative, bisulfite, might have neurotoxic effects in the developing brain not detectable by ultrasonography.

0267BRA

HIPPOCAMPAL DEVELOPMENT IN NEWBORNS WITH INTRAUTERINE GROWTH RESTRICTION

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Background/Aims: The hippocampal formation plays a significant role in learning and memory processing. This structure is known for its increased sensitivity to hypoxia, to stress hormones and to undernutrition, all likely to be present in intrauterine growth restriction (IUGR). IUGR is known to cause potential neurodevelopmental disabilities with learning deficits later in life. We have previously been able to show, by quantitative 3D-MRI studies, an alteration of cortical brain development with reduced cortical grey matter volumes in this population. Whether the hippocampus volume in particular is modified, in premature infants with IUGR compared to premature infants with appropriate intrauterine growth, is the purpose of this study. **Methods:** High-resolution 3D-MRI data sets consisting of T2-weighted images of 1.5mm slice thickness were acquired by using 1.5 Tesla clinical MR scanner. 14 preterm infants, with a MRI scan at a mean age of 40 weeks, were included. We used a specially developed 3D rendering software, 3D Slicer (www.slicer.org), that allows visualization of T2 weighted images with their associated tissue classified image and used automatic and manual segmentation. 7 preterm infants with IUGR (mean GA: 32.4 weeks; mean BW<10%ile 1220gr) were paired with 7 control infants with age-matched gestational age at birth (mean GA: 32.2 weeks; mean BW: 1740gr). **Results:** Premature infants with intrauterine growth restriction have a smaller hippocampal volume (see table) when matched with premature children with the same gestational age at birth but normal growth. There was a right-greater-than-left asymmetry of the hippocampal volume in both groups similar to the one found in older children ($p<0.001$). **Conclusions:** This study determines for the firts time the hippocampal volume of premature infants at term. Hippocampal volume was found to be significantly smaller in IUGR preterm infants at term when compared with preterm infants with normal growth. Chronic hypoxia and/or upregulation of the hypothalamus-pituitary-adrenal axis with an increased concentration of circulating corticosteroids could be responsible for the reduction of the hippocampal formation in IUGR premature infants. Whether these findings relate to learning and memory deficit in this population remains to be studied. Hippocampal formation volumes at a mean age of 40 weeks

Hippocampal formation volumes at a mean age of 40 weeks					
	IUGR (cc) mean ± SD		Normal (cc) mean ± SD		p-value (paired t-TEST)
Average of the total hippocampal formations volume	1.97	0.22	2.14	0.19	0.002
Average of the left hippocampal formation volume	0.92	0.11	1.02	0.11	0.003
Average of the right hippocampal formation volume	1.05	0.12	1.11	0.08	0.064

0287BRA

L-NAME PREVENTS HYPOXIA-INDUCED ALTERATIONS IN GUINEA PIG FETUS BRAIN

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Background: Generation of nitric oxide-mediated (NO) free radicals and subsequent increase in intranuclear Ca^{++}-influx are part of the mechanisms leading to activation of the hypoxia-induced apoptotic cascade. Previous studies have shown that cerebral hypoxia results in increased intranuclear Ca^{++}-influx in newborn piglets. It was also shown that intranuclear Ca^{++}-Influx regulates Bax (proapoptotic) and Bcl-2 (antiapoptotic) protein expression, the ratio of which is a determinant in programmed cell death. Administration of inhibitors of NO-synthase (NOS) was recently shown to prevent these increases in newborn piglet brain. Hypothesis: The present study tests the hypothesis that administration to pregnant term guinea pigs of a placenta crossing NOS inhibitor L-N-nitro-L-arginine methyl ester (L-NAME) prior to hypoxia will prevent the hypoxia-induced changes in fetal nuclear Ca^{++}-influx and proapoptotic protein expression. **Methods:** We studied guinea pigs fetuses at term: 5 normoxic (Nx), 5 hypoxic (Hx) and 6 hypoxic pretreated with L-NAME (Hx+L-NAME, 30 mg/kg intraperitoneally). Experiment was started one hour after treatment administration. Control and treated animals were matched and placed in the same hypoxic chamber. Normoxia (FiO2 0.21) or chamber hypoxia (FiO2 0.06–0.08) was then induced for 1 hr in the pregnant mothers. Cerebral hypoxia was determined biochemically by ATP and phosphocreatine (PCr) levels using the method of Lamprecht. Neuronal nuclei were isolated and ATP-dependent $^{45}Ca^{++}$-influx was determined in a medium containing 50mM TRIS (pH 7.4), 150 μg of nuclear protein, 1 mM of ^{45}Ca with and without 1mM ATP for 120 sec at 37C. Bax and Bcl-2 expression determination was performed by Western Blot analysis using specific Bax and BCl-2 antibodies. Protein bands were detected by enhanced chemiluminescence and analyzed by imaging densitometry. **Results:** ATP and PCr values were significantly decreased in the Hx and Hx+L-NAME groups compared to Nx, ($p<0.05$), although, the treated matched group showed a non significant tendency toward higher energy phosphates levels than the hypoxic group. Intranuclear Ca^{++}-influx (pmoles/mg protein) increased in Hx (8.9 ± 2.4), compared to Nx (4.6 ± 0.8), $p<0.05$ and Hx+L-NAME (4.7 ± 0.75), $p<0.05$. Bax protein (OD x mm^2) increased significantly from 69.3 ± 4.5 in Nx to 198.7 ± 9.44 in Hx ($p<0.05$) and 122.8 ± 22 in Hx+L-NAME group ($p<0.05$) whereas Bcl-2 protein was the same in all 3 groups (103 ± 15.4). The ratio Bax/Bcl-2 was increased by twofold in the hypoxic compared to the treated Hx+-L-NAME group. **Conclusions:** We conclude that NOS inhibition prevents the hypoxia-induced increase in nuclear Ca^{++}-influx and alters the gene expression in the fetus guinea pig brain at term. We speculate that L-NAME inhibits peroxidative modification of the nuclear membrane during hypoxia in the guinea pig fetus brain at term, preventing subsequent intranuclear Ca^{++}-influx and therefore modulates the upregulation of programmed cell death.

0272BRA

PERINATAL ASPHYXIA LEADS TO LONG-TERM WHITE MATTER DISTURBANCES – A DTI STUDY

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Background/Aims: About half of the children who suffer perinatal hypoxic-ischemic encephalopathy to a moderate degree are considered to have a good prognosis. However, the long-term neurological or cognitive outcomes are not known. Our aim with this study was to concentrate on this subgroup without obvious neurological impairments and use diffusion tensor imaging, an MRI method that is specific for scrutinizing white matter microstructure. **Methods:** Parents of the children without obvious neuro-impairments were interviewed by a neuro-paediatrician with respect to motor and cognitive function and found to be different from the normal population. To study the possible neurological correlates the subjects, along with a group of controls, then underwent a diffusion tensor MRI scan. From this data we calculated fractional anisotropy, a measure of white matter microstructure. Finally, the two groups were compared based on this measure. The case group consisted of 8 children (4 boys, age 17.02 years, SD 0.22 years) while there were 12 children in the control group (5 boys, age 17.72 years, SD 0.66 years) whom had been born full term without perinatal asphyxia. **Results:** Based on the lower fractional anisotropy values, our results indicate disturbances in several white matter areas in the children with the perinatal asphyxia. These areas include the posterior limb of the internal capsule bilaterally, the genu and splenium of the corpus callosum, as well as frontal and parietal white matter regions. **Conclusions:** The results of this study point to the importance of recognizing the possibility of white matter damage in children whom suffered moderate perinatal hypoxic-ischemic encephalopathy without developing any obvious neuro-impairments.

0319BRA

EFFECT OF INTERLEUKIN-10 ON CEREBRAL INFLAMMATION IN NEWBORN PIGLETS

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Background/Aim: It has been hypothesized that anti-inflammatory cytokines can protect against perinatal brain injury. In newborn piglets with hypoxic/ischemic and endotoxin induced cerebral inflammation, we assessed (1) if the cytokine interleukin-10 (IL-10) had beneficial effects on brain metabolism and microcirculation, and (2) if IL-10 was harmful in itself. **Methods:** Anaesthetized piglets were randomized to control (n=8), IL-10 (n=10), endotoxin (ETX) (n=10), endotoxin and interleukin-10 (IL-10/ETX)(n=10), after pretreatment with 0.9% saline, IL-10, ETX, or IL-10/ETX. Cerebral hypoxia and ischemia was induced by bilateral clamping of the common carotid arteries and ventilation with 8% O2 for 30 minutes, followed by 4 hours of reoxygenation and reperfusion. Extracellular levels of lactate, pyruvate, glycerol, microcirculation and tissue oxygenation were monitored periventricularly and parasagittally with microdialysis and laser Doppler flow with oxygen tension probe. We estimated area under the concentration-time and flow-time curves (AUC) and maximum peak concentration (Cmax) and compared (1) the ETX and ETX/IL-10 groups, and (2) the control and IL-10 groups. **Results:** Periventricular and parasagittal measurements showed similar results. Hence, we only report the periventricular measurements. We found no difference in microcirculation and tissue oxygen tension between (1) ETX and IL-10/ETX, and (2) control and IL-10 groups. Further results:

	Controls	IL-10	p	ETX	ETX/IL-10	p
AUC (mmol/L-min)						
Lactate/pyruvate ratio	72 (28)	37 (13)	0.23	74 (33)	34 (17)	0.29
Glycerol	24 (4)	17 (2)	0.15	19 (2)	12 (2)	0.07
Cmax (μmol/L)						
Lactate/pyruvate ratio	623 (187)	352 (82)	0.16	633 (299)	329 (143)	0.23
Glycerol	133 (22)	113 (9)	0.37	97 (8)	66 (9)	0.02

Conclusion: IL-10 administration did not have neuroprotective effects in newborn piglets exposed to inflammation, and IL-10 did not attenuate metabolism in the presence of inflammation.

0330BRA

WHERE IS BRAIN INJURY LOCATED IN VERY LOW BIRTH WEIGHT (VLBW) INFANTS?

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Background: Actually the increased survival of VLBW infants has rised the interest in their subsequent intellectual and functional development. However, sometimes the outcome does not correlate with neonatal neuroimaging findings. Objective: Firstly, to test the hypothesis that the prevalence of gray and diffuse white matter damage is understimated in the neonatal period. Secondly, to stablish, by means of cerebral ultrasound (CUS) and neuropathological (NP) correlation, which damage could be anticipated. **Methods:** Setting: University-affiliated tertiary center, between July ′97 to July ′02. Patients: neonates with birth weight (BW) <1501g or <32wk gestational age (GA) who died during their stay at the Dept of Neonatology and had pathological studies. CUSs were performed with a 7,5 MHz transducer with an angle of insonation of 90 degree. The brain was scanned in several axes of the coronal, sagittal and parasagittal planes through the anterior fontanelle. Cortical-subcortical regions were systematically assessed by tangential planes. **Results:** The study includes 73 infants, BW 974±406g and GA 27.5±3.2wk, deceased at a mean age of 10.7±22.4 days. Dysmorphic syndrome was present in 20.5% and congenital infection in 2.7%. Forty nine of the patients had CUS. Antenatal brain damage (CUS and/or NP) was present in 23% infants. NP diagnoses: Intracranial hemorrhage: Germinal matrix (GMH) 58%, intraventricular (IVH) 49%, subarachnoid 53%, cerebellum 10%; Gray matter: Selective neuronal necrosis 42% (widespread 40%, focal 60%); White matter damage (WMD): Periventricular leukomalacia (PVL) 56% (focal 10%, diffuse 90%), Periventricular hemorrhagic infarct (PHI) 23%; Other parenchymal necrosis at: cortex 15%, brain stem 3%, cerebellum 4%, thalamus and basal ganglia 6%; Ventricular dilatation 19 % (43% without IVH).CUS&NP correlates (sensibility/especificity,%): IVH 90/94; WMD 92/92 [PVL (focal or diffuse) 93/89; PHI 93/97]; cortical-subcortical involvement in PHI 100/83. All patients with persistent periventricular echogenicity lasting ≥15 days had PVL in NP. Cortical-subcortical echogenicity was associated with cortical gliosis in NP (p<.005). **Conclusions:** CUS is a useful tool to identify patients with PVL, both focal or diffuse. This study supports our hypothesis that brain damage in VLBW infants is more extense than reported. We speculate that some of the lesions seen in this population of deceased patients could explain certain late disabilities observed in surviving VLBW infants.

0331BRA

ULTRASONOGRAPHY (CUS) AND POWER DOPPLER (PD) IN POSTHEMORRHAGIC VENTRICULAR DILATATION (PHVD): A DEEPER APPROACH.

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Background: Management of PHVD in premature infants involves controversy. The morbidity associated with this condition is high, and the mechanism involved in the development of brain damage remains unclear. There is not available information regarding the prevalence of CSF-obstruction sites, and data about the associated perinatal-neonatal brain damage are scarce. Objetives/ Aims: To identify the site of impairment of CSF flow in infants with progressive PHVD. To define the type of brain lesion associated with PHVD. **Methods:** All preterm infants with intraventricular hemorrhage (IVH) and progressive PHVD (ventricular index of Levene >4mm P97) admitted to the NICU between 1995–2002 were included. The brain was explored on several axes of the coronal, sagittal, and parasagittal planes, through the anterior fontanelle, to visualize brain parenchyma and the ventricular system . To evaluate the brain surface (cortical-subcortical region) and the extra-axial space, the transducer was angled (tangential planes). PD was used to study CSF flow through the ventricular system. Adverse outcome was considered in patients who died or had severe handicaps (cerebral palsy, developmental delay and/or severe neurosensory impairment). **Results:** Progressive PHVD was diagnosed in 34 babies (GA: 27.2+2.5 wk; BW: 948+299 g). The initial CUS findings were: grade 3-IVH 31 (97%); periventricular hemorrhagic infarct (PHI) 15 (44%); periventricular echogenicity (PVE) 24 (70.5%); cortical-subcortical involvement 19 (56%); cystic PVL 10 (3%); thalamus and basal ganglia 6 (18%) and cerebellum 1 (3%) involvement. In 4 patients (12%) brain damage was considered to be antenatal. Lumbar taps (LT) were started at a mean age of 19.4+7.3 days. In only 22% of patients ≥10ml/K of CSF per LTcould be obtained. LTs failed (persistent ventricular dilatation and tension) in 90.6%. As a whole, ventricular dilatation had a non-surgical arrest (serial LTs) in 3 infants whereas 29 needed ventriculoperitoneal shunt (VPS) at a mean weight 1443+392g (12 and 1, out of 29, with previous subcutaneous reservoir –SCR- and external drainage, respectively). There were two deceased patients, one before surgery and another with SCR. By means of CUS-PD characterization of CSF flow-impairment sites was possible: aqueduct of Sylvius (G-1) 14 (41%), 4th ventricle foramina (G-2) 15 (44%) (Obstructive PHVD) and posterior fossa cisterns and arachnoid villi (G-3) 5 (15%) (Communicating PHVD). LTs failed in all G-1 and G-2 patients and in 40% of G-3 (p<.05). On evolution, adverse CUS findings were associated with: G-2, ventricular dilatation with irregular margins, PVL and cerebral and cerebellum atrophy (p<.01); and with G-1 and G-2, thinning of the corpus callosum (p<.001). Fourteen infants had adverse outcome: 38.5% G-1, 61.5% G-2 and 20% G-3 (NS). **Conclusions:** 1. CUS-PD is a powerful tull for early characterization of CSF-outflow impairment in PHVD, helping to deal with diagnostic and management dilemas. 2. There is a high rate of associated brain injury diagnosed at the time of onset of PHVD. Speculation: An earlier and more precise diagnosis of CSF obstruction is essential to avoid the extent of brain damage resulting from mechanisms triggered by ventricular distention.

0346BRA

TITLE:INTRAVENTRICULAR HEMORRHAGE AND PLASMA ACTIVIN A LEVELS IN PRETERM NEWBORN

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Background: The pathogenesis of intraventricular hemorrhage (IVH) is multifactorial and not fully elucidated. Perinatal hypoxia is an important risk factor in the pathogenesis of IVH by altering cerebral blood flow regulatory mechanisms and causing sustained depressed cerebral function at birth and days or weeks afterwards. **Aim:** The present study was designed to explore the association between plasma activin A, a biochemical marker of perinatal hypoxia, and IVH detected by brain ultrasonography in premature infants. The hypothesis was that activin A is associated with detectable IVH and could be a factor involved in hypoxia-induced brain hemorrhage in preterm newborns. **Methods:** 50 consecutively born preterm infants of 32 weeks' gestation or less were studied. Nucleated red blood cells (NRBC) count, hypoxanthine (Hx), xanthine (Xa) and activin A plasma levels were determined in arterial blood samples collected in the first hour after birth. NRBC count was expressed as absolute erythroblast count. Hx and Xa plasma levels were evaluated by HPLC, Activin A concentrations were measured in a single matrix using specific two-site enzyme immunoassays (Serotec, Oxford, UK). Pulsed Doppler sonograms of the anterior and middle cerebral arteries and brain ultrasonography were performed within 48 hours of birth. Brain ultrasonography were serially repeated at five, six day intervals until the age of 4 weeks to detect IVH. **Results:** Hx, Xa, activin A and NRBCs were higher in newborns developing IVH than in controls. A significant association was only found between activin A and NRBC (rank correlation coefficient = 0.43, p = 0.002). Logistic regression analysis performed between IVH as dependent variable and activin A, Hx, Xa, Apgar score at 5 minutes, pH, base deficit and NRBC showed that activin A plasma levels were predictive of detectable IVH (p=0.036). **Conclusions:** This is the first report showing an association between increased levels of Activin A and IVH in the newborn infants. The data offers exciting new perspectives for clinical and experimental studies into the mechanisms underlying the pathophysiology of IVH. Acknowledgment: Grants from the Italian Ministry for the University and Scientific-Technological Research (MIUR 2001: "Identification of etiopathogenetic factors characteristics of newborn at high risk of brain damage in perinatal period. Clinical and experimental study).

0381BRA

HIPPOCAMPAL DEVELOPMENT AFTER HYDROCORTISONE TREATMENT FOR NEONATAL CHRONIC LUNG DISEASE

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Background/Aims: High doses of corticosteroids, in rhesus monkeys, have been shown by Uno H et al (1994) to cause a reduction of hippocampal volume (HV), when given in the antenatal period. Dexamethasone, when given to premature infants for chronic lung disease in the neonatal period, has further shown to be responsible for impaired cortical growth (Murphy B.P. et al, 2001). The aim of the current study was to determine the HV, at 9 years, in a group of premature infants, who were treated with hydrocortisone (HC) in the neonatal period. **Methods:** 58 children had an MRI scan at a mean age of 8 years and 8 months, 22 preterm infants (mean GA of 28.2 weeks, BW 1088gr) were treated with HC (at a starting dose of 5 mg/kg/d, tapered over three weeks), 32 preterm infants had not received HC (mean GA of 30.36 weeks, BW 1386gr). Four children were excluded for technical reasons. A sequence of image processing algorithms was used to segment each of the MRI slices (6 mm thickness) into the following separate tissue classes: cerebral cortical gray matter, white matter, and cerebrospinal fluid. The hippocampus was then manually segmented on IR-weighted images of 1.5mm thickness and corrected for intracranial volume. **Results:** There is a right-greater-than-left asymmetry in the studied population (paired t-test p<0.0001). Girls (f) have a tendency to have a smaller hippocampus than boys (m) regardless of the type of ventilation or treatment received (p=0.15). There is no effect of HC treatment on HV (see table). There is also no effect of HC on cortical gray matter volume (mean volume in the treated group =647cc±57, in the none treated group =640cc±56). **Conclusions:** HC given at a much lower dose, than used in prior studies, has no effect on hippocampal growth or on cortical development. It remains to be studied whether hydrocortisone has an effect on hippocampal function in these patients.

	+ hydrocortisone mean ± SD	Ø hydrocortisone mean ± SD	p-value (t-test)
Total hippocampal vol. (m+f)	5.809±0.81	5.816±0.78	0.97
Corrected vol. (cc)	5.831±0.86	5.816±0.62	0.94
Total hippo. vol. (f)	5.654±0.92	5.633±0.81	0.95
Corrected vol. (cc)	5.895±0.85	5.868±0.67	0.93
Total hippo vol. (m)	5.938±0.71	5.977±0.73	0.89
Corrected vol. (cc)	5.777±0.91	5.77±0.63	0.98
Left hippo. vol. (m+f)	2.78±0.4	2.795±0.41	0.89
Corrected vol. (cc)	2.802±0.54	2.795±0.36	0.96
Right hippo. vol. (m+f)	3.029±0.39	3.021±0.43	0.84
Corrected vol. (cc)	3.051±0.61	3.021±0.32	0.82

0393BRA

DIFFUSE OPTICAL BRAIN IMAGING OF FULL-TERM NEWBORN INFANTS

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Background: Diffuse optical imaging (DOI) is a new functional brain imaging modality, where near-infrared light is delivered into the tissue and the transmitted and reflected light are measured. Changes in the measured signals reflect changes in the optical properties of the tissue. Such changes are normally mainly related to the changes in the concentrations of the two main forms of hemoglobin ($[HbO_2]$ and [Hb]). Images of the hemodynamic changes in the tissue can be obtained by using several source and detector positions. In pediatrics, DOI has several benefits over other functional brain imaging modalities, such as the safety and the comfort of the patient, and suitability for bedside monitoring. **Objective:** Our aim was to develop methods for the use of DOI to study auditory short-term memory of newborn infants. **Subjects:** 12 healthy full-term newborn infants at 0.5–4 days of age. **Method:** A 4-channel frequency domain instrument, which uses optical fibers to deliver near-infrared light into the tissue and back to the detectors, was used in these measurements [1]. A special adaptable fiber-coupling helmet for newborn infants was developed to ensure a safe and comfortable interface between the instrument and the patient. Activation studies were done to measure hemodynamic responses to somatosensory (tickling of the left heel) and auditory (beeping sound at 1 kHz with 0.7 s ISI) stimuli. Two different experimental paradigms were used: the block design, and the event-related design. **Results:** In the measurements using the block paradigm, clear hemodynamic responses to somatosensory (3 μM change in $[HbO_2]$ and -0.7 μM change in [Hb]) and auditory stimuli (1.6 μM change in $[HbO_2]$ and -0.5 μM change in [Hb]) were found. The concentration changes are averages over the measured volume, and the changes in the cortex are thought to be significantly larger. Locations of the responses match the anatomical location for the somatosensory and auditory cortex. Movement artefacts were occasionally severe, which made analysis unsuccessful in the event-related measurements of hemodynamic response. **Conclusions:** We have shown that DOI can be used to successfully study brain functions of newborn infants. Although the block-style measurements were successful, more research is needed before we can achieve results from event-related measurements. There might be a possibility to use the event-related paradigm to measure the fast optical responses, which are directly related to the electrical activity of the neurons. However, measurement of the fast optical response is more challenging and needs a more carefully designed experimental paradigm than the measurement of the hemodynamic response. [1] I. Nissilä, K. Kotilahti, K. Fallström and T. Katila, Instrumentation for the accurate measurement of phase and amplitude in optical tomography, Rev. Sci. Instr. 73, 3306–12 (2002).

0401BRA

NEAR INFRARED SPETROSCOPY FOR INDUCED CEREBRAL OXYGENATION CHANGES BY TACTILE STIMULATION IN TERM NEONATES

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Background: The noninvasive assessment of the functional capacity and the progress of brain injury in neonates due to perinatal asphyxia, infection or other reasons remains a largely unsolved problem in neonatal medicine. Near-infrared spectrophotometry (NIRS) is an emerging technique which offers the possibility to assess reliably the changes in cerebral oxy- and deoxyhemoglobin (O_2Hb and HHb) concentrations associated with normal and pathologic processes. In the past NIRS has proven its usefulness as a noninvasive technique for continuous and repetitive bedside measurements of critically ill neonates. It appears to be well suited for the purpose of functional brain analysis. **Aim:** Our aim was to develop a NIRS instrument to detect images of slow regional changes in cerebral hemodynamics due to neural activity induced by a stimulus. **Methods:** The NIRS instrument consists of the measuring system, the stimulation unit and the sensors. The measuring system is running with uClinux (a Linux based embedded operating system). To allow a mapping of different brain regions more than 8 locations can be analyzed simultaneously. Efforts were taken to engineer the sensor, which is the most critical part for studies in neonates. The sensor uses LEDs and photodiodes, is soft and easy to attach to the head. Dedicated data channels carry the stimulation pattern from the stimulation unit which allows a precise correlation of the physiological signals with the stimulation patterns. The stimulation unit drives ultra-miniature vibration motors for tactile stimulation, which were attached to the left and right hand of a term neonates (after obtaining parental informed consent). 4 sensors were attached above the left somatosensory cortex. The left and the right hand were stimulated alternatingly for 20s. After each stimulation period, there was a period of 10s without stimulation. Stimulations were repeated up to a total measurement time of 10min. O_2Hb and HHb concentration changes were calculated from the optical changes in the tissue by established methods. By back projecting the changes in O_2Hb and HHb and color coding the concentrations we created images of the hemodynamic status of the brain. These can be displayed in real time as a video of functional activation in the neonatal brain and contain spatial information as well. **Results:** Sessions of up to 30 minutes were well tolerated. The application and removal of the sensor did not cause any distress and was quickly performed without waking up the infant. No sedation was necessary. A total of 15 measurements in 10 neonates were recorded. Separated localized functional activations were only visible in a few infants. In the other infants hemodynamic changes in O_2Hb and HHb due to slow vasomotion (autoregulation) were superimposed to the functional signal and larger in the amplitude. The slow vasomotion was not localized. **Conclusions:** Distinct local haemodynamic changes could be induced in healthy term newborns by tactile stimulation. These localized changes reflect spots of brain activity. Compared to adults the effect of slow vasomotion due to immature autoregulation is much larger in neonates. Algorithms to separate these two effects need to be developed.

0413BRA

INTEGRATION OF EXOGENOUS STEM CELLS INTO STRIATAL ORGANOTYPIC CULTURES

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Background/Aims: Neuronal stem cell transplantations have been shown to ameliorate a multitude of CNS pathologies and may have a potential therapeutic value in the future. To determine formation of neurons and functional neuronal networks in vitro during progressive stages of differentiation cells from the murine stem cell clone C17.2 were used. Initial cell characterization was done using calcium imaging and patch-clamp recordings followed by immunostaining for NeuN, GFAP, MAP2 and synaptotagmin. **Methods:** An organotypic model of the striatum was obtained by isolating 250 μm striatal slices from postnatal day 5 rat brains. Undifferentiated and differentiated stem cells were transplanted beside or on top of the slice 1, 3 or 7 days after establishment of the organotypic culture. Cultures were then grown for an additional 1–3 weeks before final characterization. Several independent criteria were used to identify stem cell derived cells as functional neurons. Utilizing Fluo-4 calcium imaging we examined spontaneous and induced calcium fluctuations. Voltage dependent calcium channel activity was demonstrated using application of 10–50 mM K^+, glutamate, NMDA and ATP. Whole cell patch clamp current/voltage recordings were performed to determine membrane properties and the cells were filled with Lucifer Yellow allowing subsequent immunostaining of recorded cells. **Results:** Results indicate that organotypic culture cells exhibit immunostaining, calcium fluctuations and membrane properties after 3–4 weeks in culture resembling acute slices. Transplanted C17.2 cells seem to survive, differentiate and integrate into the organotypic model system. **Conclusions**: The results support the use of this technique to characterize functional properties of stem cells and their integration into CNS tissue during different stages of development. We will present and discuss optimal conditions for differentiation, integration into and support of host tissue.

0447BRA

HEMATOPOETIC STEM CELLS AMELIORATE HYPOXIC ISCHEMIC BRAIN DAMEGE IN NEONATAL MICE

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Backgound/aims: Cerebral hypoxic ischemia (HI) of the newborn remains an important cause of cerebral palsy, epilepsy, mental retardation or death. The immature brain may provide a beneficial environment for transplants due to its pronounced plasticity. Nevertheless, few studies have examined strategies for repair in the immature brain. In a model of ischemic stroke in adult rats, it was shown that bone marrow cells ameliorated brain damage (Chen J et al. Stroke 2001) and furthermore that pharmacological mobilization of endogenous bone marrow cells leads to reduced infarction volume (Six I et al. Europ J of Pharm 2003). In the present study, we have studied the effect of mononuclear bone marrow cells (mBMC) and sorted hematopoietic stem cells (HSC) on hypoxic ischemic brain damage in immature mice evaluated with behavioural tests and morphology. **Methods:** Donors: Bone marrow cells (BMC) were harvested from the femur and tibia of transgenic mice carrying the gene enhanced green fluorescent protein (EGFP). Mononuclear cells were sorted by using Ficoll Hypaque density centrifugation and resuspended in PBS + 3% fetal calf sera (FCS). Hematopoetic stem cells (HSC) were further sorted by using c-kit (CD117) and sca-1 antibodies in a magnetic cell sorting (MAC) system. Recipients: HI was induced in 10-day-old C57 black 6 mice by exposure to 10% oxygen for 60 minutes after occlusion of the left common carotid artery. An intraperitoneal injection of 800000 mononuclear bone marrow cells (mBMC) or 5000 c-kit+sca-1+sorted hematopoetic stem cells (HSC) or vehicle (FBS+3%FCS) was given directly after HI. The resulting unilateral focal lesion was evaluated two weeks after HI with behavioral tests (beam-walking and rotarod) and with histopathological scoring. **Results:** The brain injury (morphological scoring) was reduced in animals that received c-kit+, sca1+ sorted HSC compared to controls ($p<0.05$). HSC-treated mice were also significantly less impaired in the beam walking ($p<0.05$) and rotarod test ($p<0.05$) than controls. Mononuclear BMC-treated mice did not differ from controls in any of the measured parameters. The donor-derived cells are currently being identified in different organs including the brain. **Conclusions:** These data suggest that administration of hematopoietic stem cells seems protective in neonatal hypoxic ischemic brain damage. The neuroprotective mechanism is unknown but might speculatively be explained by local secernation of survival-promoting factors.

0461BRA

RESUSCITATION WITH 100% O_2 IN HYPOXIC NEWBORN PIGLETS INCREASES CEREBRAL MMP-2 ACTIVITY

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Background: Matrix Metalloproteinases (MMPs) play a significant role in extracellular matrix remodelling. Birth asphyxia is defined as a severe disturbance of oxygen supply to the fetus, which develops during the first or second stage of labour. During resuscitation it is important to prevent cerebral damage but the mechanisms, which lead to cerebral damage, are not completely understood. **Objective**: To investigate MMP-2 and MMP-9 expression in hypoxic brain-damaged piglets, resuscitated with ambient air or 100% O_2. We tested the hypothesis that hypoxic newborn piglets can be equally successful resuscitated with ambient air as with 100% O_2. We also studied the effects of different pCO_2-levels during resuscitation. **Material and methods:** Newborn piglets (12–36 hours old) were made severely hypoxic by ventilation with a gas mixture of 8% O_2 in N_2, until mean arterial blood pressure (MABP) had fallen to 15mmHg or base excess (BE) ≤ -20mmol/l. The groups were normalised with respect to the number of animals, age, weight, haemoglobin and hypoxemia time. The piglets were randomly resuscitated by ventilation with ambient air (n=30) or 100% O_2 (n=30). pCO_2 during resuscitation was kept low, normal or high. The piglets were resuscitated for 30 minutes and thereafter observed for 150 minutes, while they were normoventilated with ambient air. At the end of the experiment, brain tissue from corpus striatum was immediately frozen with liquid nitrogen and stored at -70°C. MMP-2 activity was analysed by gelatine zymography, and the results were calculated using one normal control sample not included in the study as equal to 1, as well as using an internal standard on every zymography gel. All values are given as mean (±SEM). **Results:** MMP-2 activity was twice as high in brain tissue from resuscitated animals as compared to controls (0,58±0,09 and 11±0,06, respectively, p=0,006). Furthermore, brain MMP-2 activity was significant higher (p=0,001) in piglets resuscitated with 100% O_2 (1,34±0,08) compared to piglets resuscitated with ambient air (0,88±0,05). The CO_2 level did, however, not influence MMP-2 activity. MMP-9 activity could not be detected by gelatine zymography. Haemodynamic parameters (MABP, HR) and blood gases (pH, BE, pO2, pCO2) were normalised in all groups at the end of the experiment, but no other significant differences between the groups were found. **Conclusion:** Resuscitation with 100% O_2 induces higher cerebral MMP-2 activity than resuscitation with ambient air in this global hypoxic piglet model. pCO_2 levels during resuscitation had no influence on MMP-2 activity.

0462BRA

MR ASSESMENT OF ISCHEMIA IN A PIGLET MODEL

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Background/Aims: MR perfusion and diffusion imaging have proved to be sensitive tools for early detection of brain injury and to monitor interventions aimed at minimizing or preventing irreversible brain injury (1,2).The purpose of the current study was to assess the utility of functional and structural MRI to assess the functional extent of brain injury in a hypoxia/ischemia model in piglets. A secondary aim was to use MRI to validate that the desired ischemic injury was successfully induced. **Methods:** MR imaging was performed at 1.5 T (Siemens Vision, Siemens Medical, Erlangen, Germany) in piglets (n=10; age 12– 36 hours) under general anaesthesia. Hypoxia was induced by ventilation of a gas mixture containing 8% O_2 in N_2 (AGA, Oslo, Norway). Ischemia was induced by bilateral clamping of the common carotid arteries (CCA). Relative cerebral flow (rCF) was estimated using a single shot SE-EPI sequence (TE = 85 ms, voxel size 1x1x5 mm^3), measuring the first-pass response following bolus injection of an intravascular iron oxide nanoparticulate contrast agent (NC100150 Injection, Amersham Health, Oslo, Norway) at a dose of 4.5 mg Fe/kg. rBF maps were generated on a pixel-by-pixel basis from the peak height of a gamma-variate function fitted to the first-pass contrast agent response. The presence of total carotid occlusion was assessed by MR angiography (MRA) and phase contrast angiography (PCA). MRA images (3D-GRE, TR/TE 4.4 ms /1.8 ms, voxel size 0.9 x 0.9x1.5 mm^3) were acquired after contrast administration; utilising the T1-effect of NC100150 Injection. PCA images were generated in a single slice at the level just proximal to the rete mirabile (V_{enc} = 45 cm/s; voxel size 0.8 x 0.8 x 10 mm^3). Apparent diffusion coefficient (ADC) maps were generated using a single shot SE-EPI sequence (TE=103 ms, voxel size=0.8x0.8x3 mm^3) with b-values of 0 and 1000 s/mm^2 applied in three orthogonal directions. Perfusion, diffusion , MRA and PCA acquisitions were performed pre HI, during HI and post HI at 30 min and 2.5 hrs. **Results:** The combination of morphological and functional images enabled consistent assessment of both the presence of absence of complete occlusion as well as the functional significance of the occlusion. In animals with successful bilateral clamping, the ADC was significantly reduced during ischemia compared to baseline values (p=0.01). The ADC mean ± SD was 1.0 ± 0.09 x 10^{-3} mm^2/s and 0.78±0.14 x 10^{-3} mm^2/s at baseline and during HI, respectively. Fig. 5 shows the evolution of mean ADC during the experimental observation period. Post HI, the mean ADC increased slightly compared but did not return to baseline values during the 2.5 hrs of observation (p=0.03). **Conclusions:** We have developed a pig model to assess the effect of HI in newborn pigs using diffusion and perfusion MRI in combination with PCA and contrast enhanced MRA. Using an intravascular contrast agent, both perfusion and MRA can be assessed following a single contrast agent administration; providing a comprehensive tool for both a morphological and functional assessment of ischemia and hypoxia.

0014EPI

DOES PREDOMINANT RATHER THAN EXCLUSIVE BREASTFEEDING AT BIRTH SHORTEN THE DURATION OF BREASTFEEDING?

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Background: It is unknown whether predominant, rather than exclusive, breastfeeding (according to WHO definitions) at the maternity ward may influence the duration of breastfeeding. **Methods:** To describe reasons for the babies are predominantly breastfed during the first 48 h after birth, and to examine whether any difference in the duration of breastfeeding exists between infants exclusively or predominantly breastfed at birth, a one-year longitudinal telephone survey has been conducted, 1999 to 2000, on a total of 2450 healthy, term infants randomly recruited among singleton newborns occurred in Italy, November 1999. Main outcome measure was the percentage of breastfed infants through the first year of life using WHO criteria for breastfeeding. **Results:** The national rate of initiation of breastfeeding within the first 48 h after birth ("at birth") was 91.1% (95% confidence interval, CI, 90.0–92.2%). Breastfeeding at birth was exclusive in 38.7% (36.8–40.6%) and predominant in 28.9% (27.1–30.7%) of babies. The main reasons for predominant breastfeeding at birth were "persistent crying" (35.9%, 32.4–39.4%) and "customary routine at maternity ward" (29.0%, 25.6–32.3%). At birth, 28.0% (24.7–31.3%) babies were given fluids due to clinical problems of baby and/or mother. No difference was found in the duration of breastfeeding between infants exclusively or predominantly breastfed at birth (mean [median] of 5.6 [6] months vs. 5.3 [6]), independently of reason for predominant breastfeeding. **Conclusions:** Predominant, rather than exclusive, breastfeeding at birth may not negatively influence the duration of breastfeeding in industrialized countries. Unwarranted predominant breastfeeding is currently supplied to many babies at the maternity wards.

0152EPI

ORAL HEALTH IN YOUNG ITALIAN DOWN PATIENTS.

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Objective: The aim of this study has been to evaluate the oral health status in patients suffering from Down's Syndrome living both within their families and institutionalized structures. **Methods:** Among the recruited patients, in total 160 subjects aged between 20 and 24, 83 were taking part to the Olympic Games in Caorle (June 2002). DMFT (D=decayed, M=missed, F=filled, T=teeth) and CPITN (C=community, P=periodontal, I=index, T=treatment, N=needs) have been used as epidemiological parameters in conformity with the World Health Organization standards. **Results:** The index of caries experience has resulted to be DMFT=6,67 (D=3,00; M=0,99; F=2,68). The periodontal conditions examination has evidenced the following CPTIN values: healthy=26,69%, gingival bleeding=1,50%, calculus=41,35%, 4–5mm periodontal pockets=13,90%, deep periodontal pockets=3,00%, excluded patients for edentulism=13,56%. Sextants: healthy=3.01, gingival bleeding=0,13, calculus=1,58, 4–5mm pockets=0,28, deep pockets=0,03, excluded sextants for edentulism=0,97. During odontoiatric visits, a presence of dental agenesia has been diagnosed with an incidence of 15,90% concerning the whole dentition in the following percentage: frontal incisors=8%, lateral incisors=52%, canines=12%, first premolars=4%, second premolars=16%, first molars=0%, second molars=8%. Moreover, the presence of soft oral pathologies has been observed, in particular fissured tongue and macroglossia (39,70% and 19,20% incidence, respectively). Data relative to epidemiologic indexes DMFT and CPITN of the patients suffering from Down's Syndrome have been compared with the same indexes of a group of military recruits. This comparison shows that there are differences in the values of DMFT (DMFT Down subjects=6,67; military recruits=5,23) and CPITN. These disparities are caused by a low oral hygiene level in the Down patients. **Conclusions:** it is essential for Down Patients to receive regular odontoiatric cares and suitable instructions in order to maintain an adequate level of oral hygiene since a childish age. Furthermore, it would be appropriate to combine it a correct fluorine prophylaxis, in order to avoid the beginning of dental caries.

0156EPI

ORAL HEALTH IN 12 YEARS OLD ITALIAN POPULATION .

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Background: Since 1978 the aim of the Milan WHO's Cooperation Institute has been to evaluate the oral health status in 12 years old patients living within their home territory, to monitor teenager dental-periodontal condition and to program suitable oral-hygiene instructions within Italian school system. **Methods:** DMFT (D=decayed, M=missed, F=filled, T=teeth) and CPITN (C=community, P=periodontal, I=index, T=treatment, N=needs) have been used as prevailing index of oral-periodontal pathologies in conformity with World Health Organization standards. In consulting medical rooms junior high-school teenagers were subjected to a close inspection realized by properly trained personnel. **Results:** DMFT and CPITN survey differ absolutely from the years depending on where indexes were evidenced. 1978 DMFT particularly resulted to be 6,9 where index of caries evidenced 5,7 while an incidence of 0,51% of examined subjects were gingival healthy. **Conclusion:** Collected data showed years after years a DMFT gradual level decrease particularly concerning caries in twelve years old Italian people. Therefore it has resulted in a considerable improvement of periodontal health conditions, and the incidence of patients having no need of suitable odontoiatric cares exceeded 14%. These achievements are confirming the oral health status improvement in 12 years old Italian teenagers from 1978 to present days. Preventive information, as well as prophylaxis of oral periodontal pathologies developed and pursued during the last few years, have been essential to get these results.

0158EPI

NEONATAL SERVICES' ACTIVITY AND IN-HOSPITAL MORTALITY OF VLBWI IN ITALY

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Background/aims: The number and outcome of newborn infants with birthweight <1500 g (very low birthweight infants, VLBWI) are the best synthetic indicators of activity levels and quality of care in neonatal intensive care services. In Italy striking differences in health services delivery and outcome exist among geographical areas, including a persisting north-south gradient in infant mortality. We performed the present national investigation in order to: 1) know the number of VLBWI admitted to any single neonatal service in 2001, separately by inborn/outborn status and birthweight classes; 2) calculate in-hospital mortality by inborn/outborn status and birthweight; and 3) evaluate possible differences among geographical areas. **Methods:** All the regional sections of the Italian Society of Neonatology were asked to fill in a special questionnaire with the following data about VLBWI admitted during 2001 to any single neonatal units in each region: number, inborn/outborn status and death before discharge, separately by birthweight classes of 250 g. Malformed infants were included. The medians and interquartile ranges (ir) of the number of subjects admitted to each unit, the frequency of inborn infants, and in-hospital mortality rate for all VLBWI and by birthweight classes were calculated; the analysis was performed for the whole country and for each geographical area (northern, NR, central, CR, and southern, SR, regions). **Results:** A total of 125 units and 4679 infants were surveyed. Since 531880 babies were born in Italy in 2001, the estimated VLBWI rate was 0.88%, and that of infants <1000 g was 0.33%. The median number of subjects admitted to each unit was 34 (ir 16–52). The medians were 29 in the NR, 34 in the CR and 36 in the SR; the differences were not statistically significant (p=0.49). The inborn rate was 80.7%, with a north-south decreasing trend: 86.5% in NR, 83.8% in CR and 74.6% in SR. No difference in the inborn rate was found among the birthweight classes, both at national level and in the three geographical areas. Nine hundred and nineteen infants died before discharge (19.64%). Mortality was 59.95%, 25.34%, 9.62% and 5.52% respectively in the birthweight classes <750 g, 750–999 g, 1000–1249 g and 1250–1499 g. The risk of death was higher for outborn than inborn babies (23.17% vs 18.80%; rate ratio 1.23); this difference was common to all birthweight classes. Death rates were 14.54% in NR, 19.89% in CR, and 23.45% in SR; this trend was mainly explained by a north-south increasing mortality among inborn babies, while in outborn infants nearly no difference was evident. No variations in crude death rates in the three geographical areas were found after adjustment for birthweight distribution and inborn/outborn status by means of direct standardization. **Conclusions:** This is the first national-based epidemiological study performed in Italy on VLBWI, which specifically investigated and analysed the patient volume in neonatal units, the inborn/outborn status and in-hospital mortality by birthweight classes and geographical areas. It demonstrated a too wide variation in patient volumes, with one quarter of units admitting less than 16 VLBWI per year, and a still important gradient in mortality between southern and northern regions (rate ratio 1.6). These findings probably reflect not only the known social deprivation in the south compared to the north but also different models of organization and quality of neonatal/perinatal care among geographical areas.

0159EPI

CONGENITAL CYTOMEGALOVIRUS SCREENING: FIRST RESULTS

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Background: Cytomegalovirus(CMV) is considered the first cause of congenital infection in developed countries. The estimated incidence is 0.2–2.5%. Five to 15% of infected babies are symptomatic in neonatal period and 30–60% develop sequelae such as hearing loss, neuromuscular defects, chorioretinitis, microcephalia and mental retardation. Therefore many congenital CMV infections are neither diagnosed nor eventually treated, although they are related with long term sequelae. The aims of this study was to enhance knowledge on incidence, morbidity, mortality and sequelae of congenital CMV infection. **Methods:** Between May-August 2002, 757 consecutive newborns were screened for CMV congenital infection. The laboratory diagnosis was performed by both Polymerase Chain Reaction (PCR) and isolation of CMV and *shell-via* from urine, during the first days of life. In 653 cases cord blood was available and PCR was also performed. Maternal data and information concerning neonatal outcomes were recorded. Follow up at 3 and 6 months included neurologic, audiologic, ophthalmologic and development assessment. **Results:** Congenital CMV infection was diagnosed in 5 out of 757 (0.7%) cases by virus culture in urine. PCR in cord blood was negative in all cases. All infants were asymptomatic at birth. Two newborns showed symptoms of congenital CMV infection within the first 3 weeks of life: pneumonia (1); bone marrow failure (1); hepatitis (1); basal ganglia vasculitis (2). At 6 months, all infected infants had a normal development, neurologic and ophthalmologic assessment. **Conclusions:** The rate of CMV congenital infection was 0.7%. Symptomatic newborns ratio was 2/5 (40%). We didn't detect viral genome by PCR in cord blood and CMV diagnosis from urine was a reliable method. Although normal 6 months assessment, these five asymptomatic babies need a long period follow up, to detect sequelae. Funded by Science and Technology Foundation

0163EPI

A NEW DIAGNOSIS RELATED GROUP (DRG) CLASSIFICATION FOR NEWBORN INFANTS.

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Background: The HCFA-DRGs classification is used in many Countries including Italy. The purpose of the HCFA-DRG system is to classify in-hospital patients into homogeneous categories with similar utilization of resources, thus providing a guide for appropriate reimboursement.In the current classification, one Major Diagnostic Category (MDC-15) is dedicated to diseases of the perinatal period, grouped into 7 DRGs. This classification does not adequately represent the neonatal case-mix, which is highly heterogeneous within each DRG in terms of length of hospital stay (LOS),case-mix complexity (CMC) and costs. Aims. The aim of our study was to costruct a new and more reliable classification system which could describe the neonatal case-mix appropriately. **Methods:** A group of experts (Authors),based on their clinical experience and on data from the neonatal case-mix of the Lazio Region,devised a new algorithm.This new classification was then tested in two neonatal populations: 1) Retrospectively, in all infants discharged from all Italian Hospitals in the year 2000 (Source,Italian Ministry of Health; N°= 526.005 infants); 2) Prospectively,in infants discharged from16 Italian Hospitals during the study period (N°=2.674).In both groups individual LOS were registred and, in the second group, data on CMC and costs were also collected. The performances of the old (HCFA-DRG 10th edition) and the new classification were evaluated and compared by the R^2 statistics ,which measures the fraction (R^2) of the variance in LOS, CMC and costs that can be explained by the system. **Results:** Only the results from the "inlayer" case-mix (i.e. with a LOS > 2 days and < threshold value) are reported.The performance of the new classification was significantly better than the old one for both LOS (R^2=0.64 vs 0.47; Δ=+36%) and costs (R^2=0.63 vs 0.45; Δ=+40%). This improved performance was confirmed when the comparison was made with the 19th revision of the HCFA-DRGs (ΔR^2 +23.3% for LOS and +31.3% for costs). **Conclusions:** The new classification criteria include: age (< 29 d.) birth weight (5 classes), some complex procedures (such as: mechanical ventilation, peritoneal dyalisis, etc.) surgical interventions, cardiac surgery, associated pathologies or complications, and type of discharge (alive/dead/transferred),without increasing too much the number of DRGs (from7 to 18).It is significantly more efficient than the current HCFA-DRG system and needs to be tested in other socio-economic and sanitary contexts, different from the Italian one. (Supported by Grants N° 9901068 and 02Q000123 from the Italian Ministry of Health)

0179EPI

QUALITY OF NEONATAL CARE AND SURVIVAL AT 27–28 WEEKS GESTATION IN UK

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Aim: To identify variations in standards of neonatal care in the first week of life that might contribute to deaths in preterm infants born at 27 to 28 weeks gestation and from these to make recommendations for future practice. **Methods:** Design: Case control study. Cases: 366 neonatal deaths < 28 days occurring in England, Wales and Northern Ireland in the period 1st of September 1998 to 31st of August 2000. Controls: 395 controls randomly selected from the group who survived beyond 28 days during the same period. Exposure: departure from standards of care or deficiencies in neonatal care in the first week of life assessed by regional panels from anonymised medical records. Standards for Enquiry: based on pre-established clinical standards and expert opinion of best practice. Measure of effect: odds ratio (OR) crude and adjusted* for gender, birth weight ≤ 5th centile and severity of illness of the baby shortly after birth. **Results:** Standards of care: resuscitation standards were often met in the same proportion of babies who died and survived, but timely attendance of full complement of skilled staff was not achieved in 45% of all deliveries. Temperature < 36^0C on admission was more frequent in babies who died (73%) than in those who survived (59%), OR*: 1.71 (1.21–2.43). Most intubated babies received surfactant (96%) but delays in administration were frequent (40%) and equally distributed. Efforts to achieve standard of ventilatory support were poorer amongst babies who died (18%) than in those who survived (7%), OR*: 3.29 (1.97–5.49). The same pattern was found for cardiovascular support standard: 15% versus 7%, OR*: 2.37 (1.36–4.13). **Deficiencies in care:** Panels identified more deficiencies in babies who died in all aspect of neonatal care except the management of infection. Main areas for concern were: intubations skills; delay in surfactant administration, poor management of temperature control, ventilation technique, volume expansion, inotropic support, ex utero transfers; staffing levels and lack of senior support. Overall substandard care likely to have contributed to death, were more frequent amongst babies who died (28%) than in those who survived (6%). Stratification by poor condition of babies at birth showed a higher risk of dying of major substandard care when babies were born in good condition OR* 11.53 (6.21–21.41) than if babies were poorly at birth OR*: 6.04 (1.68–21.77). **Conclusion:** Our data suggests a strong association between quality of neonatal care and neonatal deaths. Poor quality of care may have more effect on neonatal deaths if baby is in good condition at birth. Implementation of neonatal recommendations at local hospitals, national and commissioning levels based on these findings may improve the survival of premature babies born at 27–28 weeks gestation.

0216EPI

COMPARISON OF THE EFFICACY OF HEPATITIS B VACCINATION BETWEEN NORMAL AND LOW BIRTH WEIGHT NEONATES

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Backgroud and objective: Hepatitis B Vaccination is one of the most effective methods to prevent and control of the disease. Concerning its importance in children and intervention of variable factors in vaccine efficacy , we carried out a study to compare the production of AntiHBS after routine vaccination in low birthweight and normal birth weight infants in our country. **Material and Method:** This case- control study performed on 120 children less than seven years old who were referred to Amirkola children hospital during 2000–2001. They had recieved three doses of hepatitis B vaccine(at birth, at 1.5 month and at 9 month of life) .We divided them in to 2 groups: Low birth weight or ≤ 2500gr (group A) and normal range of weight;more than 2500 grams at birth (group B). We checked HBSAb and HbcAb in blood by ELISA method and Radim kit. Data collected and analyzed by T-test, fisher exact test and chi-square test. P value less than 0.05 was significant. **Results:** In this study, the children were divided in two groups: There was 40 cases in group A (25=male , 15=female) and 80 cases in group B (43=male, 35=female). Two children of group B were excluded. Mean age of children in group A and B were 35.5 months (Std. Error mean= 3.58) and 33.6 months (Std. Error mean=2.32) respectively (p=0.64). In group A, 36 cases (90%) had protective levels of AntiHBS(more than 10mIu/ml) and in 4 cases (10%) AntiHBS levels were lessthan protective level. The protective levels of AntiHBS had been produced in all of the children in group B (p=0.012). Between protective levels of AntiHBS in group A (90%) and ideal response in children (95%) was not significant difference (p=0.015). The mean of AntiHBS levels in group A was 182.07mIu/mL (Std Error mean=45.9) and in group B was 334.73mIu/mL (Std Error mean=41.4). **Conclusion:** Although the mean level of anti- HBS in the lowbirth weight infants is less than the normal birth weight infants but between this response in LBW(90%) and ideal response in children(95%)there is not significan difference. Therefore we advise to continue routine vaccination in LBW and normal birth weight infants similarly. Key word : vaccination, hepatitis, HBS Antigen.

0305EPI

ASSESSING VERY LOW BIRTH WEIGHT INFANTS MORTALITY USING CART TREES

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Background/Aims: Classification and Regression Trees (CART) are tree-structured classifiers built so as to minimize misclassifications. They also estimate the probability associated with an outcome. Thus, they would be an ideal technique to predict risk of death. Our aim was to test the performance of CART trees in assessing mortality in VLBWI (<1500 g) and to compare the results with those achieved by means of Clinical Risk Index for Babies (CRIB) score and logistic models. **Methods:** Data relative to 1809 VLBWI assisted in 12 neonatal Intensive Care Units in Lombardy (Northern Italy) from 1999–2002, and participating in a regional network (www.ospedalevirtuale.it/nnl), were analysed. Outcome was in-hospital death. CRIB was computed by adding the coded values of 6 variables: gestational age (GA), birth weight (BW), highest and lowest FiO2 and worst base excess during the first 12 hours of life, and severity of congenital malformations. Higher CRIB scores correspond to higher mortality risk. Logistic models and CART trees were fitted to the same set of variables, and their performance was compared by computing percentage of dead infants correctly classified (sensitivity), percentage of alive infants correctly classified (specificity), and total percentage of misclassified infants. **Results:** Mean BW and GA of the sample was 1093 g and 29.2 w, respectively. There were 259 deaths (14.3% of the sample). Median CRIB score was 1 in survivors, and 10 in non-survivors. The ROC curve area for CRIB was 0.908. The table shows the results obtained by using logistic models and CART trees with the following sets of variables: 1) variables used to compute the CRIB score, all coded ; 2) as in set 1, but GA and BW are used with their actual values, to evaluate whether codifying them produced an important loss of information; 3) as in set 2, plus other variables that influence VLBWI survival (Apgar score at 1 and 5 min, type of delivery, multiple gestation and antenatal steroid prophylaxis). In the table Sensitivity (Se), specificity (Sp), and total misclassifications (Miscl) are shown as percentages.

	Set 1			Set 2			Set 3		
	Se	Sp	Miscl	Se	Sp	Miscl	Se	Sp	Miscl
Logistic	57	97	8.7	58	97	8.7	61	97	7.8
CART	52	98	8.8	68	98	6.8	72	97	6.2

Conclusions: All models have very high specificity, but a lower sensitivity. In more complex situations (sets 2 and 3), the results obtained by using CART trees are remarkably better than those of the logistic models, probably because they make powerful use of conditional information. Moreover, CART trees provide a very clear characterization of the conditions which drive the classification process, so that they can be very useful to understand the factors that contribute most to increase the risk of mortality. Finally CART trees handle very easily the presence of missing values. In conclusion, for the aim of classifying cases, CART trees appear to be superior to logistic models.

0410EPI

POPULATION-BASED STUDY OF CHRONIC LUNG DISEASE INCIDENCE AND RISK FACTORS IN VERY LOW BIRTH WEIGHT INFANTS

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Objective: To assess the pulmonary outcomes of very low birth weight (VLBW) infants in Switzerland in 1996 and 2000 and to identify risk factors in chronic lung disease. **Methods:** Data were collected prospectively by collaborators from all 10 neonatal intensive care units in Switzerland to determine survival and pulmonary outcomes of infants with birth weights ranging from 500 to 1500 g. CLD was defined as oxygen dependency at 36 weeks' postmenstrual age. **Results:** Outcome data were available for 555 VLBW infants in 1996 and 603 in 2000 respectively. The overall rate of CLD at 36 weeks PMA was 16.5 % in 1996 and 13.4 % in 2000 as percent of infants hospitalized at 36 weeks PMA. Children with surfactant treatment had a significantly higher rate of CLD in both cohorts tested whereas the well known links between CLD and infection proven by positive blood culture, or between CLD and Patent ductus arteriosus (PDA) or mode of respiratory support (mechanical ventilation versus Nasal continuous airway pressure - NCPAP) could not be upheld. In 1996, postnatal transport may have been an additional risk factor and in 2000 there were significantly more male infants with CLD than female. Multivariate logistic regression could not alter this impression. **Conclusion:** For both years, the incidence of CLD is lower in Switzerland than listed in the comparable prospective studies by the Vermont Oxford Network. Surfactant could be confirmed as risk factor whereas infection, PDA and choice of ventilation strategy could not. Postnatal transport and gender may also have an effect on pulmonary outcome.

0423EPI

ASTHMA AMONG GREEK CHILDREN FROM BIRTH TO 18 YEARS OLD. A LONGITUDINAL STUDY.

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1st Department of Pediatrics, Athens University City: Arhens, Greece The recent increase in the incidence of asthma in industrialized countries has stimulated research related to the triggering factors as well as to the natural course of the disease throughout childhood.

Aim: To identify the overall incidence and the clinical course of asthma from birth up to the age 18 years in Greece. **Methods-Population:** Representative birth cohort consisted of 2,139 children born throughout Greece during April 1983 were followed up by self-completed questionnaires at the age of seven and eighteen years. **Results:** Asthma symptoms confirmed by a physician and needed treatment were reported by 24% of the cohort at least once during their life. Boys were more susceptible than girls ($p=0.02$). One out of two from these children were free from symptoms at the age of seven years and almost one out of four (24%) between the age of seven and eighteen years. In 16% of children symptoms appeared between seven and eighteen years of age. Asthma has been present during the entire study period in 12% of the affected children (2,7% of the total cohort). From all environmental and hereditary factors a statistical significant positive association was found between child's asthma and history of atopic disease in the family. Great variations were detected among the various regions of the country, which may indicate different environmental influences. **Conclusions:** The above findings illustrate over the time the size of the problem among the Greek children and adolescents, information which can be obtained only from longitudinal studies.

0440EPI

ON THE ANTIBODY AGAINST CHLAMYDIA PNEUMONIA AMONG PATIENTS SUFFERING FROM PROLONGED COUGH-AN OBSERVATION FROM A PEDIATRIC-INTERNAL PRACTITIONER-

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Background: 2001 to October 2002, 141 patients suffering from prolonged cough visited our clinic. The age distribution ranged from 0 to 90 years with an average of 29.6 years. 154 samples from those patients were used to measure their antibodies against Chlamydia Pneumonia titers. Additionally, the antibody titers against Mycoplasama Pneumonia, Chlamydia Psitaci titers, and the cold agglutination test were tested in order to examine relations with other resembling infectious diseases. **Methods & Results:** In our small clinic where most patients suffer less severe illness in comparison with a large hospital Chlamydia Pneumonia antibodies were detected from many patients. 26% of Chlamydia Pneumonia antibody positive patients showed only positive Chlamydia Pneumonia antibody and no positive results of Mycoplasama Pneumonia, Chlamydia Psitaci titers, and the cold agglutination. The male and female ratio of Chlamydia Pneumonia antibody positive patients was 40:47. A seasonal deviation among Chlamydia Pneumonia antibody positive patients was noticed. Many Chlamydia Pneumonia antibody positive patients were found in January, February, and September while fewer cases occurred in November and December. **Conclusion:** Previous reports stated that patients below the age of 15 years with Chlamydia Pneumonia antibodies positive are less common. The findings of our sample suggest the necessity to consider the possibility of Chlamydia Pneumonia when approaching patients belonging to that age group.

0302HAE

INFLAMMATION POTENTIATES HYPOXIA-INDUCIBLE FACTOR 1 PROTEIN EXPRESSION UNDER HYPOXIC CONDITIONS

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Background: Hypoxia-inducible factor 1 (HIF-1) regulates the transcription of genes whose products are involved in erythropoiesis, angiogenesis, cell proliferation and migration. Most of these conditions are also involved in inflammation. HIF-1 alpha protein steadily increases in cells when exposed to hypoxia, but decays rapidly upon reoxygenation. We investigated whether the subsequent exposure of human lymphocyts and monocyts under hypoxia to the inflammatory stimulus and protein kinase C activator phorbol-myristate-acetate (PMA) influenced the HIF-1 alpha protein expression. **Measurements:** HIF-1 alpha protein expression was detected in 60 μg cellular protein extracts with Western blotting technique using a monoclonal HIF-1 alpha antibody. **Results:** HIF-1 alpha protein was increased by at least one order of magnitude in lymphocyte-monocyte populations after 6 hours of simultaneus exposure to hypoxia and 50 ng/ml PMA as compared to normoxic controls with or without PMA. A similar effect was seen in cells exposed to PMA and hypoxia for 6 hours after a prior 24-hour period of normoxia. The PMA effect was partially blocked by 1 μM Wortmannin, a specific phosphatidylinositol 3-Kinase inhibitor. **Conclusions:** Protein kinase C activation synergizes with Hypoxia in stabilizing HIF-1 alpha. This provides a mechanism for inflammation-triggered augmentation of hypoxia-induced gene transcription.

0339HAE

ELECTIVE TRANSFUSION LEADS TO AN INCREASE IN FUNCTIONAL CAPILLARY DENSITY IN THE SKIN OF PRETERM INFANTS

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Background/Aims: Direct studies of the microcirculation at the levels of the skin capillaries may provide information on how oxygen is delivered to tissue. Orthogonal polarization spectral imaging (OPS) enables non invasively direct observation of changes in microvascular perfusion. **Methods:** OPS was applied to the upper arm of 13 preterm anemic infants before and after transfusion (Tx). Off –line quantitative data of microvascular perfusion were obtained by measuring functional capillary density (FCD), vessel diameter, RBC velocity and flow. Data are presented as median and 95% CI and analyzed using ANOVA with a post hoc test for linear trend, followed by paired Student t-Test for parametric data. Clinical data such as heart rate, blood pressure, body and incubator temperature were recorded simultaneously. **Results:** The 13 infants (median [95% CI]: gestational age of 26 [25–26] weeks; birth weight 730 [652 – 789] g) were transfused with 10 [9,3 – 14,2] mL RBC/kg at age 30 [19 - 39] days and current weight of 1075 [897 – 1338] g. We found a significant increase in FCD 2hrs after transfusion with an additional significant rise after 24 hrs, thus indicating improved microvascular perfusion. Vessel diameter, RBC velocity and flow did not change significantly (Table 1). There were no significant changes in clinical variables, such as blood pressure, heart rate or body temperature.

	Diameter[µm]	RBC vel[µm/s]	Flow [µm²/s]	FCD[cm/cm²]
prior	10,78 (9,7 – 11,2)	349 (336 – 402)	29 392 (26 625 – 37 616)	14,2 (13,4 – 15,5)
2 hrs	10,1 (9,4 – 10,7)	343 (316 – 378)	27 797 (24 228 – 31 366)	18,5*(16,6 – 19,6)
24 hrs	10,3 (9,2 – 11,3)	371 (323 – 392)	30 425 (24 506 – 36 343)	20,6*# (18,5 – 21,9)

*2 hrs and 24 hrs post Tx compared to prior to Tx ($p < 0.001$); # 24 hrs post Tx to comapred 2 hrs post Tx ($p < 0.001$)

Conclusion: Whereas conventional monitoring methods did not show any changes after transfusion quantitative analyses of OPS images indicated improved perfusion, hence it seems a useful monitor for assessing the response to therapies aimed to improve tissue perfusion.

0050NUT

DIETARY HABITS AND SERUM FATTY ACIDS IN NORMAL AND OVERWEIGHT CHILDREN.

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Aim: To investigate the associations between dietary habits and the serum pattern of fatty acids (FA) in a school-age population and to look at the associations between dietary habits and the pattern of serum FA levels in overweight children. **Subjects and methods:** In 105 healthy 8-years old children out of a population of 171 infants enrolled at birth the nutritional habits have been evaluated by means of a Food Frequency Questionnaire and a 24-hr recall. FA analysis was performed by capillary gas-chromatography. Children with Body Mass Index (BMI) beyond the 85th percentile within the group were defined overweight. Statistics: non-parametric tests. **Results:** The most favourable fatty acid patterns were associated with high consumption of pasta and low intake of red meats. A high (n = 16) vs medium (n=71) or low (n = 18) consumption of pasta was associated with lower serum levels of C18:0 and higher levels of C20:5n-3, C22:6n-3 and total polyunsaturated FA. A low (n=31) vs medium (n=48) or high (n=26) meat consumption was associated with lower serum levels of total saturated FA and higher levels of monounsaturated FA. The children with high pasta and low meat consumption (n=9) compared with the others (n=96) showed lower levels of total saturated (29, SD 4, vs 35, SD 2) and higher levels of total monounsaturated (31, SD 6, vs 24, SD 4) FA in serum (P= 0.001 and P=0.04, respectively). Sixteen children were overweight (BMI 19.2 to 25.6) compared to the other 89 (BMI 12.4 to 18.9). No differences in macronutrient intakes and FA levels were found between the two groups. Anyway, the ratio between the two major long-chain polyunsaturated (LCP) FA (C22:6n-3/C20:4n-6) was lower in overweight (0.20, SD 0.04) vs non-overweight (0.29, SD 0.32) children (P = 0.02). **Conclusions:** Our data suggest that a high consumption of pasta coupled with a low intake of meat may be marker of a more favourable pattern of circulating FA. Moreover, a trend towards a decrease of n-3 LCP vs higher levels of n-6 LCP may be an early marker of changing insulin sensitivity in overweight children.

0079NUT

CHRONIC INTESTINAL PSEUDO-OBTRUCTION ASSOCIATED WITH GLUTARIC ACIDURIA TYPE 1

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Background: Chronic intestinal pseudo-obstruction (CIPO) is a rare clinical syndrom characterized by recurrent episodes of intestinal obstruction in the absence of a mechanically obstructing lesion. Vomiting, abdominal pain and distension, constipation and loose stools are common. Gastrointestinal motility disorders result from disturbances of gut motor activity, produced by disease involving enteric nerves and muscle and altered central nervous system input. Both congenital and acquired diseases may produce these pathogenetic mechanisms. We found a CIPO associated with glutaric aciduria type 1 (GA-1). GA-1 is an inborn error of metabolism caused by a deficiency of the mitochondrial enzyme glutaryl-Co enzyme A dehydrogenase. A hipercaloric and relatively hypoproteic diet with controlled amount of lisina and triptofano is necessary to maintain the metabolic balance. **Clinical data.** R.F. was born at 41° weeks of gestation. Auxologic parameters were normal. He suffered a neonatal distress and needed oral intubation and 30' ventilation. The patient developped in the next hours hypertonia and seizures and was administered sedative and antiepileptic drugs in large dose. Magnetic resonance imaging findings revealed signs of anoxia in lateral talamus and globus pallidus. Analysis showed raised plasmatic levels of glutaric acid and lisina. The diagnosis of GA-1 was confirmed by enzimatic and molecular tests and appropriate diet was administered. The next months have been marked by frequent vomiting. At 6 months we performed a gastrotomy to ameliorate nutrition, but vomiting persited and total parenteral nutrition was needed. He remained with diarrhoea in the first months, turned constipated, with evident abdominal distension and crisis of pain. We didn't find evidence of intestinal obstruction at abdomen Rx. The patient is now 2 years old and is always hospitalized. A complete paralysis is present. Total parental nutrition allows normal growth and good metabolic compensation. Venting gastrotomy alleviates but don't eliminate vomiting and abdominal distension. Constipation is present. In a periodic rewiew of the case we found that the situation fulfills the conditions for diagnosis of CIPO (JPNG 1997; 24:102). We are planning further investigations to confirmate CIPO: a manometric registration, a radiosopic transit, a full thickness intestinal biopsy. **Conclusions:** GA-1 tipical presentation is after 12 months of life, with dyskinesia and dystonia accompanied by chorea and athetosis. The symptoms are linked to a supposed neurotoxicity of the excess of glutaric, glutaconico and 3 OH- glutaric acids on the central nervous system caused by the enzimatic deficit. Vomitus is frequent in no treated patient. We know that CIPO can be caused by cerebral damage by itself. We presume that the precocious neurological sindrome and the successive intestinal syndrome have been caused by the association of GA-1 with the neonatal distress. An important co-factor is the need of large amount of drugs to controle convulsions. We conclude that GA-1 can join the list of metabolic deseases correlating with CIPO.

0095NUT

FATTY ACID COMPOSITION OF PLASMA LIPIDS DURING AND AFTER DIABETIC KETOACIDOSIS

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Background: At the ESPR Congress 2001, we reported significantly higher plasma values of the essential fatty acid, linoleic acid (C18:2n-6) but significantly lower plasma values of the long-chain polyunsaturated fatty acids, dihomo-gamma-linolenic acid (C20:3n-6) and arachidonic acid (C20:4n-6) in diabetic children than in healthy controls [Decsi et al., Prostaglandins, Leukot Essent Fatty Acids 67: 203–210, 2002]. It remained to be clarified, however, whether the differences were related to the disease or its dietary treatment. Here we report data on the acute effect of diabetic ketoacidosis (DKA) on the fatty acid composition of plasma lipids. **Subjects and methods:** Diabetic children (n = 9, age: 16.1 [3.3] years, duration of diabetes: 5.0 [5.3.] years, body mass index: 19.5 [8.0] kg/m^2, daily insulin dose: 0.87 [0.66] unit/kg body weight/day, glycated haemoglobin: 13.4 [2.8]%, median [IQR]) were investigated at admission for DKA (during DKA) and at the end of the treatment of DKA (after DKA). Fatty acid composition of plasma lipid classes was determined by high-resolution capillary gas-liquid chromatography. **Results:** Blood glucose (27.0 [8.5] versus 6.5 [1.6] mmol/l), pH (7.28 [0.35] versus 7.36 [0.06]) and base excess (-8.9 [15.1] versus -2.2 [6.3] mmol/l) were grossly abnormal before but not after DKA. Values of C18:2n-6 were significantly lower after than during DKA (table). In contrast, values of gamma-linolenic acid (C18:3n-6), C20:3n-6 and C20:4n-6 as well as the product/substrate ratio for the delta-6-desatuase enzyme ([C18:3n-6+C20:3n-6]:C18:2n-6) were significantly higher after than during DKA (table). Table: Fatty acids and the product/substrate ratio for delta-6-desaturase (delta-6) in diabetic children (n = 9) during and after diabetic ketoacidosis (DKA). % wt/wt, median [IQR], *P<0.05, **P<0.01

	Non-esterified fatty acids		riacylglycerols		Phospholipids
	During DKA	After DKA	During DKA	After DKA	During DKA	After DKA
C18:2n-615.55 [2.79]	13.35 [7.00]**	20.84 [11.40]	17.40 [8.17]*	21.59 [7.80]	16.96 [5.25.]*
C18:3n-60.86 [0.48]	2.34 [3.25]*	0.22 [0.65]	0.65 [0.58]	0.32 [0.30]	0.48 [0.23]
C20:3n-60.26 [0.20]	0.74 [0.41]*	0.19 [0.16]	0.21 [0.26]	1.13 [0.54]	1.06 [0.73]
C20:4n-61.39 [0.65]	1.33 [1.29]	1.37 [1.01]	1.74 [0.63]*	10.73 [5.01]	12.02 [3.11]
Delta-60.07 [0.11]	0.28 [0.55]*	0.03 [0.05]	0.05 [0.04]	0.06 [0.06]	0.09 [0.06]*

Conclusions: 1. In this study, successful treatment of diabetic ketoacidosis was associated with significant decrease of plasma linoleic acid and significant increase of plasma n-6 long-chain polyunsaturated fatty acid values. 2. Product/substrate ratio for the delta-6-desaturase enzyme indicated significant enhancement of enzyme activity by the cessation of diabetic ketoacidosis. 3. These data suggest that the disturbances of essential fatty acid metabolism in diabetic children are related not only to diet but to the level of insulinisation as well.

0096NUT

FATTY ACIDS IN EARLY HUMAN MILK FOLLOWING PRETERM AND FULL-TERM DELIVERY

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Background: It has been much debated whether fatty acid (FA) composition of human milk (HM) differs following preterm as compared to full-term delivery. Here we report data on FA composition of HM close to delivery. **Subjects and methods:** HM samples were obtained from mothers of preterm (n = 8, gestational age: 28.0 [4.2] weeks, birthweight: 1235 [420] g, median [IQR]) and full-term (n = 10, gestational age: 38.5 [2.7] weeks, birthweight: 3375 [282] g) infants. FA composition was measured by high-resolution capillary gas-liquid chromatography. **Results:** Maternal age (30.5 [4.2] and 28.0 [4.5] years, preterm and full-term) and body mass index (22.0 [3.5] and 24.3 [5.4]) did not differ. Food frequency questionnaire did not reveal significant differences in diet between the two groups. Fat contents of HM did not differ between the two groups. Values of linoleic acid (C18:2n-6) and alpha-linolenic acid (C18:3n-3) did not differ throughout the study. Values of the intermediary metabolites C18:n-6 and C20:3n-6 (table) as well as C18:4n-3 and C20:3n-3 were significantly higher following preterm as compared to full-term delivery. Arachidonic (C20:4n-6) and docosahexaenoic acid (C22:6n-3) values were significantly higher in samples of mothers of preterm than of full-term infants (table). Table: Principal long-chain polyunsaturated fatty acids in human milk following delivery of preterm (n = 8) and full-term (n = 10) infants. Data are % wt/wt, median (IQR), * = P < 0.05, ** = P < 0.01

	Dihomo g.-linolenic (C20:3n-6)		Arachidonic (C20:4n-6)	Docosahexaenoic (C22:6n-3)	
Day	Preterm	Full-term	Preterm	Full-term	Preterm	Full-term
1	0.66 (0.27)	0.44 (0.32)	0.96 (0.47)	0.65 (0.43)	0.36 (0.20)	0.18 (0.17)
2	0.63 (0.25)	0.42 (0.30)	0.89 (0.38)	0.61 (0.38)	0.39 (0.25)*	0.15 (0.18)
3	0.58 (0.23)*	0.36 (0.12)	0.90 (0.33)	0.47 (0.37)	0.38 (0.22)*	0.15(0.18)
4	0.58 (0.23)**	0.28 (0.14)	0.82 (0.40)*	0.44 (0.28)	0.33 (0.23)*	0.15 (0.14)
5	0.51 (.027)**	0.23 (0.15)	0.83 (0.32)**	0.37 (0.33)	0.33 (0.16)*	0.12 (0.19)
6	0.38 (0.26)*	0.28 (0.14)	0.56 (0.37)*	0.36 (0.31)	0.24 (0.18)**	0.10 (0.18)
7	0.44 (0.18)**	0.23 (0.14)	0.61 (0.25)**	0.34 (0.25)	0.26 (0.16)**	0.13 (0.15)
14	0.43 (0.33)*	0.26 (0.13)	0.47 (0.43)	0.39 (0.25)	0.21 (0.18)	0.09 (0.14)
21	0.41 (0.42)**	0.22 (0.11)	0.44 (0.41)*	0.33 (0.18)	0.21 (0.17)*	0.11 (0.08)
28	0.55 (0.35)*	0.28 (0.09)	0.64 (0.46)*	0.36 (0.26)	0.22 (0.27)	0.13 (0.13)

Conclusion: In this study, values of arachidonic and docosahexaenoic acids as well as the values of the intermediary metabolites of essential fatty acid metabolism were all significantly higher in early human milk samples of mothers giving birth to very-low-birth-weight preterm as compared to full-term infants.

0115NUT

RANDOMIZED CONTROLLED TRIAL ON NUTRITIONAL EFFICACY OF PRETERM HYDROLYZED FORMULA

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Background/Aims: It is not clear whether hydrolyzed proteins are really needed for preterm infants. Some studies suggested that hydrolyzed proteins are easier to digest, whereas others emphasized their poor nutritional quality. We designed a randomized controlled trial to test the effects of a preterm formula with hydrolyzed cow's milk proteins on short term growth and urinary and plasma amino acids levels. **Methods:** Infants with birth weight < 1750 and gestational age < 34 weeks fed exclusively with formula were recruited into the study when they reached and tolerated 150 ml/kg/day. They were randomly assigned to receive, for 4 weeks or until discharge, a conventional preterm infant formula (Formula B) or an isocaloric isonitrogenous hydrolyzed formula (Formula A). In the hydrolyzed formula all amino acids were also found as free amino acids except for Pro and Cys, whereas in the formula containing the intact protein only Gly, Ala, Trp, His, Arg were free. Weight was measured daily; length, head circumference, midarm circumference and total skinfold thickness were measured weekly. Blood and urine were analyzed for nutritional indexes and amino acid concentrations at the start of the study period, and at 14 and 28 days after randomization. Both caretakers and investigators were blind to subject assignment. **Results:** Twenty-one infants met the criteria for randomization; no infants were removed from study for acute illness necessitating the discontinuation of enteral feedings or for protocol violations. There were no significant differences in baseline characteristics of the two groups at birth and at the time of recruitment. The daily feeding volumes were similar: Formula A 172.8±5.6 vs Formula B 170.1±2.8 ml/kg/day. No significant differences were found either in caloric (129.6±4.2 vs 127.6±2.1 Kcal/kg/day) and protein intake (3.5±0.1 vs 3.4±0.1 g/kg/day). Infants fed with Formula A showed slower weight gain (17.4±3.4 vs 20.5±3.3 g/kg/d; $p = 0.045$) and lower mean change in Z scores for weight (-0.18±0.16 vs 0.00±0.09; $p = 0.009$) and for head circumference (-0.06±0.13 vs 0.06±0.13; p = 0,049). Arm muscular area (24.7±7.1 vs 34.4±10.5 mm^2/wk; $p = 0.027$) and arm fat area changes (16.7±4.1 vs 20.8±4.2 mm^2/wk; $p = 0.042$) were significantly greater in those fed with Formula B. No significant differences were found in plasma amino acids. However, after 14 days, infants receiving Formula A had significantly higher urinary levels of essential amino acids compared to infant receiving Formula B. A similar trend was observed after 28 days. **Conclusions:** Our results support the hypothesis of less nutritional value of hydrolyzed versus conventional preterm formulas. Impaired growth performance could be explained by the quicker absorption kinetic of free amino acids leading to higher temporary plasma levels and causing an increased renal excretion. These findings and their interpretation must be confirmed by further studies with larger sample sizes and involving protein hydrolysates with different degrees of hydrolysis, leading to different amounts of free amino acids and smaller peptides

0148NUT

GASTROINTESTINAL DYSMOTILITY IN INFANTS WITH COW'S MILK ALLERGY

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Background: Neuroimmune interactions have been described as a lead factor in order to provoke cow's milk allergy in infants (1). Gastric luminal antigen challenge results in IgE-mediated mucosal mast cell degranulation and in the release of various substances, which might determine an alteration of gastrointestinal motility involving intestinal primary afferent nerve fibres (IPAN) (2,3). Epigastric impedance is an experimental method that evaluates gastric emptying by measuring tissue impedance variations during the transit of a mild (800 microAmpere) AC current (50 kHz). Aim: To evaluate gastrointestinal motility through epigastric impedance in infants with cow's milk protein allergy (CMPA). **Methods:** We studied 5 atopic infants, aged 2 to 4 months, with symptoms related to CMPA such as regurgitation, vomiting, excessive crying and/or colicky abdominal pain and eczema, diagnosed on the basis of a clinical remission after the beginning of a cow's milk-free diet, with or without a positive skin prick test and a positive response to cow's milk challenge. All the infants had a positive family history for atopy, at least one first-degree relatives affected by allergic reactions of any kind but related. 5 age-matched healthy infants without any gastrointestinal symptoms were studied as control subjects. Gastric emptying was monitored for 90 minutes, after the ingestion of cow's milk based starting formula, by impedance analyser (Computerised Plethysmograph IPG & PPG-Akern-Firenze) connected to a personal computer in order to record impedance values and to elaborate a graph representation of the data. For each measurement was obtained the trend line, whose angle (α), indicating gastric emptying velocity, was calculated with formula: $\alpha = \text{arctang}(a/b)$ where a = decrease of impedance and b = time of observation. Statistical analysis was performed using T test and significance was set at $p < 0.05$. **Results:** The average of the angles (α) of infants with CMPA was 0.37° with standard deviation (SD) 0.08°; in healthy infants average α was 1.72° with SD 0.32°. **Conclusions:** In sensitized infants, cow's milk induces delayed gastric emptying supporting the hypothesis of gastrointestinal dysmotility in food allergy. Further studies are required to confirm the role of mast cell-nerve interaction in the production of this dysmotility. References: 1) Ravelli AM, et al. Vomiting and gastric motility in infants with cow's milk allergy. J Pediatr Gastroenterol Nutr 2001; 32: 59–64. 2) Borrelli O, et al. Mast cell-nerve interaction is critical for food allergic intestinal dysmotility. J Pediatr Gastroenterol Nutr 2001; 32: 348. 3) Heuschkel R, et al. Cow's milk induces T-cell proliferation and mucosal mast cell degranulation with neural tropism in an in-vitro organ colture model. J Pediatr Gastroenterol Nutr 2003; 36: 527.

0175NUT

TRACKING THE FATE OF A PROBIOTIC LACTOBACILLUS PARACASEI STRAIN DURING A HUMAN TRIAL IN THE PRESENCE OF ANTIBIOTIC TREATMENT.

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Background: Orally consumed viable bacteria with proposed beneficial health effects, the so-called probiotics, are increasingly used to treat disorders like viral, bacterial and radiotherapy-induced diarrhoea, constipation, inflammatory bowel disease and food allergy. An assessment of the survival and persistance of the ingested probiotic bacterium is required in order to correlate the observed effects to its action. The real in vivo persistance of some strains has been assessed by means of genetic tools, based on DNA amplification and analysis such as RAPD, REP, PFGE fingerprinting. While it has been shown that several probiotic are able to survive and reproduce themselves into the gut of healthy individuals, it is poorly known the potential of probiotic to survive into the gut of unhealthy individuals treated with antibacterial drugs. **Aim.** We have tried to gain knowledge on the potential of a probiotic bacterium (Lactobacillus paracasei DN-114001) contained in a fermented milk product (Actimel). **Methods:** Actimel was given (one 125 ml pot per day) to a group of seven children aged 48.2 months (range, 39–52) with recurrent respiratiry tract infections and likely to receive antibiotic treatments. Subjects were sampled 3 times (once per month) for feces in a space time of 90 days after starting Actimel. Faecal samples were plated counted for the presence of lactobacilli and a statistically significant number of Colony Forming Units were genetically identified by means of REP fingerprinting (a PCR-based technique able to discriminate the identity of lactobacilli at the strain level). **Results:** The presence of the specific strain has been shown in all the fecal samples throughout the study period, except than in one single sample, despite the fact that different antibiotic treatments (including various beta-lactamics and macrolides) have been used. It is also to note that the used technique, based on genetic identification of CFUs allows to detect one specific strain only if it is present in high concentration. **Conclusion:** This is, as far as we know, the first report on the possibility to use a probiotic product in children also in presence of antibiotic treatment for its persistance in feces.

0293NUT

PLATELET AGGREGATION, BLOOD VISCOSITY, LIPID PROFILE IN ADOLESCENT OBESITY

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Background: Prevalence of obesity is increasing worldwide and epidemic of childhood obesity also reached Hungary. Hypertension and serum lipid abnormalities are common features in obesity. Besides the activation of the sympathetic nerve and renin-angiotensin system, several other factors have been proposed in the development of obesity induced hypertension: 1) hormones (insulin, aldosterone, leptin, etc.); 2) vasoactive mediators (angiotensin II, prostaglandins, nitric oxide, etc.); 3) rheological parameters (platelet activity, blood viscosity). The role of these pathogenic factors is well-known in adults but rarely investigated in children. **Aims** of this study were to investigate the possible role of platelet aggregation, blood and plasma viscosity and changes in serum lipids (total cholesterol, TG, HDL-, LDL-cholesterol) in obese and hypertensive adolescents. **Methods:** Four groups of adolescent subjects with either sex (n; mean age in years ± S.D.) were investigated: normotensive obese (n=15; 13.4 ± 3.5), obese hypertensive (OHT: n=17; 13.5 ± 3.2), essential hypertensive (EHT: n=15; 14.4 ± 2.7) and controls (n=20; 16.1 ± 5.4). Blood pressure (BP) was measured by ambulatory blood pressure monitoring, in vitro platelet aggregation (in aggregation unit, AU) with collagen by laser rheoaggregometer and whole blood and plasma viscosity by viscosimeter. Lipid profile, measured by routine laboratory methods, consisted of plasma cholesterol, triglyceride, high density lipoprotein (HDL) and low density lipoprotein (LDL) serum levels. ANOVA and Pearson correlation were used for statistical analysis, $p<0.05$ were considered to be significant. **Results:** (see Table; means ± SD; * $p<0.05$ vs. controls, # $p<0.05$ vs. obese, + $p<0.05$ vs. EHT)

Conclusions: In obesity and obesity induced hypertension of adolescents raised platelet activity, blood viscosity and changes in serum lipids were found. These rheological parameters might be additional risk factors for cardiovascular complications in childhood obesity.

	Obese	OHT	EHT	Controls
BMI (kg/m^2)	31.1 ± 6.0 *+	32.8 ± 2.7 *+	21.1 ± 2.3	22.9 ± 1.9
Systolic BP (mmHg)	119.3 ± 5.0	141.6 ± 9.7 *#	136.9 ± 6.5 *#	111.2 ± 6.2
Diastolic BP (mmHg)	65.6 ± 4.7	81.8 ± 11.4 *#	76.9 ± 9.4 *#	66.3 ± 5.6
Platelet aggregation (AU)	22667 ± 6540 *	29886 ± 1940 *#	26671± 5608 *	15624 ± 3359
Blood viscosity (mPAs)	2.81 ± 0.14	3.06 ± 0.26 *#	2.67 ± 0.20	2.82 ± 0.12
Cholesterol (mmol/L)	5.26 ± 0.52 *+	5.57 ± 0.57 *+	3.92 ± 0.54	3.87 ± 0.58
Triglyceride (mmol/L)	1.71 ± 0.59	2.05 ± 0.31 *+	0.93 ± 0.40	1.01 ± 0.32

0296NUT

BODY COMPOSITION AND BASAL METABOLIC RATE IN PAEDIATRIC PATIENTS

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Background: Accurate prediction of energy expenditure is required for adequate nutritional support. Fat free mass (FFM) measurements might improve prediction of basal metabolic rate (BMR) compared to body weight. Aims: (1) To analyse agreement between FFM measurements by deuterium dilution versus bioelectrical impedance analysis and skinfold thickness. (2) To compare several BMR predictive models with measured BMR. **Patients and methods:** 49 hospitalised patients admitted for surgical (n=18) and medical reasons were included (median age 2 (range 0–6) yrs; median weight 10.5 (range 3.5–24.5) kg).We measured total body water (TBW) from urine deuterium enrichment, 4 hrs after a weighted oral deuterium dose. TBW from impedance was calculated using an adjusted algorithm of Beertema (2000): $\{0.52x[Weight^{2/3}x(Height^2/Resistance)]^{2/3}+1.53\}$. For both methods FFM was calculated using age-matched hydration factors. Furthermore, FFM from the sum of 4 skinfolds was calculated. BMR was measured with a metabolic monitor. For prediction of BMR, we used the linear Schofield equations for gender, age and weight (1985) and two power models of Butte et al. (1995), using body weight and FFM. Comparison was performed by Bland-Altman analysis. **Results:** Mean FFM (% bodyweight) was 9.3 (88%), 9.5 (88%) and 9.3 (86%) kg for deuterium dilution, impedance and skinfolds respectively. Mean measured BMR was 2.16 (range 0.69–3.96) MJ/day. Agreement between paired observations of FFM and BMR are shown in table 1 and 2 respectively. Table 1 Comparison of FFM in kg (%) by impedance and skinfolds versus deuterium dilution (n=49)

Method	Bias	Limits of agreement	
		Lower limit	Upper limit
- impedance	-0.3 (=-3%)*	-2.0 (=-24%)	1.4 (=17%)
- skinfolds	-0.1 (=-1%)	-1.7 (=-19%)	1.4 (=17%)

Table 2 Comparison of BMR in MJ/day (%) by several predictive equations versus measured BMR (n=49)

Method	Bias	Limits of agreement	
		Lower limit	Upper limit
- Schofield equations	-0.22 (=-5%)**	-1.15 (=-47%)	0.71 (=37%)
- Butte 1: $0.471xWt(kg)^{0.63}$	0.11 (=1%)*	-0.57 (=-39%)	0.80 (=41%)
- Butte 2: $0.571xFFM$ from deuterium $(kg)^{0.63}$	-0.08 (=-7%)	-0.76 (=-49%)	0.61 (=34%)

*p<0.05; **p<0.001

Conclusions: FFM measurements by impedance and skinfolds showed the same accuracy compared to deuterium dilution with small bias and acceptable limits of agreement. However, FFM does not improve BMR prediction compared to body weight, with clinical significance. As predictive equations show wide limits of agreement in this paediatric population, energy expenditure measurements are preferred for adequate nutritional support.

0310NUT

ENHANCED CELL PROLIFERATION AND MAPK ACTIVATION OF A HUMAN FETAL SMALL INTESTINAL CELL LINE WITH EGF, TGFA-4052M AND IGF-1

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Background/Aims: EGF, TGFα, and IGF-1 have been implicated in gut epithelial proliferation and integrity. Using an in vitro model, the trophic and interactive effects of these proteins on fetal human small intestinal (FHs-74) cell proliferation and total and active MAPK phosphorylation were measured. **Methods:** FHs-74 cells were grown in 96-well plates. Recombinant EGF, TGFα or IGF-1 was added to wells at increasing logarithmic concentrations (range 0.001–1000-ng/mL serum-free medium). Combinations of the growth factors (0.005 or 500-ng/mL medium) also were added to the cells. After 24 hr of growth factor exposure, cell proliferation (expressed as % control) was measured. In addition, total and active MAPK phosphorylation was measured 20 minutes after growth factor exposure by Western blot analysis and densitometric analysis of blots. Data were analyzed using logistic regression and ANOVA. **Results:** There was a dose-dependent increase in FHs-74 cell proliferation with each growth factor ($p<0.0001$). EGF's maximal effect on proliferation was at 0.5-ng/mL; TGFα and IGF-1's maximal effect occurred at 100-ng/mL. Proliferation declined at concentrations above 0.5-ng/mL for EGF and above 100 ng/mL for TGFα and IGF-1. When IGF-1 and TGFα or EGF and TGFα were added concomitantly, the proliferation profiles resembled that of TGFα alone; however, when EGF and IGF-1 were added together, proliferation increased above that of each growth factor alone. The proliferation profile of all 3 growth factors together was less than EGF or TGFα alone, but above that of IGF-1 alone. When compared with EGF or TGFα alone, IGF-1 had a diminished effect on cell proliferation. Follow-up post-hoc testing showed physiologic high and pharmacologic concentrations for each growth factor to be statistically significantly different from physiologic low concentrations (TGFα $p<0.001$; EGF $p<0.004$; IGF-1 $p<0.002$). However, physiologic high concentrations of the growth factors were not statistically significantly different from pharmacologic concentrations. Western blot analysis for total MAPK showed no differences following exposure to each of the three growth factors; however, there was a dose-dependent increase in active MAPK at the higher doses of the three growth factors singly and in combination. **Conclusions:** FHs-74 proliferation varied as a function of growth factor type and combination. EGF, TGFα and IGF-1 had a dose-dependent, trophic effect on cultured human small intestinal cells that was associated with an increase in active MAPK synthesis and cell proliferation.

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0336NUT

CASEIN HYDROLYSIS REDUCES OPIOID ACTIVITY LIBERATED DURING DIGESTION

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Background: Protein hydrolysis accelerates gastrointestinal transit (GIT) and feeding advancement in preterm infants on formula feeding. In rat pups opioid receptor agonists derived from casein during digestion such as β-casomorphins slow down GIT. We hypothesized that hydrolysis of casein reduces the opioid activity liberated during digestion thereby accelerating GIT compared to native casein. **Aim:** Aim of the present study was to investigate whether hydrolysis of casein accelerates GIT compared to native casein and whether pretreatment with naloxone, an opioid receptor blocker, abolishes this difference in rat pups. **Methods:** In a randomized controlled trial following a 2x2 factorial design 216 female Wistar rat pups were fed with pellets based on hydrolyzed or native casein. After pretreatment with naloxone or normal saline carmine red was administered by orogastric gavage as a tracer for GIT velocity measurement. Four hours later the animals were sacrified. Their intestine was removed and the length of the colon from the coeco-colonic junction to the anus was measured. GIT was recorded as percentage of the total colonic length (percentage of colonic transit) containing carmine red. Data as mean ± SD. **Results:** There was a significant difference in GIT between the two formulas (77.4 +/- 17% vs. 51.2 +/- 20%; hydrolyzed vs. native casein respectively), however, there was no difference after naloxone pre-treatment (77.1+/-16% and 76.5+/-17%). **Conclusion:** The present data suggests that hydrolysis of casein accelerates GIT via reduction of the casein derived opioid activity liberated during digestion.

0355NUT

PROTEIN REQUIREMENTS OF PREMATURE AND TERM INFANTS.

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Background/Aims: Protein requirement is defined as that protein intake that is needed for realization of full growth potential. Protein requirement depends on body size, body composition and rate of growth. Because these parameters change rapidly in premature and term infants, protein requirements also change rapidly, making experimental establishment of requirements exceedingly difficult. The factorial approach fills this void and provides specific estimates of protein requirements for any age and size. **Methods:** Based on data on growth and body composition of the fetus, protein requirement has been calculated for preterm infants of various sizes. Using similar data for normal term infants, protein requirement has been determined for monthly age intervals from term to 6 months of age. **Results:** The results are shown in the tables. The values for preterm infants agree generally with experimentally obtained requirements. In the case of term infants there is close agreement between factorial estimates and protein intakes observed in breastfed infants.

Preterm infants

Preterm infants					
Body weight (g)	500-700	700-900	900-1200	1200-1500	1500-1800
Fetal weight gain (g/d)	13	16	20	24	26
(g/kg/d)	21	20	19	18	16
Protein (g/kg) (NX6.25)					
Inevitable loss	1.0	1.0	1.0	1.0	1.0
Growth (accretion)	2.5	2.5	2.5	2.4	2.2
Required intake					
Parenteral	3.5	3.5	3.5	3.4	3.2
Enteral	4.0	4.0	4.0	3.9	3.6
Protein/Energy (g/100kcal)					
Parenteral	3.9	4.1	3.5	3.1	2.9
Enteral	3.8	3.7	3.4	3.1	2.8

Term infants						
Age interval (months)	0-1	1-2	2-3	3-4	4-5	5-6
Protein (g/kg) (NX6.25)						
Inevitable loss	0.93	0.93	0.90	0.89	0.88	0.89
Growth (accretion)	1.03	0.78	0.56	0.38	0.30	0.29
Required intake	1.98	1.71	1.46	1.27	1.18	1.18
Protein intake breastfed	2.09	1.59	1.18	1.06	1.00	0.95
Protein/Energy (g/100kcal)	1.76	1.51	1.46	1.35	1.31	1.31

Conclusions: Feedings must provide the highest protein/energy ratio pertaining to the class of infants for whom the feeding is designed.

0417NUT

EFFICACY OF MATERNAL VITAMIN D (VITD) SUPPLEMENTATION DURING LACTATION

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Background: Vitamin D-deficient rickets has risen dramatically during the past three decades, mainly among darker pigmented, breastfeeding (BF) infants. In response, some organizations have advocated for universal vitD supplementation of breastfed infants. Maternal supplementation has not been considered a viable option because of toxicity concerns. Recently, supplementation to 10,000 IU/day or 25 X's the current DRI (400 IU/day) for up to 5 mos was shown to be safe in a diverse adult population. The effectiveness and safety of such therapy in lactating women and their BF infants previously has not been evaluated. **Objective:** To determine the vitD status of BF mother-infant pairs during high-dose maternal vitD supplementation.Design/Methods: Complete data are available on 9/30 dyads in an ongoing study. Fully BF mothers receiving 400 IU/day vitD were recruited and enrolled during the first month postpartum. Mothers were randomised to receive either 2,000- or 4,000 IU/day vitD_2 (ergocalciferol) for 3 mos. The sole infant source of vitD_2 was breast milk. Maternal serum and milk and infant serum were assessed monthly for antirachitic activity: vitD_2, D_3, 25(OH)D_2 and 25(OH)D_3 levels were measured. Maternal serum Ca and urinary Ca/Cr ratios were monitored monthly. Sun exposure was monitored utilizing a diary. **Results:** Supplementation with 2,000 or 4,000 IU vitD/day safely increased maternal serum and milk and infant serum vitD levels above baseline as shown in the table below: Vitamin D Status of BF Dyads According to Maternal Vitamin D Dose

2000 IU/day		Mother (n=4)			Infant (n=4)	
	Baseline	Month 1	Month 2	Month 3	Baseline	Month 3
25(OH)D_3	<0.5	13.4±3.3	18.5±3.5	16.4±2.8**	<0.5	7.23±0.7**
Total 25(OH)D_2	28.3±14.0	40.8±9.9	44.9±6.9	34.8±4.6**	6.1±1.3	20.0±7.3**
Total Milk VitD (IU/L)	39.6±8.9	65.9±6.3	79.7±23.4	73.3±15.0**		
4000 IU/day		Mother (n=5)			Infant (n=5)	
25(OH)D_3	2.6±3.6	13.4±3.0	17.3±5.8	23.4±6.8**	0.7±1.3	10.2±3.7**
Total 25(OH)D_2	35.5±7.4	35.6±9.1	40.5±13.5	43.3±15.3**	17.1±10.6	26.7±16.6**
Total Milk VitD (IU/L)	42.6±13.1	88.8±22.5	76.5±20.6	110.0±72.0**		

*25(OH)D_2 and Total 25(OH)D expressed in ng/mL serum; (**$p<0.05$) In this cohort, there was no evidence of hypervitaminosis D, even in mothers who had increased sun exposure. Maternal and infant serum calcium levels and maternal urinary calcium/Cr ratios remained in the normal range throughout the study period.

Conclusions: High dose oral vitD supplementation up to 4,000 IU/day in lactating mothers appears to be safe and effective in increasing maternal and milk vitD levels and improved the nutritional vitD status of recipient BF infants. Further work is necessary to confirm these data with a larger sample size to establish the optimal range of vitD supplementation as a function of latitude, cultural practices and race. Funded in part by a grant from the University Research Committee, Medical University of South Carolina.

0432NUT

THE ROLE OF LONGCHAIN POLYUNSATURATED FATTY ACIDS IN THE PERINATAL PERIOD

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The perinatal supply of long-chain polyunsaturated fatty acids (LC-PUFA) is critical for infant growth and neurodevelopment. The mechanisms for the preferential, materno-fetal LC-PUFA transfer have not been elucidated. We studied the in vivo placental transfer of stable isotope labelled palmitic (PA), oleic (OA), linoleic (LA) and docosahexaenoic acids (DHA) given as an oral bolus 4 hours before caesarean section. At the time of birth, ^{13}C-enrichment of fatty acids was higher in placental triglycerides than in cord plasma triglycerides, whereas non esterified fatty acid enrichments were higher in cord plasma than in placenta. The distribution ratio between tracer fatty acid concentration in placenta and maternal plasma was significantly higher for ^{13}C-DHA than for other fatty acids (^{13}C-PA: 7.1 ± 1^{ab}; ^{13}C-OA: 3.8 ± 0.4^{a}; ^{13}C-LA: 9.2 ± 1.3^{b}; ^{13}C-DHA: 25.9 ± 3.4^{c}). These results suggest that only a part of the placental non esterified fatty acids participated in the fatty acid transfer process. Placental tissue shows a preferential incorporation of tracer DHA relative to LA, OA and PA at the studied time point, which may reflect preferential materno-foetal DHA transfer. After birth, breast fed term and preterm infants receive appreciable amounts of preformed AA and DHA with human milk lipids. Although milk LC-PUFA content is influenced by maternal dietary composition, compositional studies have given indications for some metabolic control of milk PUFA contents. We studied the turnover of U-^{13}C-labeled fatty acids acid in lactating women. Milk transfer and oxidation were measured. We estimate that about 30 % of milk LA is directly transferred from the diet, whereas about 11 % of milk dihomo-γ-linolenic acid and 1.2 % of milk AA originate from direct endogenous conversion of dietary LA. In contrast, the major portion of human milk PUFA is derived from maternal body stores and not directly from the maternal diet. This results in a relatively constant milk PUFA supply to the recipient infant, which might be of biological benefit. In a more recent study, we evaluated the contribution of dietary and of endogenously synthesized AA to its milk secretion in undernourished Mexican women on a low fat diet. The cumulated 72 h recovery of ^{13}C-linoleic acid in milk was 16.3 ± 6.4 % of the dose, but only 0.01% of the label was found as ^{13}C-AA. The calculated transfers of dietary linoleic and AA into milk were 32.8 ± 18.0% and 11.8 ± 6.6 %, respectively. AA stemming from conversion of dietary linoleic acid contributed only 1.1% to total milk AA. In this population, 70% of linoleic acid and almost 90% of AA secreted in milk were not derived from direct intestinal absorption. Only a minor fraction of milk AA stemmed from conversion of linoleic acid. Our results suggest that maternal body stores are the major source of human milk linoleic acid and AA. We also studied supplementation of lactating women with n-3 LC-PUFA and found that this intervention can effectively prevent the postnatal decline of milk DHA without changing the proportional utilization of 13C-labeled n-3 fatty acids. The proportional transfer of labeled ^{13}C-DHA from the diet to human milk is similar to that of other long-chain fatty acids and is not altered by dietary supplementation of n-3 LC-PUFA. In view of a very limited endogenous LC-PUFA synthesis by infants, functional consequences of the perinatal n-3 LC-PUFA supply documented in a number of controlled trials and our data on maternal utilization of LC-PUFA, pregnant and lactating women should have a regular dietary supply of preformed n-3 LC-PUFA. Supported by European Commission (QLK1-CT-1999–00888, NUHEAL; QLK1–2001-00138, PERILIP) and German Research Council – Deutsche Forschungsgemeinschaft (Ko 512/5–2).

0045OTH

INCREASED MMP-8 IN THE TRACHEAL ASPIRATE AT BIRTH AND RISK FOR THE ATYPICAL CLD

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Background/Aims: We tested the hypothesis that preterm infants who develop atypical chronic lung disease (CLD) of prematurity which occurred without preceding RDS have higher levels of metalloproteinase-8 (MMP-8) in the tracheal aspirate at birth compared to those who do not develop atypical CLD of prematurity. **Methods:** The relationship between levels of MMP-8 in the tracheal aspirate and the development of atypical CLD was examined in 26 preterm infants. Levels of MMP-8 in the tracheal aspirate were measured by specific immunoassay. **Results:** Median levels of MMP-8 were higher in preterm infant who develop atypical CLD of prematurity than those who do not develop atypical CLD of prematurity(44.42 ng/ml vs. 3.28 ng/ml, $P<0.05$). The difference persisted significantly after we made adjustment for the effect of gestation age and birth weight, and presence of histologic chorioamnionitis by logistic regression analysis(OR, 3.19 per 0.45 ng/ml increment of logMMP-8, 95% CI 1.01–10.22). **Conclusions:** Increased levels of MMP-8 in the tracheal aspirate of preterm infant at birth may be one of predictors for the development of atypical chronic lung disease of prematurity

0070OTH

EFFECTS OF RETINOIDS IN EARLY AND LATE LUNG GROWTH IN EXPERIMENTAL CDH

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Background/Aims: Early and late lung underdevelopment in congenital diaphragmatic hernia (CDH) are predominantly due to non-mechanical (directly mediated by nitrofen) and mechanical (mediated by thoracic herniation) factors, respectively. Antenatal treatment with vitamin A attenuates lung hypoplasia in CDH. Our purpose was to assess whether vitamin A enhances lung growth by interfering with non-mechanical or mechanical factors. **Methods:** Thirty-two pregnant Wistar rats were exposed on gestation day 9.5 to 100 mg of nitrofen or just olive oil. At the same day nitrofen-exposed rats were treated either with 15,000 IU vitamin A or just the vehicle. At selected gestation ages (E18, E20 and E22), the lungs were harvested, weighed and analysed for DNA and protein contents. Lung hypoplasia was estimated through total lung weight-to-body weight ratio. Foetuses (n=471) were assigned to five experimental groups: Sham (not exposed to nitrofen or vitamin A), Nitrofen (nitrofen without CDH), CDH (nitrofen with CDH), Nitrofen-Vit A (nitrofen without CDH+vitamin A) and CDH-Vit A (nitrofen with CDH+vitamin A). In both groups with CDH. **Results:** Incidence of hernia was significantly reduced in foetuses treated with vitamin A. At E18, lung hypoplasia was similar in foetuses with and without hernia (Nitrofen 1.92±0.05; CDH 1.92±0.04), whilst vitamin A attenuated it, in relation to sham group (2.45±0.05), in 5% in nitrofen (nitrofen-vit A 2.05±0.03) and 6% in CDH (CDH-vit A 2.08±0.04) groups. At E20, lung hypoplasia was higher in foetuses with hernia (Nitrofen 2.54±0.1; CDH, 2.39±0.05), whilst vitamin A attenuated it, in relation to sham group (3.20±0.07), in 16% in nitrofen (nitrofen-vit A 2.96±0.03) and 14% in CDH (CDH-vit A 2.60±0.03) groups. At E22, lung hypoplasia was significantly higher in foetuses with hernia (Nitrofen 2.13±0.06; CDH 1.48±0.03), whilst vitamin A attenuated it, in relation to sham (2.38±0.04), in 8% in nitrofen (nitrofen-vit A 2.29±0.06) and 8% in CDH (CDH-vit A 1.69±0.05), respectively. **Conclusions:** The enhancement of lung growth due to vitamin A varies during gestation. At each time point, however, vitamin A attenuates lung hypoplasia in both CDH and nitrofen foetuses on a similar degree. Therefore, vitamin A attenuates lung hypoplasia in CDH by interfering only with early acting non-mechanical factors

0071OTH

RARE DISEASES RESEARCH THROUGH SURVEILLANCE: THE CANADIAN EXPERIENCE.

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Background: Traditionally, anecdotal data and retrospective case reports provide insight into the natural history, epidemiology and case management of rare diseases. This approach generates insufficient numbers to enable meaningful analysis for subsequent development of interventions. **Aim:** To describe the role, methodology and accomplishments of an active pan-Canadian surveillance system in advancing research into rare diseases. **Methods:** Using a monthly report form, over 2300 paediatricians and paediatric subspecialists actively report 10–12 different rare diseases according to preset definitions and protocols. Principal investigators analyze case-specific clinical data provided on follow-up questionnaires. Confidentiality and ethical approval are mandatory and external validation of case ascertainment is sought. As a member of the International Network of Paediatric Surveillance Units (INoPSU), the CPSP facilitates sharing of information and collaboration between researchers of different countries to advance paediatric research. **Results:** CPSP active surveillance greatly improved case ascertainment completeness for acute flaccid paralysis and congenital rubella syndrome over pre-existing passive reporting systems. CPSP case definitions and protocols increased awareness and knowledge of rare diseases. For Smith-Lemli-Opitz syndrome (SLOS), the program estimated the first Canadian population-based incidence rate and provided insight into the SLOS mutation spectrum with identification of 3 new mutations. This was pivotal to the continued funding of a multi-centred international study on prenatal screening. For CHARGE association/syndrome, the study clarified the diagnostic criteria permitting earlier diagnosis and providing new research data on medical, developmental and behavioral needs of patients now surviving into adolescence. Even for well-known diseases, the CPSP produced new perspectives. The anaphylaxis study, with 700 cases affecting children aged 1 month to 17 years, depicted a clearer picture of symptoms, signs and treatments in infants and very young children. Through INoPSU, the CPSP compared different prophylactic vitamin K regimens (IM versus oral) for hemorrhagic disease of the newborn in Australia, Germany, Netherlands, New Zealand, Switzerland and the United Kingdom. These results reinforced Canada's recommendation for administration of IM vitamin K in all newborns. **Conclusions:** CPSP's real-time active surveillance tool offers tremendous research possibilities by contributing reliable national epidemiological incidence data to advance scientific knowledge and guide medical and public health decisions. International collaboration exemplifies enhanced global village surveillance where all children will ultimately benefit.

0080OTH

ORAL VASCULAR NETWORK GEOMETRY IN INFANTILE HYPERTROPHIC PYLORIC STENOSIS

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Background/Aims: Idiopathic infantile hypertrophic pyloric stenosis (IHPS) is a common surgical condition of unknown etiology. Recent evidence suggests an extra-cellular matrix (ECM) abnormality in IHPS and as ECM is known to play an important role on angiogenesis and blood vessel geometry. The hypothesis of a vascular network geometry abnormality in IHPS families was tested. **Methods:** 25 consecutive children with IHPS (M: 18; F: 7; age at surgery [mean ± SD]: 5.3 ± 1.5 wk; age at examination: 5.0 ± 2.3 yr) and their parents (age of fathers and mothers: 36.1 ± 4.5 and 33.2 ± 4.0 yr, respectively) participated in the study. Familiar IHPS was excluded. A total of 75 age- and sex-matched control subjects [M: 54 ;F: 21; mean age: 4.9 ± 2.5 yr; and their parents (age of fathers and mothers: 35.8 ± 5.0 and 32.5 ± 4.3 yr, respectively)] were also included. The lower gingival and vestibular oral mucosa was chosen as the study-area, due to the high vasculature pattern visibility and easy accessibility. Fractal dimension (D) at two scales (D 1–46, and D 1–15), tortuosity (minimum-path dimension, Dmin), and relative Lempel-Ziev complexity (L-Z) of the vascular networks from the lower gingival and vestibular oral mucosa were measured. **Results:** The oral vascular networks of IHPS patients and their unaffected parents exhibited a significantly increased complexity, with higher D (1–46) ($P<.00001$) and D (1–15) ($P<.00001$) than control vascular networks, together with a significant trend towards non-structured randomness, as indicated by higher L-Z values ($P<.00001$). IHPS patients showed significantly higher D (1–46) ($P=.0001$), D (1–15) ($P=.0001$), and L-Z values ($P=.03$) than IHPS parents. Conversely, no statistically significant differences in Dmin between IHPS (patients and unaffected parents) and controls ($P=.067$) were present. No significant differences in the examined vascular pattern characteristics between control children and control parents were observed ($P \geq .45$). **Conclusions:** The findings of the present study indicate the presence of a previously unrecognized increased vascular network complexity on the oral mucosa of IHPS patients and IHPS unaffected parents. Qualitatively similar changes in the unaffected IHPS parents confirm the presence of a subclinical ECM abnormality in the IHPS families; may provide a useful phenotypical marker for identifying couples potentially at risk for the birth of an affected infant; and strongly support the importance of a genetic component in IHPS.

0081OTH

CRY FEATURES REFLECT PAIN INTENSITY IN TERM NEWBORNS: AN ALARM THRESHOLD

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Objective: To assess differences in sound spectra of crying of term newborns in relation to different pain levels. **Methods:** Fifty-seven consecutively born neonates were evaluated during heel-prick performed with different analgesic techniques. Crying was recorded and frequency spectrograms analyzed. A pain score on the DAN (Douleur Aiguë du Nouveau-né) scale was assigned to each baby after the sampling. Three features were considered: 1) whole spectral form; 2) the fundamental frequency of the first cry emitted (F_0); 3) root-mean-square (rms) sound pressure normalized to its maximum. These three parameters were correlated with the corresponding DAN scores. **Results:** After emission of the first cry, babies with DAN scores >8, but not with DAN scores ≤8, ($p<0,001$) showed a pattern ("siren cry") characterized by a sequence of almost identical cries with a period of the order of 1 s. A statistically significant correlation was found between rms ($r=89\%$, $p<0.01$), F_0 ($r=32\%$, $p<0.05$), siren cry ($r=68.2\%$, $p=0.02$) and DAN score. F_0 did not show significant correlation with DAN score in the subset of neonates with DAN scores ≤8 ($r=1.4\%$, $p=0.94$) and babies with a DAN score >8 had a significantly higher F_0 than those with lower DAN scores ($p=0.016$). **Conclusions:** An alarm threshold exists between high (>8) and low (≤8) DAN scores: crying has different features in these two groups. When pain exceeds a DAN score of 8, usually a first cry at a high pitch is emitted, followed by the siren cry, with a sound level maintained near its maximum. This may be considered a signal of unbearable pain.

0082OTH

SENSORIAL SATURATION: AN EFFECTIVE ANALGESIC TOOL FOR HEEL-PRICK IN PRETERM INFANTS: A PROSPECTIVE RANDOMIZED TRIAL

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Aims: Pain is traumatic for preterm infants and can damage their CNS. We wanted to assess whether multisensorial stimulation can be analgesic and whether this effect is only due to oral glucose or sucking. **Methods:** We performed a randomized prospective study, using a validated acute pain rating scale to assess pain during heel-prick combined with five different procedures: (A) control, (B) 10% oral glucose plus sucking, (C) sensorial saturation (SS), (D) oral water, and (E) 10% oral glucose. SS is a multisensorial stimulation consisting of delicate tactile, vestibular, gustative, olfactory, auditory and visual stimuli. Controls did not receive any analgesia. We studied 85 heel-pricks (5 per baby) performed for routine blood samples in 17 preterm infants (28–35 weeks of gestational age). We applied in random order in each patient the five procedures described above and scored pain. **Results:** SS and sucking plus oral glucose have the greater analgesic effect with respect to no intervention ($p < 0.001$). The effect of SS is statistically better than that of glucose plus sucking ($p < 0.01$). **Conclusions:** SS promotes interaction between nurse and infant and is a simple effective form of analgesia for the NICU.

0083OTH

EFFECT OF MULTI-SENSORY STIMULATION ON ANALGESIA IN TERM NEONATES: A RANDOMIZED CONTROLLED TRIAL

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Aims: Many attempts have been made to obtain safe and effective analgesia in newborns. Oral glucose-water has been found to have analgesic properties in neonates. We investigated whether other sensory stimulation added to oral glucose provided more effective analgesia than oral glucose alone. **Methods:** In a randomised prospective double-blind trial we studied 120 term newborns during heel prick. The babies were divided randomly into six groups of 20 and each group was treated with a different procedure during heel prick: A) control; B) 1 ml 33% oral glucose given 2 minutes before the heel-prick; C) sucking; D) 1 ml 33% oral glucose + sucking; E) multisensory stimulation including 1 ml 33% oral glucose (sensorial saturation); F) multisensory stimulation without oral glucose. Sensorial saturation consisted in massage, voice, eye contact and perfume smelling during heel prick. Each heel prick was filmed and assigned a point score according to the Douleur Aigue du Nuoveau-né (DAN) neonatal acute pain scale. Camera recording begun 30 seconds before the heel-prick, so it was impossible for the scorers to distinguish procedure A (control) from B (glucose given 2 min before), C (sucking water) from D (sucking glucose) and E (multisensory stimulation and glucose) from F (multisensory stimulation and water) from the video. **Results:** Procedure E (multisensory stimulation and glucose) was found to be the most effective ($p<0.0001$) and the analgesia was even more effective than that produced by procedure D (sucking glucose) ($p=0.004$). **Conclusions:** We conclude that sensorial saturation is an effective analgesic technique that potentiates the analgesic effect of oral sugar. It can be used for minor painful procedures on newborns.

0084OTH

INTRACRANIAL PRESSURE DURING PROCEDURAL PAIN

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Background: Physiological changes provoked by pain may threaten the integrity of the CNS. In particular, intracranial pressure (ICP) regulates brain perfusion and its sudden increase may trigger brain haemorrhage. **Methods:** We measured intracranial pressure (ICP) in 51 healthy newborns (gestational age: 35–41 weeks) during blood sampling, by means of a tonometer applied to the anterior fontanelle. Peak ICP values were compared during three different types of blood sampling: from the external jugular vein, by heel prick and by heel prick with sensorial saturation. Sensorial saturation consists in giving sensorial stimuli during pain to arrest the transmission of pain to the cerebral cortex. **Results:** ICP peak values during heel-prick were higher than during jugular vein sampling ($M=26.22$ mmHg vs 21.036 mmHg; $p<0.0001$), though babies who underwent the latter procedure had high ICP values before sampling due to the body position required. Heel-prick with sensorial saturation was associated with a lower ICP peak ($M=11.75$) than sampling from jugular vein ($p<0.0001$). **Conclusions:** We concluded that heel-prick caused a greater rise in ICP than sampling from jugular vein and that sensorial saturation moderated the rise associated with heel-prick

0107OTH

DATA FROM FOS-THE FABRY OUTCOME SURVEY. CLINICAL FEATURES OF CHILDREN.

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Background: Fabry outcome survey (FOS) is a unique European database on the natural history of Anderson-Fabry disease (FD) and the effect of enzyme replacement therapy (ERT) with agalsidase alfa (Replagal). **Methods:** Data from 35 children (18 boys and 17 girls) below 18 years of age with Fabry disease, are analysed here. The median age at entry into FOS was 14.3 and 15.9 years in boys and girls, respectively. All diagnoses were confirmed by enzymology/mutation analysis. **Results:** More frequent signs and symptoms, affecting 50 -60% of the patients, were neurological and gastrointestinal features of the disease, including acroparaesthesia, altered temperature sensitivity, dyshydrosis, abdominal pain and altered bowel habits. Tinnitus, vertigo, fatigue and angiokeratoma were also present in more than 50% of patients. These clinical features were noted in early childhood (< 12 years of age) with a similar frequency in both sexes. **Conclusions:** Contrary to the common view that females heterozygous for Fabry disease are asymptomatic, these results have shown a similar distribution of signs and symptoms in both males and females at a very early age. This is the largest cohort of children with Fabry disease that has been studied. The clinical phenotype of this progressive disease in children is very different from that known in adults and most of its features are difficult to recognize because they are mainly based on subjective symptoms reported by the child. Misdiagnosis is common, and clinicians should be aware of the variety of signs and symptoms that even young children may present with, particularly as enzyme replacement therapy is now available.

0108OTH

FLUCTUATING OXYGEN INDUCES GLIOSIS IN NEONATAL RAT BRAIN

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Background and Aims: Frequent fluctuations in transcutaneous (blood) oxygen of preterm infants receiving supplemental oxygen, have been associated with the incidence and severity of the potentially blinding disease, retinopathy of prematurity (ROP)[1]. By translating the fluctuations recorded in a preterm infant into equivalent levels for rats, it has been possible to replicate these fluctuations in a computer-controlled laboratory model, and to reproduce some of the retinal changes observed in ROP in rats[2]. With more extremely preterm infants surviving than ever before, but many of them with neurological problems, the aim of the study was to use our laboratory model to investigate the effects of oxygen fluctuations on the developing immature rat brain. **Methods:** Newborn rats were either reared in room air (controls) or in a computer-controlled fluctuating oxygen (8kPa) chamber for 5, 7 and 14 days. At the end of each time period, rats were sacrificed and half the number of brains processed for immunohistochemistry and the other half for western blotting analysis of glial fibrillary acidic protein (GFAP) and myelin basic protein (MBP). **Results:** In rats exposed to fluctuating oxygen for 14 days (our standard exposure paradigm), GFAP expression was significantly increased in all regions of the brain, but by different amounts (30–100%). Similar data was obtained from rats exposed for 5 and 7 days. MBP expression was reduced by up to 40% in some brain regions of rats exposed to fluctuating oxygen for 14 days. **Conclusions:** The significant increase in GFAP, which is a sensitive marker of injuries to the CNS, is an indication that fluctuating oxygen causes injury to the developing immature brain. The reduction in MBP expression would suggest white matter regions to be vulnerable to oxygen fluctuations. Oxygen fluctuations may contribute to the brain injuries and neurological problems observed in preterm infants who survive. Acknowledgement: The project is funded by a grant from Action Research References: 1. Cunningham S, Fleck B, Elton RA, McIntosh N (1995). Transcutaneous oxygen levels in retinopathy of prematurity. Lancet 346: 1464–1465. 2. Cunningham S, McColm JR, Wade J, Sedowofia K, McIntosh N, Fleck B. (2000) A novel model of retinopathy of prematurity simulating preterm oxygen variability in the rat. Invest Ophthalmol Vis Sci. 41: 4275–4280

0110OTH

EARLY ABNORMAL COAGULOPATION PREDICTS MORTALITY IN PEDIATRIC TRAUMA

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Background: Coagulopathy early after injury has been shown to be a predictor of mortality in the adult Trauma population. The relationship of coagulopathy to mortality in pediatric trauma patients is unknown. **Methods:**Initial coagulation tests performed in a cohort of pediatric trauma patients treated at a Level I trauma center from January 1, 1995 to December 31, 2000 was analyzed. A multiple logistic regression was performed for prothrombin time(PT), partial thromboplastin time-(PTT), platelet count and their ability to predict mortality when controlling for pre-determined factors. **Results:**There were 3,359 patients(<19 years old) admitted to the Trauma Center in the study period. Of these, 2,224 patients had complete disposition data and 1,076 were in the final statistical model. The overall mortality rate was 5.26%(117/2,224). The median time to lab draw was 32 minutes, and 75 % of the patients having their labs drawn by 53 minutes. A PT >14 seconds was found in 35.6% (543/1,524) and a PTT >34 seconds in 10.2%(1540/1472) of patients. Platelet count of less than $100{,}000/10^3$cells/μl was found in 1.84%(38/2028). A multiple logistic regression model generated the odds of dying, with SDs, after controlling for:age, ISS, RTS, penetrating versus blunt trauma, gender, scene and trauma bay systolic blood pressure, hemoglobin, acidosis, head injury, time from injury to arrival, time of arrival to laboratory evaluation and length of hospital stay, of 4.19(1.88–9.84) for PTT, 2.19(1.00- 4.85) for PT and 0.19(0.013–2.92) for platelet count. **Conclusions:**The prevalence of early coagulation abnormalities in the pediatric trauma population is high and conveys an increased risk of death. Abnormal initial PTT is a strong independent predictor of mortality in this cohort.

0119OTH

CARDIAC ANOMALIES IN MULTIPLE GESTATIONS AND INVITRO FERTILIZATION

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Background/Aims: There is an increased incidence of congenital anomalies in neonates resulting from multiple gestations. Invitro fertilization, which is commonly related to pregnancies with 2 or more fetuses, has also been associated with increased risk of birth defects. We studied the incidence of congenital heart disease in a population of premature twins and triplets and its relationship with invitro fertilization. **Methods:** During the period 1997–2002 a total of 369 premature neonates resulting from 150 twin and 23 triple gestations were admitted in our Neonatal Intensive Care Unit. Sixty of 173 pregnancies (35%) were the result of invitro fertilization. Transthoracic echocardiography was performed to document the presence of structural heart disease when clinically indicated. **Results:** In the group of infants conceived with invitro fertilization 8/139 (5.7%) had congenital heart disease compared to 9/230 (3.9%) neonates conceived naturally. Although the incidence of congenital heart disease in neonates conceived with invitro fertilization was 1.5 times higher than that of neonates conceived naturally, the difference was not statistically significant ($p=0.45$). In the group of infants conceived with invitro fertilization 3/139 (2.2%) had chromosomal abnormalities (2 Trisomy 18 and 1 Trisomy 21), all of which had congenital heart disease. On the contrary, there were no cases of caryotypic abnormalities in the 230 neonates conceived naturally ($p=0.05$). When the cases of congenital heart defects related to chromosomal abnormalities were excluded, the incidence of congenital heart disease in the group of invitro fertilization was 3.6% versus 3.9% in the group conceived naturally. **Conclusion:** There is an increased incidence of chromosomal abnormalities in multiple births resulting from invitro fertilization, compared to those resulting from natural conception. Infants with chromosomal abnormalities have an increased risk of congenital heart disease. Therefore, detailed antenatal screening including fetal echocardiography and probably amniocentesis should be offered to all mothers carrying multiple fetuses, especially post invitro fertilization technology.

0124OTH

PLASMA CYTOKINES AND PROGNOSIS IN PERINATALLY ASPHYXIATED INFANTS.

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Background/Aims: To determine the relation between the initial plasma cytokine responses and the prognosis in term infants with perinatal asphyxia. **Methods:** Infants who were exposed to perinatal asphyxia (fetal distress, low 1-min. Apgar score) and admitted to the neonatal intensive care unit (n=23) were studied prospectively. Cytokine concentrations were measured from umbilical cord blood at 3 and 12 hours after birth. They were divided into 2 groups according to the survival and the presence of follow-up cerebral palsy (CP), ie, poor prognosis (death or positive CP, n=9) and good prognosis group (n=14). Enzyme-linked immunosorbent assays were performed for interleukin (IL)-1beta; IL-6; IL-18. **Results:** Cord IL-1beta and IL-18 concentrations were similar in both group infants. But infants with poor prognosis had significantly higher IL-6 concentrations than infants with good prognosis at 3 hours (369+/-291 vs 61+/-81 pg/mL, p=0.001) and 12 hours (403+/-320 vs 88+/-128 pg/mL, p=0.011). **Conclusions:** There was a significant association between neurologic outcome and plasma cytokine concentrations in perinatally asphyxiated infants, high plasma IL-6 levels may be an indicator of poorer prognosis in infants with perinatal asphyxia.

0132OTH

CEREBRAL BLOOD FLOW DECREASES AFTER DOXAPRAM ADMINISTRATION IN PRETERM INFANTS

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Background: Doxapram is used to treat apnea of prematurity when other treatment options failed. Effects of doxapram on cerebral perfusion have not yet been studied. However, this seems important, as developmental delay has been recently reported to be associated with doxapram therapy in preterm infants (Sreenan C et al. J Pediatr 2001; 139: 832–7). **Methods:** Fifteen preterm infants treated with doxapram were included in the study. Birth weight ranged from 380g to 1150g (Median 740g), gestational age from 24 to 27 weeks (Median 26 weeks). Infants received doxapram 2.5 mg/kg over a 30-minutes period followed by a continuous infusion of 0.5 mg/kg/h. Using Doppler sonography, blood flow velocities and the pulsatility index were measured in the anterior cerebral artery. Measurements were performed at baseline and 30 and 120 minutes after the start of doxapram. **Results:** Maximal systolic blood flow velocity (Vmax) decreased significantly from baseline at 30 minutes (Vmax baseline: 41 cm/sec +6.9; Vmax 30 min.: 35 cm/sec +8.9; p = 0.0017). At 120 minutes, the difference from baseline was no longer significant. Other parameters did not change significantly. **Conclusions:** Doxapram induced a significant decrease in maximal cerebral blood flow velocity. Further studies are necessary to confirm our findings and to assess clinical relevance.

0142OTH

LUNG MECHANICS, FUNCTIONAL RESIDUAL CAPACITY, AND DISTRIBUTION OF VENTILATION IN PRETERM INFANTS AND IN INFANTS WITH CONGENITAL DIAPHRAGMATIC HERNIA (CDH) DURING THE FIRST YEAR OF LIFE.

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Background: Normal respiratory function in childhood depends on lung development during the first year of life, which, in turn, could be markedly influenced by perinatal events such as premature birth, respiratory distress syndrome (RDS), chronic lung disease (CLD) and lung hypoplasia. **Aims:** The aim of this study was to compare the development of the breathing pattern, pulmonary mechanics, lung volumes and distribution of ventilation in "healthy" preterms (PREM) and in infants with CDH surgically corrected during the first days of life. **Subjects:** 14 preterm (BW 1372±414 gr; GA 30.5±1.7 wks) and 10 CDH infants (BW 3198±561 gr; GA 39.0±2.3 wks) were studied at a mean postnatal age of 6.3±2.7 and 7.8±4.5 months respectively. **Methods:** Breathing pattern (Tidal Volume, Vt; Respiratory Rate, RR) was measured with an ultrasonic flow meter. Pulmonary mechanics (Compliance and Resistance of the respiratory system, Crs and Rrs; Time Constant, Tc) was assessed by the single occlusion technique. Functional Residual Capacity (FRC) and distribution of ventilation, expressed as Lung Clearance Index (LCI), were measured by the sulphur hexafluoride washin/washout method. Measurements were performed in unsedated sleeping subjects. **Results:** Vt, RR, Crs were normal in both groups (Vt: PREM = 8.37±2.18 ml/kg; CDH = 8.75±2.26 ml/kg. RR: PREM = 41.35±17.26 b/min; CDH = 39.70±11.07 b/min. Crs: PREM = 2.35±1.12 ml/cmH_2O/kg; CDH = 2.16±0.51 ml/cmH_2O/kg). FRC was normal in preterms and significantly decreased in CDH infants (PREM=21.63±3.95 ml/kg; CDH=16.43±3.17 ml/kg; $p<0.005$). LCI was normal in preterms and significantly higher in CDH infants (PREM=7.94±1.11 ml/kg; CDH=12.30±1.68 ml/kg; $p<0.001$). **Conclusions:** Our study suggests that "healthy"preterm infants (without severe RDS and/or CLD) have a normal development of lung function in the first year of life. Infants with CDH continue to have some lung abnormalities (i.e. lower lung volumes and less homogeneous distribution of ventilation) suggesting the persistence of lung hypoplasia and dishomogeneity,even if the values of Vt, RR, Crs and Rrs are within normal limits. (Supported by Grant N° 02P000316 of the Italian Ministry of Health)

0157OTH

LATE EFFECTS OF PERINATAL HYPOXIA ON THE PULMONARY CIRCULATION

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Background: Adverse events occuring either in utero or during the neonatal period may result in a definitive imprint predisposing to a pathological response later in life. Chronic pulmonary vascular diseases and abnormal pulmonary vasoreactivity in adulthood may be associated with a hypoxic insult occuring around birth. In particular, human and animal studies have shown that individuals born in a hypoxic environment show later in life an exaggerated response following a prolonged re-exposure to hypoxia. **Aims:** To study the influence of perinatal hypoxia on chronic or acute secondary exposures to hypoxia in adulthood. To investigate mechanisms implicated in the abnormal pulmonary vasoreactivity in adult individuals born in hypoxia, with particular attention to the nitric oxide/cyclic guanosine monophosphate (NO/cGMP) signaling pathway. **Methods:** Pregnant mice were placed in a hypoxic environment (12% O2) 5 days before delivery and left in hypoxia with their litter for 5 days after birth. Pups were then raised in normoxic conditions until adulthood, when some were re-exposed to hypoxia before studies. Hemodynamics was assessed in anesthetized mice in normoxic and acute hypoxic conditions. Experiments consisted of closed chest measurements of systemic arterial pressure (SAP) and right ventricular pressure (RVP). RVP was used as an estimation of pulmonary arterial pressure. Pulmonary artery (PA) reactivity was tested by isolated vessel tension studies. Total lungs and PA mRNA expression was assessed by RT-PCR analysis, and endothelial nitric oxide synthase (eNOS) and soluble guanylate cyclase (sGC) activities by biochemical assays. **Results:** Under normoxic conditions, basal systolic RVP (sRVP) was different in each group. sRVP was higher in mice born in hypoxia than in control mice. Adults exposed to chronic hypoxia showed an increase range of sRVP as compared to controls, the highest sRVP being measured in mice born in hypoxia and re-exposed in adulthood. Isolated vessel tension studies showed no significant difference in the relaxation induced by acetylcholine (Ach) between PAs of control mice and mice born in hypoxia. However, PAs of mice exposed to hypoxia in adulthood showed a greater response to Ach than control vessels, the highest response being observed in PAs from mice born in hypoxia and re-exposed to hypoxia in adulthood. RT-PCR analyses in adult lungs showed a decrease in expression of eNOS mRNA in mice born in hypoxia, whereas expression of this mRNA was increased in mice exposed to hypoxia in adulthood. sGC activity was enhanced in lungs of mice exposed to perinatal and/or adult hypoxia, as compared to controls. **Summary:** Our results show that a perinatal hypoxic insult induces long term modifications on adult pulmonary circulation. These changes could be explained by permanent alterations of the contraction-relaxation mediators balance such as agents implicated in the NO/cGMP signaling pathway, by structural remodelling of the pulmonary vessels, or by both.

0176OTH

FINGERPRINT RECOGNITION PROVIDES CONFIDENTIALITY IN A NEONATAL UNIT.

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Background/Aims: As electronic medical records become more common, more notes exist without a written signature. It is important to identity those accessing a medical data system for reasons of confidentiality and for medico-legal reasons to verify who is entering a patient note or who is modifying an existing note. With our cotside computer system we have had parents accessing data about their own infant, and potentially they also have access to data on other parents' babies. There have always been these problems: in paper based records, a signature identifies the first person to make a note, but has the risk that someone can add or delete information at a later point without identifying themselves. Most existing systems electronic medical records use usernames and passwords for identification; passwords can be forgotten, exchanged or guessed. A biometric solution offers more reliable authentication and may be easier to manage and use. Our aim was to introduce fingerprint recognition to our computer system to establish confidentiality of access of patient medical data. **Methods:** In our neonatal unit, each cotside computer running the Badger Patient Data Management System has database and monitoring facilities. We have equipped each station with a Siemens ID mouse, with a built in fingerprint sensor. The fingerprint identification software we have developed is built in as a module on the system, so that whenever a member of the medical staff enters a new note or makes any changes to a patient record, a confirmation box asks the user to place their finger on the sensor. Within one or two seconds, the system takes the image of the users fingerprint, transmits it across the hospital network to a server which compares it to all the users who have been enrolled on the system; This retrieves their names and positions. The notes are then saved and this information is appended along with a date and time. **Results:** Speed of user recognition: the system being implemented in Edinburgh has been tested using a database of 20 users: recognition was almost instantaneous. The system is expected to identify a user within two seconds for up to 150 users, though for a larger user base there may be performance issues. **Confidentiality:** In no case has an unidentified user been able to get into the system using the fingerprint mouse. One of the advantages of using fingerprints to identify who is making or changing notes is that an audit trail can be kept on exactly which changes where made in the notes, by who and when. **Potential difficulties:** Whilst the technology is not difficult to integrate into an existing electronic records system, the addition of any new technology means a change in working practices and the way things are done on the unit. One of the difficulties in getting the system to work is getting the involvement of the people who will be using it and addressing security concerns. Implementation from the staff users, however, has been without problem. **Conclusions:** Biometric authentication, if used properly, can be more reliable than either a password based system or the signatures traditional on paper notes.

0184OTH

GHRELIN PLAYS A ROLE IN PATHOGENESIS OF LUNG HYPOPLASIA IN CDH

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Background/Aims: It was suggested that ghrelin (endogenous ligand for growth hormone secretagogue receptor (GHSR)) might be involved in foetal lung growth (mainly pseudo-glandular stage). To establish whether ghrelin plays a role in the pathogenesis of lung hypoplasia in congenital diaphragmatic hernia (CDH), we investigated the gestation-specific expression of ghrelin in foetal lung and the effects of prenatal treatment with ghrelin in nitrofen-induced CDH rat model. **Methods:** Nitrofen or just the vehicle (olive oil) was administered to Sprague-Dawley pregnant rats at day $9^{1/2}$ of gestation (term 22 days). Foetal lung mRNA gene expression of ghrelin was investigated by in situ hybridisation (ISH) at E18 and E22 both in normal and nitrofen-exposed foetuses. A group of nitrofen-treated rats was randomly selected in order to receive from day 14 to 18 either ghrelin (rat ghrelin 1–5: 100mg/kg BID, subcutaneous, Peptides International Inc.) or just saline solution. Total lung-to-body weight ratio was evaluated and lung samples were collected to measure total DNA and proteins. Five groups were created: Control (not exposed to nitrofen); Nitrofen-saline (exposed to nitrofen with no hernia); CDH-saline (exposed to nitrofen with hernia); Nitrofen-ghrelin (exposed to nitrofen and ghrelin with no hernia); CDH-ghrelin (exposed to nitrofen and ghrelin with hernia). Results are presented as mean±SEM. **Results:** In normal lung foetuses and at all gestational data points, ISH analysis revealed ghrelin expression (predominantly localized to the airway epithelial cells), which was stronger at E18 than E22. In nitrofen-exposed foetuses, however, ghrelin mRNA expression was significantly decreased particularly in those foetuses that presented CDH. Exogenous administration of ghrelin did not affect foetal body weight (Nitrofen, 4.9±0.1; Nitrofen-ghrelin, 4.8±0.1; CDH, 4.9±0.1; CDH-ghrelin, 4.9±0.1 g). However, ghrelin administration significantly increased the lung-to-body weight ratio both in nitrofen (Nitrofen-saline, 2.3±0.1; Nitrofen-ghrelin, 2.8±0.1; $p<0.01$) and in CDH (CDH-saline, 1.6±0.04; CDH-ghrelin, 2.1±0.1; $p<0.01$) groups. Of note, in Nitrofen-ghrelin group lung-to-body weight ratio was similar to control foetus (Control, 2.7±0.1; N-ghrelin, 2.8±0.1; p=n.s.). **Conclusions:** These findings suggest that: i) ghrelin has a role in foetal rat lung development; ii) expression of ghrelin is down-regulated in pulmonary hypoplasia associated with CDH; iii) prenatal exogenous administration of ghrelin enhance lung growth in nitrofen-induced CDH rat model. Further research is necessary to evaluate the potential clinical application for therapy based on ghrelin–GHSR signalling pathway in CDH.

0200OTH

INFANTILE ONSET POMPE DISEASE (IOPD) NATURAL HISTORY: A STUDY REPORT

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Background: Pompe Disease is an autosomal recessive neuromuscular disease caused by the deficiency of acid alpha glucosidase (GAA). Clinical forms range from a rapid fatal infantile onset disease associated with cardiomyopathy to a slowly progressive late-onset myopathy frequently evolving to respiratory insufficiency. Estimated incidence is 1:40,000. To characterize the natural history of IOPD, data from medical records were reviewed in a systematic fashion. **Methods:**This was a multinational, multicenter, historical cohort study. Inclusion in the study required documentation of onset of symptoms in the first 12 months of age and GAA enzyme deficiency or GAA mutation(s). Data abstracted from the medical records included demographics, family history, progression of signs and symptoms by organ system, diagnostic process, ancillary evaluations, treatment modalities, and resource utilization. **Results:** 300 cases were screened for inclusion in the study. A total of 168 IOPD cases from 33 study sites met all eligibility criteria. Geographical origin of cases was 54 (32%) from N. America, 46 (27%) from Asia, 36 (22%) from the EU, and 32 (19%) from the Middle East. 83 cases were male (49%) and 85 cases were female (51%). Ethnic distribution of cases was 80 (48%) Caucasian, 52 (31%) Asian, 22 (13%) Black, and 14 (8%) Other. 93 cases (55%) were born from 1995 to present; the remaining 75 cases (45%) were born before 1995. The median age at presentation of first symptoms + SD was 2.0 + 2.5 months (n= 166). Median age + SD at diagnosis was 4.7 + 8.8 (n= 165). Median age + SD at first ventilator use was 5.9 + 6.3 (n= 165). Median age + SD at death was 8.7 + 1.1 (n= 163). Kaplan-Meier distribution of survival confirmed previous smaller reports of early mortality in IOPD: By 12 months of age, 74% of IOPD cases had succumbed to the disease; by 18 months of age, mortality approached 86%. The most common signs/symptoms at presentation included cardiomegaly (92%, n=154), hypotonia (88%, n=148), cardiomyopathy (88%, n=147), and respiratory distress (78%, n=131). Failure to thrive was documented in 89 cases (53%), congestive heart failure in 84 cases (50%), and at least one episode of pneumonia in 76 cases (45%). At least 29% of patients (n=49) required one or more episodes of ventilator assistance during the course of the disease. IOPD diagnosis was confirmed by GAA activity measurement in 164 cases (98%) and by GAA mutation analysis in 10 cases (6%). 157 cases (94%) were hospitalized at least once in the course of the disease. Median number of hospitalizations + SD was 3.0 + 1.8 times. The median hospital stay + SD was 25.0 + 41.0 days. 90% of cases (n=151) were treated with medications. The most common used medications were cardiac (82%, n=138) and antibiotics (76%, n= 127). 130 cases (77%) received nutritional support. 93 cases (55%) received other support, including respiratory, physical and/or occupational therapy. **Conclusions:** This is the largest retrospective case review study performed to date in IOPD. In spite of widespread use of medications and other therapeutic modalities, mortality has changed little across the decades. Systematic chart review has allowed detailed documentation of the frequency, as well as the age at presentation of signs/symptoms in IOPD. This information is vital in the selection of clinical end points that measure the efficacy of therapeutic interventions in IOPD. A subgroup analysis on patients who survived beyond 12 months of age is needed. Such analysis could potentially identify clinical characteristics predictive of survival beyond 1 year of age in patients affected with IOPD.

0215OTH

OUTCOME OF ANTENATALLY DIAGNOSED CONGENITAL HEART DISEASE

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Aims: To assess the accuracy of diagnosis and outcome of all antenatally diagnosed congenital heart disease in a regional foetal centre. **Methods:** Prospective analysis of all specialist foetal echocardiography (September 2000 to October2002) where a diagnosis of congenital heart disease was made before or after birth. **Results:** Eighty-six women aged 16 to 43 years were seen at a median gestation of 23 weeks. The majority (72%) were referred because of an abnormal four-chamber view at routine 20-week scan. 19% had a chromosomal abnormality. 66% were born alive, 21% opted for termination of pregnancy (TOP), 5% had an intrauterine death (IUD) and 8% are awaiting delivery. The commonest lesions were a complete atrioventricular septal defect and Hypoplastic left heart syndrome. A ventricular septal defect was commonly found in association with other complex conditions. In 31% of fetuses, the diagnosis was not confirmed because TOP or IUD was not followed by postmortem, or they have not delivered yet. In 83% of those with a confirmed diagnosis, this was correct. 7% had significant differences from the antenatal diagnosis and in 10% the diagnosis was incorrect. Inaccuracies were in relation to complex lesions or the presence of associated congenital diaphragmatic hernia. Of the 57 babies born alive, 67% have survived, 28% died in the neonatal period and 5% in infancy. **Discussion:** Survival in infants born alive has improved significantly, despite their complex problems. The number of pregnancies terminated after cardiac diagnosis is less than other studies. Precise diagnosis remains difficult in the presence of complex lesions and congenital diaphragmatic hernia.

0217OTH

COMPARISION OF THREE DIAGNOSTIC MODALITIES OF HELICOBACTER PILORI INFECTION IN CHILDREN : HISTOLOGY, RAPID UREASE TEST AND SEROLOGY

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Backgroud and objective: Helicobacter pylori (H. Pylori) has been known to be a culprit in many diseases of children. During the last decade several modalities have been employed for diagnosis of H. pylori infection. Our objective was to compare three of these diagnostic tests in children: Histology, Rapid urease test (Rut) and serology (ELISA). **Material and Method:** This prospective study was performed on 50 children (3–14 years old age) with various complaints requiring upper gastrointestinal endoscopy in a pediatric center at the north of Iran (Babol city) from April 2000 to May 2001. In addition to histopathologic examination of each gastric antral speciemen (Giemsa staining) and performance of Rut on it (in endoscopy suit), a blood sample was sent for ELISA examination in each case. Our gold standard of H.pylori infection was any 2 positives of 3 tests. **Results:** Of the 50 individuals studies, 38% (n=19) were infected with H.pylori. The frequency of this infection was 45.1% in boys and 26.3% in girls. In our study, ELISA with an optimal and specific cut-off value calculated according to our studied population (o-23 ur/ml in ELISA supplied by RADIM) had a sensitivily of 89.4% and a specificity of 96.7% . Histology yeilded sensitivity and specificily resemble to ELISA. Also Rut had 89.4% sensitivity and 100% specificity. **Conclusion:** With standardization of ELISA in our study . We concluded that these three diagnostic tests had similar sensitivity but Rut was more reliable than others. Sensitivity and specifity of ELISA without standradization in children were lower. Key Words: Helicobacter pylori, Children, Serodiagnosis, Immunological tests, Diagnosis.

0228OTH

GENDER AND INTELLECTUAL ABILITIES IN ADOLESCENTS WITH LOW BIRTHWEIGHT

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Background/Aim: In adolescents with birth weight < 1500 gram or born small for gestation age, impaired intellectual development has been reported. Few studies have explored gender differences at this age. The aim of this study was to assess intellectual abilities in adolescent boys and girls with low birth weight. **Design/methods:** At the age of 14, two groups of adolescents with low birth weight (54 prematures with birth weight <1500 g (VLBW, 24 girls, 30 boys) and 60 small for gestational age born at term (SGA, 32 girls and 28 boys)) were compared to 83 controls with normal birth weight at term (NBW, 48 girls, 35 boys). Intellectual abilities were assessed by four subtests from WISC-III (Arithmetics, Vocabulary, Picture arrangement and Block design). Verbal IQ was estimated from Vocabulary and Arithmetics, Performance IQ from Picture arrangement and Block design. Full scale IQ was estimated from Verbal and Performance IQ, using the WISC-III manual. **Results:** Full scale estimated IQ for the groups were: VLBW: 78.2 (+22.0) (mean SD), SGA: 90.4 (+17.7) and NBW: 94.6 (+16.5). The girls in the VLBW group scored lower than the SGA and NBW on full scale IQ (26.6 and 26.9 points, p<.001), Verbal IQ (17.8 and 18.7, p<.005) and Performance IQ (32.2 and 30.5 p<.001) and on all the WISC-III sub tests (p<.01). There were no differences in Full scale IQ or Verbal IQ between the boys in the three groups. In the SGA boys, Performance IQ was slightly lower than in NBW boys (p<.05). Differences in scores between VLBW girls and VLBW boys were significant for Full scale IQ, Verbal IQ and Performance IQ (p<.005) and all the sub tests (p< .02). VLBW girls scored lower than the NBW girls on all subtests, the boys on Arithmetic's (# p<.01) and slightly lower on Picture arrangement (* p<0.05, table). For the SGA group, there was a slight

	Arithmetic	Vocabulary	Picture arrangement	Block Design
Girls	5.2 (2.7)#	6.2 (3.7)#	5.9 (3.6)#	5.1 (2.5)#
Boys	6.9 (2.4)#	9.3 (3.4)	8.1 (3.0)*	9.2 (3.0)

gender difference in Block design (p.<05) with girls outperforming the boys. For Full scale IQ and Verbal IQ, no differences were found either between groups or between girls and boys when comparing SGA to NBW. **Conclusion:** When assessed for intellectual abilities in adolescence, VLBW boys performed similar to NBW boys with exception of Arithmetics. VLBW girls performed lower on all items. This gender difference was unexpected and warrants further studies.

0240OTH

MENINGOCOCCAL MENINGITIS IN A PATIENT WITH COMPLEMENT C7 DEFICIENCY

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C7 deficiency is an autosomal recessive disorder that is mostly reported in Caucasians. It is a part of the deficiencies of terminal complement components which is associated with an increased susceptibility to infection of Neisseria species. We have experienced a patient of C7 deficiency, which was proven by cytogenetic studies, and was infected with Meningococcal meningitis. An 11-year-old girl was hospitalized complaining of fever, headache, vomiting, clouding of consciousness and skin rashes that had developed a day before admission. The cerebrospinal fluid (CSF) assay demonstrated bacterial meningitis by detecting Neisseria meningitidis Group B from the CSF culture. Accompanying with a substantial drop of serum C7 concentration (less than 0.5mg/dL), a decreased activity of complements (less than 14/CH50) was noted based on the hemolytic test. In order to identify mutations in the C7 gene, we performed a sequencing analysis of all exons and their flanking introns of the C7 gene. The patient was homozygous carriers of a splicing mutation (IVS4–1GT) and three polymorphisms of the C7 gene (c.665GA, c.1166GA, and IVS14+10GA). As expected, the patient's mother was heterozygous carrier of the mutation and all three polymorphisms but the patient's father had wild type alleles for all these variations. An extended haplotype analysis with 7 microsatellite markers flanking C7 gene revealed that a large deletion or a uniparenteral disomy of the C7 gene might be the cause of C7 deficiency in this patient. In summary, we have reported a patient with C7 deficiency carrying a yet unidentified mutation as well as a splicing mutation. When a meningococcal infection was noted in a relatively healthy child, the underlying complement deficiency should be identified.

0248OTH

A FATAL CASE OF SEVERE HEMOLYTIC DISEASE OF NEWBORN ASSOCIATED WITH ANTI-JK^B

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The most of isoimmune hemolytic disease of newborn (HDN) is induced by ABO & Rho(D) incompatibility, and the minor fraction was by the minor blood groups. Among these groups, Kidd system-induced HDN is rarely occurred, and is known to have mild symptoms with favorable prognostic outcome. On the contrary authors experienced a case exhibiting severe HDN which was associated with anti-Kidd (JK^b) antibodies. A male patient, blood type of AB, Rho(+), was admitted for jaundice on the fourth day after birth. His body weight was 3,000 g following a normal vaginal delivery by 39-year-old mother, with the birth history of gravida 3, para 2, during the gestational age of 37 weeks and 5 days. At the time of admission, the patient was lethargic and had decreased Moro reflex, with the laboratory data indicating hemoglobin value of 11.4 g/dL, reticulocyte count of 14.9%, and the appearance of moderate anisocytosis and severe polychromasia in peripheral blood smear. The seroanalysis showed total bilirubin of 46.1 mg/dL, direct bilirubin of 1.1 mg/dL, and strong positive result (+++) of direct Coomb's test. As a result of the identification of irregular antibody from the maternal serum, anti-JK^b was detected, which was also found in eluate made from infant's blood as well. Despite the management of exchange transfusion and intensive phototherapy, the patient died of intractable seizure and acute renal failure. Consequently, HDN was very likely due to JK^b incompatibility, since the fetal blood type was AB, Rho(+), JK^b(+), while the mother was indicated as AB, Rho(+), JK^b(-). Although minor blood group incompatibility-induced HDN is rarely occurred and generally shows mild clinical symptoms and favorable prognosis, we experienced one apparent case of HDN with severe clinical symptoms and fatal outcome.

0271OTH

USE OF SEROLOGY IMPROVES THE DIAGNOSTIC YIELD IN MENINGOCOCCAL DISEASE.

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Background: Meningococcal disease (MD) is the commonest infective cause of death outside the neonatal period. Diagnosis is currently based on culture or Polymerase Chain Reaction (PCR).

Aims/Objectives: To evaluate the introduction of routine paired serology in children with suspected MD. **Method:** Over a 3-year period any child aged <12 years admitted with suspected MD had a standardised diagnostic work-up including blood for culture, PCR and paired serology. The clinical characteristics of all children positive for MD by any of the methods were analysed within subgroups and against negative controls. **Results:** A total of 391 patients were investigated for possible MD, of which 40 were positive giving a population incidence of 1 in 2700 per child per year. 18 (4.6%) were PCR positive, 17 (4.3%) serology positive and 5 (1.2%) were blood culture positive. Only 2 children were both PCR and serology positive. The use of paired serology increased the diagnostic yield by 74%. Children positive for MD were significantly sicker than negative controls. There were no significant clinical differences between children positive for PCR compared with serology. **Conclusion:** The use of serology significantly improves the diagnostic yield in children with suspected MD. Although this does not affect the acute management of MD, it enhances epidemiological surveillance.

0273OTH

IMPACT OF INTRACRANIAL HEMORRHAGE ON CEREBRAL ACTIVITY IN PRETERM INFANTS USING AMPLITUDE-INTEGRATED EEG (AEEG)

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Background: The influence of intracranial hemorrhage on cerebral activity in very preterm infants has not yet been studied in detail. The amplitude-integrated EEG (aEEG) represents a useful method for continuous, non-invasive monitoring of cerebral function. **Aim**: Aim of this study was to investigate the impact of the different degrees of intracranial hemorrhages on the development of cerebral activity in very preterm infants. **Patients and methods:** 300 preterm infants beyond 30 weeks of gestational age have been monitored weekly until discharge. 128 of these patients had intracranial hemorrhage: IVH I (n=54), IVH II (n=36), IVH III (n=23), IVH III+ (n=15) (classification according to Volpe 1989). The cerebral activity was monitored using aEEG, an amplitude-integrated EEG-Monitor. The duration of aEEG-tracings was at least 6 hours. The evaluation of the obtained tracings was done by description according to the method of Hellström-Westas and by measuring minimal and maximal amplitudes according to the method of Thornberg and Thiringer. **Results:** Patients with hemorrhages of lower degrees (I or II) showed no significant differences in their aEEG-tracings in comparison to patients without any hemorrhage. Patients with hemorrhages of higher degrees (III or III+) showed a significant flattening of their tracings in time of the acute bleeding and a switch to discontinuity. In addition these patients showed sleep-wake-cycles later in their development than infants with hemorrhages of lower degrees or infants without hemorrhage. Cerebral seizures occurred more often in infants with hemorrhages of higher degrees. **Conclusion:** Patients with hemorrhage of higher degrees showed a flattening of their tracings, a more discontinuous activity and developed sleep-wake-cycles later in their development.

0274OTH

UMBILICAL VENOUS BLOOD SAMPLING DECREASES CEREBRAL OXYGENATION IN PRETERM INFANTS

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Aim: Using near infrared spectroscopy (NIRS) we showed that blood sampling from umbilical artery catheters (UACs) induces a significant decrease in cerebral blood volume (CBV) and cerebral oxygenation (Acta Paediatr 89:862–6.2000). Changes in CBV and cerebral oxygenation may be dangerous to the immature brain. The aim of this study was to assess whether blood sampling from umbilical venous catheters (UVCs) has any effect on CBV and cerebral oxygenation in preterm infants. **Methods**: 19 preterm infants, median birth weight 940 g (480 g – 1900 g), median gestational age 27 weeks (24 - 31 weeks) were studied during routine blood sampling from an UVC. Infants were studied during the first 4 days of life (median age 29 hours). Using NIRS changes in concentrations of cerebral oxygenated (O_2Hb) and deoxygenated haemoglobin (HHb) were measured, and changes in cerebral blood volume (CBV) and cerebral oxygenation index (HbD) were calculated. Heart rate, oxygen saturation, $tcPO_2$, $tcPCO_2$ and blood pressure (Dinamap) were registered simultaneously. **Results**: During blood sampling from UVCs O_2Hb decreased significantly, whereas HHb did not change significantly. This resulted in decrease in HbD, but no significant decrease in CBV. Heart rate increased slightly but significantly from baseline. **Conclusions**: Blood sampling from UVCs induced a significant decrease in cerebral oxygenation. In contrast to sampling from UACs, CBV did not decrease significantly. Further studies are necessary to find the optimal mode of blood sampling to avoid these effects in preterm infants.

0312OTH

CONTROL OF INSPIRED O_2 BY AN ADAPTIVE MECHANISM DURING CONTINUOUS POSITIVE AIRWAY PRESSURE (CPAP) ADMINISTRATION: A POTENTIAL FOR REDUCED OXIDATIVE STRESS

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Background: One of the most commonly administered drugs in the Neonatal Intensive Care Unit (NICU) is oxygen and it is potentially toxic in large doses. Excessive O_2 delivery to the developing preterm infant has been associated with bronchopulmonary dysplasia, BPD. Therefore, prevention of BPD by limiting O_2 exposure and the subsequent free radical formation prompts the need for more careful control of O_2 delivery. **Objective:** To evaluate a closed-loop adaptive control device which adjusts inspired oxygen (FiO_2) to maintain pulse oximetry within a set range, and to compare this to an aggressive, continuous manual O_2 adjustment protocol. A difference in overall O_2 required is the primary outcome variable measured. **Design/Methods:** Ten spontaneously breathing neonatal pigs (Bwt 2.2± 0.1 kg) were anesthetized, instrumented, given CPAP of 5 cm H_2O. All were then injured with intravenous oleic acid (OA=0.08 cc/kg), and randomized to manual O_2 adjustments (FiO_2 adjusts 5% every 15 min) or the adaptive control blender (FiO_2 adjusts every 4 sec) to maintain O_2 saturation 95±2%. Arterial blood gases, vital signs, pulmonary mechanics, functional residual capacity, and thoracoabdominal motion were evaluated hourly over 4 hrs. After which animals were sacrificed, and lungs were examined. **Results:** Both methods resulted in stable vital signs, gas exchange, pulmonary function, and O_2 saturation of 95±2% for the 4-hr period. Arterial O_2 saturation and arterial O_2 tension were not different between groups; yet, there was a 26% reduction in the O_2 requirement, $p<0.05$. Gross examination of the lungs revealed atelectasis and diffuse hemorrhage. Histomorphometrical assessment is ongoing. **Conclusions:** These results demonstrate that transient, rapid responses with the adaptive O_2 blender reduce overall inspired O_2 requirement during CPAP in this model of lung injury. For long-term O_2 administration, this technology could significantly diminish oxidative stress and thus reduce the potential for chronic lung injury. Disclosure: Supported by a grant from Hill-Rom, Air Shields, Inc. (Hatboro, PA).

0313OTH

HELIOX (He_2O_2) AUGMENTED CONTINUOUS POSITIVE AIRWAY PRESSURE (CPAP) IN A NEONATAL LUNG INJURY MODEL

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Background: Chronic lung disease (CLD) is a common illness that affects many preterm and sick term infants. Although multifactorial in nature, the inability to use exogenous corticosteroids, a former mainstay of therapy, has left clinicians with a difficult treatment dilemna. In light of this, a number of alternative therapies have been offered in an effort to minimize ongoing injury, decrease the work of breathing, and aid in growth and development of healthy lung parenchyma. **Objective:** To evaluate the effect of HeO_2, a helium-oxygen mixture, relative to a more traditional nitrogen-oxygen mixture on physiological parameters, pulmonary function, and O_2 requirement in a neonatal pig model of lung injury. **Design/Methods:** Spontaneously breathing neonatal pigs (n=10, Bwt 2.6± 0.2kg) were anesthetized, instrumented, given CPAP at 5 cm H_2O. After which all were injured with intravenous oleic acid (0.08cc/kg) to reduce to 50% of baseline lung compliance, and randomized to receive either an nitrogen-oxygen mixture, C, or HeO_2, H. Oxygen saturations were maintained at 95± 2% by a closed-loop adaptive control device that adjusts the amount of O_2 delivered (100–21%) every 4 sec for both C and H groups. Vital signs, arterial blood gases, pulmonary mechanics, and thoracoabdominal motion (TAM) were evaluated every 30 minutes. At 4 hrs animals were sacrificed, and the lungs were examined. **Results:** Vital signs, gas exchange, O_2 saturation and pulmonary function remained stable throughout the 4-hr study period for both groups. The use of HeO_2 revealed a time-averaged reduction in the O_2 requirement (17%), phase angle (ϕ)(21%), and respiratory rate (RR)(33%). This beneficial response was shown within the first 30 minutes of HeO_2 administration and was maintained over the entire 4-hr study. Gross examination of the lungs reveals atelectasis and hemorrhage. Histomorphometrical analysis is ongoing. **Conclusions:** HeO_2 administration in this model of lung injury reduces the O_2 requirement and decreases the work of breathing as demonstrated by more synchronized TAM and less tachypnea. Long-term prospective clinical studies are required to corroborate these model findings and to establish the role of HeO_2 in the treatment of CLD in the Neonatal Intensive Care Unit. Disclosure: Supported by a grant from Hill-Rom, Air Shields, Inc. (Hatboro,PA).

0318OTH

MULTIFACTORIAL ANALYSIS OF VERY LONG STAY (>100 DAYS) ADMISSIONS

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Background: Prolonged hospitalisation for children has negative effects on both the child and family. Little is known about the complex interplay of factors that cause prolonged stays. **Objectives:** To describe the incidence and diagnoses associated with very long (>100 days) medical paediatric admissions within a district general hospital (DGH) ward and define the factors that contributed to the length of stay. **Setting:** Altnagelvin hospital is a DGH serving a catchment of 161,000 people with a high level of socio-economic deprivation. **Methods:** All children with stays of greater than 100 days on the general paediatric ward over a 4-year period (1998–2001) were retrospectively identified. Case note review and a structured questionnaire were used to assess the effect of medical, nursing, social and resource factors on the need for ongoing hospitalisation of each child at 3 separate time intervals (admission, 100 days and just prior to discharge). **Results:** 4505 bed-days with estimated costs in excess of £1.5 million were attributed to 11 children over the 4-year study period. Their age ranged from 0 – 14 yr (median-3 mo) at admission, with a length of stay ranging from 108-1425 days (median 310). Beds occupied by these long stay patients on the ward at any given time ranged from 1 to 6 . Primary diagnosis was neurological in 54%, genetic in 27%, cardiac in 9% and other in 9% . Medical and nursing factors preventing discharge reduced exponentially with time, and conversely social and resource factors increased over time. **Conclusions:** These children represent an emerging health care challenge with a disproportionate effect on resources. Prolonged hospitalisation is associated with a significant increase in problems with family dynamics. Resource shortfalls in the community contribute to the failure of discharge of many of these children.

0320OTH

TRANSCUTANEOUS BILIRUBINOMETRY IN KOREAN INFANTS.

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Background/aims: Since non-invasive measurement of total serum bilirubin(TSB) was introduced by Yamanouchi, the accuracy and reliability of transcutaneous bilirubinometry had been investigated. To test the usefulness of a new transcutaneous bilirubinometer JM-103 from Minolta Company, which displayed actual bilirubin level instead of index number in previous model JM-102, we compare transcutaneous bilirubin(TCB) with TSB in Korean newborn infants. **Methods:** TCB was measured on 753 full-term newborn infants aged 3 to 7 days with Jaundice Meter JM-103 (Minolta Co., Japan). TSB was measured by AO bilirubinometer within 30 minutes after TCB measurement. Study infants were divided into five groups according to the number of flashes, from one to five, using on each measurement. TCB was measured over the forehead (glabella : TCB-F) and the chest (sternum : TCB-C) at the same time. Intraclass correlation analysis was done to test correlation between TCB and TSB, Kruskal-Wallis test was used to test the difference related to the number of flashes used in TCB-F or TCB-C. **Results:** There was linear correlation between TSB and TCB-F or TCB-C. Intraclass correlation coefficient between TSB and TCB was increased as number of flashes increased from one to five in both TCB-F and TCB-C from 0.7458 to 0.8981 and from 0.7096 to 0.8897 respectively. The range of TSB was from 1.4 to 19.9 mg/dL. Correlation coefficient between TCB-F and TCB-C was also increased from 0.8569 to 0.9783 as number of flashes increased from one to five. The discrepancies between TCB-F and TSB-F were not different significantly according to the number of flashes increased from two to five (p=0.981). The discrepancy between TSB and TCB-F using two flashes on each measurement was 1.04±0.99. **Conclusions:** With these results, we conclude that TCB measurement with JM-103 on the forehead using two flashes on each measurement can be appropriate clinical screening method of serum bilirubin level in Korean full-term newborn infants.

0324OTH

A NEW NEONATAL RENAL FUNCTION MARKER: CYSTATIN C REFERNCE VALUES

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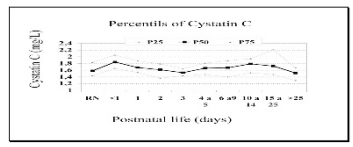
Background: Cystatin C (CC), is a proteinase inhibitor with a low molecular weight (13kDa), that is produced constantly in all nucleated cells. It is freely filtered in the renal glomeruli and reabsorbed and catabolished in the proximal tubules; so the plasma concentration of CC is determined by glomerular filtration. This makes CC an endogenous marker of renal function. Creatinine (Cr) levels depends on gender, muscle mass, and on the maternal levels in the first day of life. Recently a study showed that in the preterm tubular re-absortion of creatinine can take place. Therefore CC seems to be a better marker of glomerular filtration rate than plasma Cr in children and newborn (Pediatr Nephrol 2000; 15:105). The aim of this study is to determine the reference values of CC in pre term and full term babies, before using CC as a marker of GFR, and correlation with Cr levels.**Material and Methods:** CC was measured by nephelometric inmunoassay (Nephelometric Analyzer II, Dade Behring®) in 223 newborns. Patients were divided according to gestational age in groups : 1) 24 < 30 weeks′ GA (n= 77), 2): 30≤ 34 (n = 34), 3) >34< 37 (n = 34) and 4) ≥ 37 weeks (n= 78). CC and Cr were analysed in four intervals: A: first three days of live, B: between 3–14 days, C: between 14 -28 days and D: > 28 days. 183 blood cord samples for CC and Cr were also measured. All patients were normal for renal function, without renal impairment or malformation, and were not asphyxiated, with an Apgar test > 5 at 5 minute. The differences on the CC concentration during postnatal life was tested by the Kruskal –Wallis analysis. The studies of correlation by Spearman and Pearson tests. **Results:** Mean values and SD (mg/L) at different gestacional ages for CC were : group 1: 1,65 ± 0,47; group 2: 1,58 ± 0,41; group 3: 1,69 ± 0,26 and group 4: 1,71 ± 0,32. And for Cr (mg/dl) were: group 1: 0,8 ± 0,38; group 2: 0,67 ± 0,25; group 3: 0,8 ± 0,30, and group 4: 0,73 ± 0,2. There is a positive correlation between CC and Cr by Spearman test. Values and percentiles of CC during the first month af age are shown in figure with no significant differences. Also there is not a correlation between CC and gestacional age. There is a negative correlation between Cr and gestational age analyzing the data during postnatal life in the group A, B and C (p<0,001; <0,005 and p< 0,04 respectively).**Conclusions:** 1) Reference values for Cystatin C in newborn babies with clinically normal renal function vary between 1,58–1,71 mg/L. 2)Cystatin values are not significantly modified during the first month of life. 3) Cystatin C plasma concentrations were independent of gestacional age 4) Creatinine values are negatively correlated with gestational age during the first 28 days of live.



0326OTH

HYPOXIA INCREASES CD44 EXPRESSION IN VASCULAR SMOOTH MUSCLE CELLS

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Background/Aims: CD44 is a group of multifunctional transmembrane glycoproteins responsible for extracellular matrix interaction and migration in vascular smooth muscle cells (VSMC). Hypoxia is an inducer of pulmonary vascular remodelling, a pathology observed in several disorders, including persistent pulmonary hypertension of the newborn. We hypothesized that CD44 expression in VSMC is enhanced by hypoxia, providing thus a direct mechanism for the onset of vascular remodelling. **Methods:** Rat aortic smooth muscle cells (RASMC) were cultured in monolayers in buffered, serum-enriched medium and exposed to 21% (normoxic) or 1% (hypoxic) O_2 in the presence of 5% CO_2. CD44 gene transcription was analysed by northern blot. CD44 cell surface expression was quantified by flow cytometry after labelling with a FITC-conjugated anti-CD44H antibody (OX-49, Pharmingen). CD44 gene promoter activity was studied by transient luciferase reporter gene expression: the A7R5 fibromyoblastic cell line was transfected with the pGL2basic plasmid vector (Promega) under the control of sequences corresponding to the 5' flanking region of the CD44 gene. Promoter activity was measured by photospectrometry. Location of the hypoxia-responsive element in the promoter was then determined assessing the activity of a series of deletion mutant derivatives of the CD44 promoter. Each fluocytometry and transfection experiment was performed in duplicate. **Results:** CD44 protein and RNA are expressed by cultured RASMC under normoxic conditions. Exposure to hypoxia led to a time-dependant, 2- to 4-fold increase in protein expression. Similarly, CD44 RNA showed a 1.6 to 1.9-fold increase after 12–18 h of hypoxia. In the transfection experiments, the full-size CD44 promoter insert (1.371 Kb) showed a 2.5- to 4.2-fold increase in activity after 18 h of hypoxia, compared to a normoxic control. Promoter deletions encompassing 634 and 290 bp of the 5' flank also exhibited a strong hypoxic response (2.8 to 3.8 and 3.6 to 4.0-fold respectively). A further deletion of the promoter to 174 bp (-65 to +109) eliminated about 95% of its activity, but continued to show a 2-fold activity increase under hypoxic condition, suggesting that one or more hypoxia-responsible elements are located within the proximal promoter region. **Conclusions:** CD44 is known to be expressed at low levels by VSMC in the medial layer of arterial walls. Upregulation of CD44 gene expression has been shown to take place in VSMC during inflammatory disorders, leading to the formation of vascular occlusive lesions. We have demonstrated that hypoxia exerts a similar effect of CD44 upregulation in VSMC. The hypoxic regulatory element of the CD44 gene resides in the 65 bp proximal region of the promoter, where numerous putative transcription factor binding sites are located. The exact hypoxia responsive site remains to be determined.

0342OTH

CHORIOAMNIONITIS, FUNISITIS AND FETAL RESPONSE IN SEVERE PREMATURITY

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Background: Uncoupling protein 2 (UCP 2) of the inner mitochondrial membrane is supposedly involved in energy metabolism and control of the production of reactive oxygen species and therefore might play a role in inflammation. Aims: (i) to study the correlation between the degree of histological markers of inflammation in placenta and umbilical cord and fetal cytokine response; and (ii) possible involvement of UCP2 in fetal inflammatory response. **Methods:** In 71 infants born between 23+0 – 30+6 g.a., histological examinations of placenta and umbilical cord were performed with special regard to the localization and the degree of inflammatory infiltration (criteria by Salafia – modified). Umbilical serum levels of IL1beta and IL8 (ELISA), and umbilical whole blood levels of mRNAs for IL8, IL1beta and UCP2 (quantitative real time PCR with standardization of transcript levels using beta-actin) were measured. **Results:** The population was stratified (histological examination): without inflammation (n=10), chorioamnionitis only (n=27), moderate funisitis (n=16) and severe funisitis (n=18). We found the correlation between the degree of histological inflammation and increasing levels of IL8 (median 13 *vs* 14 *vs* 16 *vs* 54 pg/ml; $p<0.05$) and IL1beta (22% *vs* 31% *vs* 38% *vs* 65% above detection limit; $p<0.05$). Infants with funisitis were more premature (median g.a. 26+6) compared to those without funisitis (median g.a. 29+1), had higher IL8 mRNA (median 116 arbitrary units, AU *vs* 75 AU; not significant), lower IL1beta mRNA (median 27 AU *vs* 63 AU; not significant) and lower UCP2 mRNA (median 107 AU *vs* 205 AU; $p<0.05$). Significancy of the differences remained unchanged after correction for gestational age. **Discussion:** Inflammation was present in 86% of the placentas studied, funisitis in 48%, and severe funisitis in 25%. Even extremely premature fetuses are able to produce high levels of IL8. Positive correlation between the degree of histological changes in placenta, and umbilical cord and cytokine levels reflects the magnitude of fetal inflammatory response. Downregulation of UCP2 mRNA in umbilical cord blood of premature neonates may be an important part of fetal inflammatory response.

0354OTH

VIRTUAL ELIMINATION OF NECROTISING ENTEROCOLITIS FOR 5 YEARS-REASONS?

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Background: A standardised feeding regimen was adopted in 1997 for guiding enteral feeding of neonates<32 weeks' gestation during clinical trials (18 months each) involving erythromycin (n-73) as a prokinetic and carboxymethylcellulose (n=70) as a laxative as well as for during 2 years (n=155) without any trials. Most aspects of the feeding regimen (eg. milk increments-total volume/day, use of breast milk by choice etc) were not significantly different from current practices. **Results:** 298 neonates<32 weeks' gestation (<28 weeks: n=78) were enterally fed during the 5 years. Their demographic characteristics and median (interquartile) age in days at starting (AST) and days to reach full enteral feeds (FFT) of 150ml/kg.day were not significantly different during these 5 years: [AST: 5 (3–7.5), [FFT: 4 (3–7)] Only one case of definite NEC (≥Stage II) occurred during the 5 years. The time to reach full feeds was also reduced by over 54% (including for neonates<28 weeks gestation) compared with a historical cohort. **Conclusion:** Sustained reduction in the time to reach full feeds with virtual elimination of ≥Stage II NEC for 5 years indicates continued benefits of a standardised feeding regimen as a simple preventive strategy to prevent NEC. Whether our specific policy of no enteral feeds in presence of hemodynamic instability associated with PDA requiring indomethacin, and/or sepsis played a role in achieving the significant results needs controlled trials.

0370OTH

CIRCADIAN VARIATION IN MORTALITY AMONG CANADIAN INFANTS IN THE NICU

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Objective: The purpose of this study was to analyze the circadian variation in Neonatal Intensive Care Unit (NICU) mortality. **Methods:** The study used multivariable logistic regression analysis to compare the risk adjusted early neonatal mortality rates (death within 7 days of admission) of those infants admitted to the NICU during the nighttime (1700 – 0800) with the rates of infants admitted during the daytime (0800–1700). There were 5,300 infants in the study cohort. All infants less than 32 weeks gestational age with complete data who were admitted to 17 Canadian Neonatal Network NICU's from January 1996 to October 1997 were included. **Results:** 3,197 infants (60%) were admitted to the NICU during the nighttime. Infants admitted at night and those born during the day had similar characteristics regarding birth weight, gestational ages, Apgar scores at 5 minutes, incidences of antenatal corticosteroid treatment, congenital anomalies and gender. 31 neonatologists and 72 house staff (fellows, residents, clinical assistants and neonatal nurse practioners) provided NICU care during the daytime, but only 17 neonatologists and 30 house staff provided care at night. Logistic regression variables which were significantly (<0.05) predictive of early neonatal mortality included male gender, outborn status, Apgar score of <7 at 5 minutes, presence of congenital anomalies, low gestational age, high admission snap-II and admission to the NICU at night. (Odds Ratio: 1.4). **Conclusion:** The risk adjusted early neonatal mortality was 40% higher among infants < 32 weeks gestational admitted to the NICU at night compared with during the daytime. That is 19 excess deaths per 1000 infants.

0374OTH

C-MYC AND N-MYC GENE AMPLIFICATION IN MEDULLOBLASTOMA

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Background/Aims: Medulloblastoma is the most common malignant brain tumor in children. Current studies are trying to find relationships between the clinical behavior of these agressive embryonal tumors and molecular patterns of mutation in order to improve the staging system of the patients with regard to the treatment required. In the present study, we disposed of 80 medulloblastomas from patients diagnosed at 9 Spanish medical institutions. Preliminarly, we found in our series that patients with anaplastic tumors showed a markedly shortened survival. Hence, we search for genetic alterations that might correlate with this feature of poor prognosis. **Methods:** By use of real-time quantitative PCR we have analyzed in these tumors the amplification status of the human oncogenes C-myc (located on chromosome 8q) and N-myc (2p). For this purpose a short fragment of either C-myc or N-myc together with a short genomic sequence of the S18 ribosomal RNA gene, as an inner control gene, were coamplified by PCR. The fluorescence from the two differently labelled fluorescent probes for the oncogene and the control gene allowed us to determine the gene dosage in medulloblastomas of each of the two oncogenes studied. A reference range for each test gene was statistically determined from measurements of at least 40 normal tissue samples. In addition, genetic losses in several sites of the DMBT1 tumor suppressor gene (10q) were analyzed through a duplex PCR assay of both the test and a reference gene. **Results:** DMBT1 homozygous deletions were seen in approximately 15% of these tumors while genetic gains of myc oncogenes were also noted in a similar proportion of samples. DMBT1 losses did not seem associated with worse clinical outcome of the tumors. On the other hand, N-myc gene amplification did appear to be present almost exclusively in tumors of poor clinical result. **Conclusion:** While the lack of a correlative link between mutations of both C-myc and DMBT1 and survival of the patients suggests that alterations of these genes might play a role in early stages of tumor progression in medulloblastomas, N-myc alterations seem important for the acquisition of a more advanced malignant phenotype.

0385OTH

METABOLIC EFFECTS OF L-CARNITINE NUTRITIONAL SUPPLEMENTATION IN THE PRETERM NEWBORN INFANT.

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Background: After birth, an important increment of catabolic hormones (catecolamines, corticosteroids, glucagon) in plasma and a diminution and insuline peripheric resistence occurs. These mechanisms improve the transitory hyperglycemia and non esterified fatty acids, ketone bodies and amino acids (AA) are released. Carnitine (C) and branched chain amino acids (BCA) play an essential role in the neonatal response during the first period of life. The aims of the present study is: a) evaluation of C nutritional status in term (TN) and preterm (PN) neonates; b) analysis of the metabolic effect of C nutritional supplementation in TN and PN; c) study of the relationship between C and AA and the differences between both groups of neonates. **Methods:** Subjects: A total of 198 newborn infants were studied at delivery, 55 TN and 33 PN, and 5 groups of 22 TN or PN, clasified depending on the kind of nutrition they received (breast feeding, formula feeding or infant formula supplemented with 17 mg of L-carnitine/100 g of powder). Biochemistry: 1) C: Radiochemical assay based on DiDonato et al. technique (1984); 2) serum amino acids: HPLC as Peinado et al. published (1986). Statistical method: ANOVA, Tukey's test, Student-Newman-Keuls test, Kruskal-Wallis' test, χ^2 test, Fisher's test, regression analysis, Fisher's "Z" test to compare correlation coefficients. **Results & conclusions:** The TN showed insufficiency and deficiency during the early neonatal period. This fact is corrected at the end of the first month of life except for those babies fed with a non L-carnitine supplemented infant formula. The 12.12% of the PN have a C defficiency at birth (free carnitine<20 nmol/ml); the supplementation with 17 mg of L-carnitine/100 g of powder, determine higher insufficiency and deficiency of C at the end of the first month of life (45.45% and 40.91%, respectively). The infant formula supplementation with L-carnitine improve a benefitial effect in the TN, diminishing the muscle proteolisis and, so, the use of structural AA to obtain energy. On the contrary, probably due to the PN immaturity determine that this effect would not produce a benefit, causing even a higher BCA catabolism after blocking the dependent-carnitine systems. Prospective studies in PN are needed to approximate a more adequate supplementation. *CDTI –Profit Project 2000–2002. (Ministries of Industry and Science and Technology & Company-University of Granada Foundation

0386OTH

PREGNANT WOMEN DIET INFLUENCIES ON THE ORGANOCHLORINE PESTICIDES AND POLYUNSATURATED FATTY ACIDS CONTENT OF HUMAN MILK.

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Background:The diet of the breast-feeding mother impacts on the quality and quantity of the milk that she feeds her child. Milk can be a vehicle for toxins, such as drugs and their metabolites, viruses, nicotine, caffeine, alcohol, and organochlorine molecules such as PCBs, DDT, HCB, HCH and dioxins, which can harm the health of the breast-feeding child. The 24-hour recall diet was considered appropriate to adequately study the diet of breast-feeding mothers and was used in the present preliminary study to establish the possible relationship between the food items consumed and the presence of pesticides in her milk. **Material and Methods:** Subjects: 25 healthy breast-feeding volunteers aged between 17 and 35 years from two different areas were recruited [intensive agriculture zone, El Ejido (Almeria), from the "Hospital de Poniente" and urban zone, the city of Granada, from the Clinic University Hospital]. Methods: The milk samples were collected from colostrum, transition milk and mature milk. The questionnaires were administered three days before the three distinct periods of lactancy, so that every woman in the study completed nine questionnaires. A total of 225 dietary 24-hour-recall questionnaires were analysed, using a computer package based on a programme that manages a database containing the Wander food composition tables (Jiménez-Cruz, 1990), including the Spanish composition tables. Statistical analysis: Descriptive analysis, ANOVA, Bonferroni, Tahmane tests and correlation analysis were done. The SPSS 11.01 statistical programme for Windows was used. Results: Application of the Pearson correlation test to the results obtained in mature milk showed a certain positive correlation between the total intake of fats (%) and lactone-endosulfan (r: 0.39, $p<0.001$), methoxychlor (r:0.42, $p<0.0001$) and o,p'DDT (r:0.24, $p<0.03$). The intake of monounsaturated fatty acids was correlated with the amount determined in p,p′DDT in mature milk (r:0.25, $p<0.025$). The docosahexaenoic acid (DHA) concentrations measured in the milk samples analysed were close correlated with lindane, dieldrin, clordane, and different metabolites of endosulfan molecules, specially those more hydrosolubles (r:0.68, $p=0.005$; r: 0.56, $p=0.0028$; r:0.62, $p=0.0013$; lactone-endosulfan: r:0.54, $p=0.037$; diol-endosulfan: r: 0.55, $p=0.0035$). **Conclusions:** 1) The mother's fat intake directly influences the presence of some organochlorine molecules in the milk. 2) Close correlations are demonstrated between some structural long chain polyunsaturated fatty acids such DHA and the organochlorine pesticides in the mature milk. These results show that the breast-feeding could be a vehicle of non-beneficial substances that could have some deletereous effects and consequences in the baby, which have to be studied. This research was supported by a grant from the EU Commission European Project from 5th Framework Programme QLRT-1999–01422.).

0387OTH

GCK AND HNF-1A<CAPS> MUTATIONS IN CHILDREN WITH TYPE II DIABETES (MODY)

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Background: Maturity Onset Diabetes of the Young (MODY) is a genetically and clinically heterogeneous sub-type of Type II diabetes mellitus characterised by early onset, autosomal dominant inheritance and absence of autoimmunity. Mutations in six genes (MODY1-MODY6) have been shown to cause most of the MODY cases, and among them, glucokinase (MODY2) and HNF-1α (MODY3) genes are most frequently affected, representing around 70% of all MODY cases. **Methods:** Molecular analyses of glucokinase and HNF-1α genes were performed in 80 families with clinical diagnosis of MODY. Screening for sequence variants in both genes was performed by single-strand conformational polymorphism (SSCP) analysis. Samples that were seen to migrate abnormally in SSCP were sequenced to identify the mutation. **Results:** Alterations of the glucokinase gene sequence were detected in 38 out of the 80 families studied (47.5%). DNA sequencing identified 30 different mutations, 22 of them had not been described previously. HNF-1α gene was analysed in the remaining 42 families without changes in the glucokinase gene. Eight of them (10% of the total) presented mutations in this gene, being one of them a novel mutation. On the other hand, we have also noticed that most exons of HNF-1α are very polymorphic and thus, direct sequencing is the method of choice rather than SSCP analysis in this gene. **Conclusions:** 1)57.5% of MODY cases in our population are due to mutations in glucokinase (MODY2) or HNF-1α (MODY3) genes. 2)We describe 22 novel mutations in glucokinase gene and one in HNF-1α gene. 3)SSCP technique is not an efficient method for HNF-1α screening.

0388OTH

ANALYSIS OF THE GNAS1 GENE IN CHILDREN WITH PSEUDOHYPOPARATHYROIDISM

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Pseudohypoparathyroidism (PHP) consists of a heterogeneous group of endocrine diseases, whose common feature is resistance to PTH. It is divided into two types, I and II, on the basis of different responses of cAMP to PTH; in type I patients, renal cAMP production is markedly reduced after stimulus while type II patients show a normal cAMP urinary response, but a deficient phosphaturic response to PTH. PHP I can be classified in three different classes according to the presence or absence of additional endocrine abnormalities, such as resistance to TSH and gonadotropins, and the dismorphic features of Albright´s hereditary osteodystrophy (AHO), which may include short stature, obesity, brachydactyly, heterotopic ossifications and mental retardation. Individuals with AHO and resistance to PTH, TSH, and often additional hormones, are referred to as having PHP-Ia. These patients typically carry heterozygous inactivating mutations in one of the thirteen GNAS1 exons encoding the α-subunit of the stimulatory G-protein ($G_{s\alpha}$). Germline mutations of GNAS1 are also found in patients with pseudo-PHP who have AHO without hormonal resistance. Indeed, PHP-Ia and pseudo-PHP are typically found in the same family: PHP-Ia occurs if the mutation is inherited from a female carrier, whereas pseudo-PHP develops if the abnormal gene is inherited from a male. **Aim:** To analyze the GNAS1 locus in patients with pseudohypoparathyroidism and her first-degree relatives. **Patients and methods:** Five patients with PHP-Ia were studied. Genomic DNA of the subjects was extracted from peripheral blood leukocytes. The thirteen coding exons of GNAS1 gene were amplified, and then performed direct sequencing of PCR-amplified exons, in both directions (sense and antisense). E1A methylation status was determined by methylation-sensitive and insensitive retriction endonucleases (HpaII and MspI) genomic digestion and posterior amplification of the E1A promoter region with 5'- CGGGGACACTCAGTCGCGTCG-3' and 5'-GGCGCCCCTGCCT-TGTCC-3' (annealing temperature: 63°C). **Results:** The structural and methylation status analysis showed abnormal GNAS1 patterns in the five analysed patients, finding the following alterations: Gln31Stop (exon 1); 569–570delAT (exon 7); 625insT (exon 8); 283del15pb (exon 11) and anomalous methylation pattern of exon 1A. In two cases the mutation has maternal origin, whereas the other three ones occurred de novo. **Comments:** (1) PHP-Ia is associated to alteration in GNAS1 gene, which codifies for the alpha subunit of protein G. (2) The genetic alterations associated with PHP-Ia are nor merely restricted to mutations in the coding sequence but also to anomalities in the methylation status.

0389OTH

ANALYSIS OF THE CTLA4 GENE IN BASQUE FAMILIES WITH CELIAC DISEASE

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Background: Celiac disease (CD) is an autoimmune disorder caused by intolerance to ingested gluten that develops in genetically susceptible individuals. The contribution of HLA genes to the genetic risk to CD has been known for a long time, however, non-HLA genetic factors are likely to be required for the development of the disease. Several studies have associated the CD28/CTLA4 region on chromosome 2q33 with the disease in different populations. The CTLA4 gene encodes a receptor involved in the control of T cell proliferation and mediates T cell apoptosis. **Aim:** to determine the contribution of the CTLA4 gene to celiac disease in the Basque population. **Patients and methods:** 41 celiac families of Basque origin (43 patients with CD and 80 first-degree relatives). The CTLA4 A/G polymorphism at position +49 in exon 1 was typed by PCR-RFLP and the (AT)n microsatellite in the 3' untranslated region was studied by fluorescent polymerase chain reaction (PCR) followed by high-resolution electrophoresis. For disease association studies, the AFBAC (Affected Family Based Controls) approach was used and allele frequencies were compared in 2x2 tables. **Results:** The frequency of the A allele of 49 A/G polymorphism was 67,47 % in the celiac allele group compared with 70,13% in the AFBAC group. These differences were not significant. Analysis of the (AT)n polymorphism identified 17 different alleles ranging from 262 to 312 bp in length, but no allele was significantly associated with the disease. **Conclusions:** Our results did not show any evidence of association of any of the CTLA4 gene polymorphisms with the disease. This might result from population-specific differences in genetic and environmental susceptibility to celiac disease.

0390OTH

MOLECULAR ANALYSIS OF TRANSIENT NEONATAL DIABETES

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[1]Endocrinology and Diabetes Research Group, Hospital de Cruces, Bizkaia. [2]Peadiatric Endocrinology, Hospital Universitario Marqués de Valdecilla, Santander. *GEDINE: Spanish Group of Neonatal Diabetes. City: Barakaldo and Santander, Spain Transient neonatal diabetes (TND) is characterized by the appearance of hyperglycemia in the first month of life (some authors extended the time up to three months) and insulin is needed for, at least, two weeks. Genetic studies in patients with TND has shown alterations at chromosome 6q24, including paternal isodisomy (30% of cases), duplication of paternal 6q24 band (30%) and loss of the maternal methylarion pattern (10–15%).

Aim: To analyze the transient neonatal diabetes patients diagnosed in Spain. **Patients and Methods:** Eight independent families, with at least one affected individual that filled the diagnostic criteria of transient neonatal diabetes were analyzed. Duplication and isodisomy were studied employing microsatellites distributed along the chromosome 6, focusing on 6q24. Methylation status of maternal 6q was analyzed using methylation-sensitive and insensitive restriction enzymes and posterior amplification of the CpG islets of this region. **Results:** Three of the eight families presented genetic alterations. One family with paternal 6q24 duplication was identified. Two patients of two independent families presented loss of maternal methylation pattern. The principal difference among the families with genetic alterations and those who have no anomalies was the age at diagnosis: patients with transient neonatal diabetes and no genetic alterations had been diagnosed after the second month of life. **Conclusions:** (1) Diagnosed as neonatal diabetes should only refer to those patients that get the onset in the first month of life. (2) The three families that filled this criterion shown alterations on 6q24: paternal duplication in one family and loss of maternal methylation pattern in two independent families.

0391OTH

POPULATION SCREENING FOR PROGRESSION TO CELIAC DISEASE FROM BIRTH

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Background: Celiac disease (CD) is an autoimmune enteropathy that develops in genetically susceptible individuals, caused by the intake of gliadin in the diet. It has been proposed that early diagnosis of CD may reduce the risk of complications, and several studies have associated the length of the time of exposure to gluten with an increased risk of several complications and other autoimmune diseases. Thus, silent forms of CD need to be diagnosed as soon as possible. **Objectives:** To determine the prevalence of CD among children under three years of age and provide treatment to those patients diagnosed of CD. **Patients and methods:** At the time of birth, parents of 1100 healthy children born between October 1998 and December 1999 were asked to enroll their children in a screening program for early diagnosis of CD. The parents of 830 children accepted to participate and the study consisted in a first visit and anti-tTGase antibody determination at around 1.5 years of age and a second control at around 2.5 years of age. Patients positive for autoantibodies underwent intestinal biopsy for confirmation of CD. **Results:** Of the children initially enrolled, 613 and 484 returned for the first and second visits, respectively. None of them were positive for anti-tTGase antibodies in the first visit, but 9 presented anti-tTGase immunoglobulins in the second control. Of these 9 children, intestinal biopsy confirmed diagnosis of CD in seven patients, resulting in a minimum prevalence of CD of 1:118 healthy newborns. **Conclusions:** We observe a very high prevalence of CD, comparable to that observed in other European populations, which could even be higher if all of the children initially selected had returned for the second test. If the need for general screening of CD were accepted, we consider the age of 2–3 years as the best time for testing antibodies.

0394OTH

MOLECULAR ANALYSIS OF PROP-1 AND PIT-1 GENES IN CHILDREN WITH COMBINED PITUITARY HORMONE DEFICIENCY

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Introduction: The organogenesis and development of the anterior pituitary gland is under the control of several specific genes that act as transcription factors. Two of these specific pituitary genes, Prop-1 and Pit-1 are related with the differentiation and the function of thyrotroph, lactotroph, somatotroph, and gonadotroph cells. Congenital combined pituitary hormone deficiency (Congenital CPHD) has been linked with mutations in these specific pituitary transcription factors. **Aim:** To analyze Prop-1 and Pit-1 genes in a group of patients with Congenital CPHD. **Patients and methods:** Twenty-five children diagnosed of CPHD (at least two of the following hormone deficits: GH, Prl, TSH, ACTH, LH, FSH) were included in the study. Genomic DNA of the subjects was extracted from peripheral blood leukocytes. The three coding exons of Prop-1 gene, the six ones of Pit-1 and the exon-intron boundaries were amplified with a set of specific primers. Direct sequencing of PCR-amplified exons, in both directions (sense and antisense) was performed. The percentage of allelic frequencies of the following described polymorphisms: 27 T/C (exon 1), IVS1+3, and 3272 G/A (exon 3) (Prop-1 gene), versus eighteen normal controls, has been studied. **Results:** No mutations were found in Prop-1 and Pit-1 genes in any of studied patients. As it can be seen in the table, the presence of the described polymorphisms was not associated with the disease:

POLYMORPHISM	EFFECT	% allelic frequencies PATIENTS	% allelic frequencies CONTROLS
27 T/C	Ala9	42%	44,4%
IVS1+3	----------	36%	34,6%
3272 G/A	Ala86Thr	36%	34,6%

Comments: 1) The absence of molecular anomalies in these genes points out the heterogeneity of this pathology. 2) Previous studies have demonstrated that familial cases of CPHD are related to molecular alterations in the Prop-1 and Pit-1 genes. However, the percentage of sporadic cases that can be attributed to these molecular alterations is lower. 3) The presence of the polymorphisms is not associated with the pathology.

0403OTH

AGE OF GLUTEN INTRODUCTION IN SPANISH INFANTS

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Background/Aims: Age of gluten introduction has been delayed in Spanish infants during last 10 years. Nowadays, Spanish paediatric recommendation is that gluten-containing food should not be introduced in infant diet before 6 months of life. The objective of the study was to calculate the age of gluten introduction in Spanish infants and compare it with international recommendations. **Methods:** A total of 637 mothers with infants from 1 to 4 years old took part of this survey. The questionnaire has a retrospective design and was divided in three major parts: Demographic variables, breastfeeding practices and age of introduction of different food during weaning period and semi-quantitative dietary data of their younger infant. Food was categorized in the following groups:Ce-reals based products (infants cereals and bread), fruits, vegetables, beans, peas, diary products (yogurt and cow milk), eggs and meat, fish and poultry. Mothers were recruited in nurseries and in routine paediatric examinations all around Spain. The mean age of mothers in the study was 33,8 ± 4,2 years and the mean age of infants 2,3 ± 0,8 years. 15,7% of mothers had basically studies, 40,6% secondary studies and 43,7% universitary education. In a 50,7% of cases mothers were primiparous and in a 49,3% had 2 children or more. The study comprised 343 male infants and 294 female infants. **Results:** The mean age of gluten introduction was 7,3 ± 1,9 months. Normally, gluten commercial cereals were the first gluten-containing food that was introduced in infant diet but in 25,4% of cases, bread was consumed previously by infants. The mean age of gluten containing cereal products introduction was 8,0 ± 2,2 months and the bread mean age introduction 8,7 ± 2,7 months. 10,5% of infants began gluten consumption before six months of life. Age of gluten introduction was not related with maternal age, level of studies or number of children, but there was found a relationship between Spanish geographical regions and age of gluten introduction ($p=0,002$). There were found correlations between age of gluten introduction and exclusively ($p<0,001$) and total breastfeeding duration ($p=0,02$). The age of gluten introduction was significantly correlated with the age of gluten-free cereals introduction ($r=0,299$ and $p<0,01$) and age of weaning introduction ($r=0,257$ and $p<0,01$). **Conclusions:**1)Generally, Spanish paediatric recommendations are followed by mothers in relationship with age of gluten introduction (6 moths of life or later) and only 10,5% of mothers introduce the gluten before 6 moths of age in their infants diet 2) The only demographic characteristic that seems to be related with gluten introduction is the geographical region 3) It would be useful to insist mothers in the origin of gluten and which are the gluten containing foods to avoid early gluten introduction in their infants feeding.

0408OTH

A TRANSCUTANEOUS BILIRUBINOMETER AS A SCREENING TOOL FOR NEONATAL HYPERBILIRUBINEMIA

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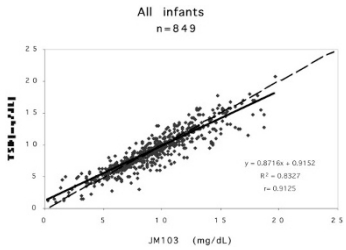
Background: Hyperbilirubinemia is a very common disorder in the immediate newborn period. The standard at present requires a heelstick serum bilirubin assessment to evaluate the level of bilirubin and, therefore, the possible need for phototherapy or further investigation to minimize the risk of kernicterus. As evaluations may be required frequently, in addition to the cost related to this there is a component of pain associated with heelsticks that may be minimized by a noninvasive approach. **Objective:** To evaluate the non-invasive Minolta/Air-Shields Transcutaneous Jaundice meter JM103 in direct comparison to total serum bilirubin levels (TSB) measured by heelstick test. **Design/Methods:** 849 newborns ≥ 35 weeks of gestation were studied in three hospitals over a one year period. TSB levels were obtained for each of the infants as part of routine newborn care. The TcB measurement was taken within 30 minutes of TSB and obtained by taking 3 measurements (head, chest, and abdomen). The JM103 were compared to the TSB by Pearon's correlation. **Results:** This non-invasive device demonstrated a tight correlation between TSB and TcB values overall. In the non-white population, the correlation was less close and differences between the TcB and TSB measurements tended to increase with rising TSB values thereby overestimating the TSB. The relationship to Pearon's Correlation as shown below:



Conclusions: The TcB using the Minolta JM103 Bilirubinometer correlated very closely with TSB levels over the range of TSB measured in this study. Because the measurement technique is so rapid and simple, it is easy to perform repeated measurements over time that will decrease the likelihood of error. The JM103 is a reliable non-invasive device that can determine the necessity of obtaining a serum bilirubin decreasing the need for the traditional heelstick test. **Disclosure:** supported by a grant from Minolta/Hill-Rom , Air-Shields, Inc. (Hatboro,PA).

0415OTH

DEGREE OF PARENTAL INVOLVEMENT IN ETHICAL DECISIONS IN SWISS NICUS

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Background: The degree of parental involvement in ethical decisions concerning term and especially extremely preterm newborns undergoing intensive care or infants presenting with major malformations remains a frequently debated issue among neonatologists. The EURONIC study (11 European countries) showed a broad range of physicians' attitudes towards parental involvement. A large number of respondents from 7 countries stated that they would implement their decision without involving parents. Interestingly, male or junior physicians and neonatologists performing follow-up were more prone to involve parents in decision making, while hospital ethics committee negatively influenced parental involvement. This survey showed moreover in every country that physicians follow parents' wishes more often when asking for continuation of treatment rather than for limitation or withdrawal. Aim: As nationality remained a strong predictor of neonatologists' attitude, we were interested to examine how neonatal care professionals in Switzerland thought about the role of parents when ethical decisions were to be taken concerning their infants. **Methods:** The anonymous, self-administered EURONIC questionnaire (kindly made available by the EURONIC Study Group) was sent to all 11 neonatal intensive care units in Switzerland. 88 physicians and 99 nurses completed the questionnaire (overall response rate 79%). **Results:** 47% of Swiss neonatologists want parents to actively take part in ethical decisions of their newborn. In contrast, 47% prefer to take into account the wishes and attitudes of the parents rather than a direct involvement, whereas only 4% think that the parents should choose the course of action for their baby. 80% of physicians against direct parental involvement argue that parents are not in the right state of mind to decide, or that they cannot fully understand the possible options and consequences and finally that they could later feel guilty and should be spared the burden of such decisions. No doctors agree on not involving parents at all. Only a minority fear that direct parental involvement could jeopardise the trust in the physician, lead to legal steps against neonatologists or put inappropriate pressure on the staff. Only 11% of physicians and 21% of nurses wish that parents' opinions should be given more weight. Once the best approach for a given baby has been found, more physicians than nurses would change their opinion in case of parents' opposition. **Conclusion:** The same percentage of Swiss neonatologists argues in favour of either direct or indirect parental involvement in decision making. Only a minority of Swiss physicians and nurses feel that parental involvement should be stronger. At our institution, we have developed a model of multidisciplinary ethical decision making in which a group of doctors and nurses directly involved in the care of the infant ("inner circle") has to formulate and find a consensus on the most appropriate course of action. The parents are then approached by their doctor and nurse and asked permission to take the approach, which is felt to be the best in the infants' interest. With this model, parents take part in the decision without being directly involved in the often difficult process of finding out the best course of action.

0416OTH

MUCOPOLYSACCHARIDOSIS TYPE I (MPS I)-GENETIC ANALYSIS OF 38 ITALIAN PATIENTS

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Background: MPS I is a rare lysosomal storage disease with recessive inheritance, due to á]-L-iduronidase deficiency. The phenotype is a "continuum" from the severe form (Hurler disease) to the mild one (Scheie disease) with different therapeutic approaches. Information on genotype/phenotype correlation could be useful for therapeutic decision in the first two years of life and for genetic counseling. Our aim was to obtain useful information for genotype/phenotype correlation by analysing IDUA gene. **Methods:** IDUAgene was analysed by direct sequencing in 38 MPS I Italian patients (25 Hurler, 9 Hurler/Scheie and 4 Scheie). **Results:** Mutations were found in 73 out of 76 alleles (91%), thus reconstructing the complete genotype in 35 patients, while only one mutation was found in 3 cases. 14 novel mutations were found out of a total number of 26. Four mutations were found in 55.37% of alleles: W402X(9.21%), Q70X(14.47%), P533R(14.47%)and G51D (17.1%). Mutations W402X, G51D and Q70X were associated to a severe phenotype as already reported. P533R resulted in mild or intermediate phenotypes in 3 homozygous patients and was found in heterozygosity in other 4 patients with intermediate phenotype. Other rare mutations (1251delC, C53X, 1902–1903del2, 755–759del5, 468–470del3, A160D, 1839–1867del29 e P183R) were associated to severe phenotypes both when homozygous or heterozygous with other known severe mutations. **Conclusions:** Our study demonstrates that genetic analysis allows genotype/phenotype correlation in many cases of MPS I, although the wide spectrum of mutations found in the Italian population makes it lacking for some patients. We thank Fondazione Pierfranco e Luisa Mariani and Associazione Italiana Mucopolisaccaridosi for their generous financial support.

0419OTH

MOLECULAR ANALYSIS OF NINE CHILDREN WITH BRANCHIO-OTO-RENAL SYNDROME

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Background: Branchio-oto-renal (BOR) syndrome is an autosomal dominant disorder characterized by the association of branchial cysts or fistulae, external ear malformation and/or preauricular pits, hearing loss, and renal anomalies, all of them with variant degrees of severity. Mutations in the EYA1 gene, a human homologue of the Drosophila 'eyes absent' gene, have been described as responsible of the syndrome. The existence of various alternatively spliced transcripts of this gene makes it difficult to identify mutations in families with the clinical diagnosis of BOR syndrome. Moreover, the existence of another gene(s) probably implicated in the pathology of BOR-related phenotypes has been proposed. **Aim:** To analyze the EYA1 gene in nine patients with branchio-oto-renal (BOR) syndrome. **Patients and methods:** We report here nine children with clinical features suggesting BOR syndrome. Genomic DNA of the subjects was extracted from peripheral blood leukocytes using standard methods. Amplification of all coding exons and flanking regions of the EYA1 gene was carried out using primers previously described. Amplified products were purified to eliminate remaining primers, and direct nucleotide sequencing was performed in both directions (sense and antisense). **Results:** Five of the cases, all of them with the complete phenotype, presented an altered genotype (a novel splice site mutation, two novel nonsense mutations, a new missense mutation and a previously described missense mutation). In one of these cases, no mutation was detected neither in the parents nor in the proband's sister, suggesting it was a 'de novo′ mutation. The other four children did not present any molecular alteration in the EYA1gene. **Comments:** Our findings support the existence of genetic heterogeneity of the BOR syndrome and other related phenotypes, with two or more genes involves, as it has been previously reported in the literature.

0436OTH

DRUG WITHDRAWAL AFTER PICU: ARE WE DOING ENOUGH?

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Background/aims: To evaluate the number of paediatric intensive care units (PICUs) identifying a problem with iatrogenic drug withdrawal. To ascertain the number of units using guidelines for weaning sedation and analgesia, using a monitoring score to assess drug withdrawal and a treatment protocol for withdrawal symptoms. **Methods:** A telephone questionnaire of all 30 English and Scottish PICUs in which the nurse-in-charge was asked five initial questions (table)

Results:	YES	NO
Do you think that there is a problem with drug withdrawal after admission to PICU?	18	10
Is there a written unit guideline on analgesia/ sedation on PICU?	18	10
Do you have a written guideline for weaning them?	7	21
Do you have a written monitoring score for drug withdrawal?	3	25
Do you have a written guideline on management of drug withdrawal?	4	24

Reasons given for a problem were: weaning too quickly (6/18), too high doses (3/19), unit guideline not followed (3/18).In the 10 units where no problem was identified, reasons cited included recent changes in practice, such as the earlier introduction of alternatives to intravenous sedation, increased continuity of care, and the particular interest of individual team members. **Conclusions:** There is evidence from the literature, that protocols to predict drug withdrawal after PICU admisión are successful.It is clear that iatrogenic withdrawal is considered a clinical problem by many UK units. The majority of UK PICUs do not have written guidelines for identifying and monitoring those at high risk of iatrogenic drug withdrawal nor do they have written guidelines on the treatment of drug withdrawal. Introduction of such guidelines could minimise or eliminate withdrawal and improve appropriate standards of care.

0437OTH

EFFECT OF PLASMA FROM PREECLAMPSIA MOTHER AND FETUS ON THE HUVEC CELLS

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Aims : We want to study the possible different effects between plasma from preeclampsia mother and her fetus on apoptosis of human umbilical venous endothelial cells and vascular adhesion molecules. Background : Current concepts of preeclampsia have been focused on dysfunction of the maternal vascular endothelium as the central pathogenetic feature of the disease. And it may also have effects on the vascular function of the fetus. But it is uncertain that maternal preeclampsia has a harmful effect on fetal or neonatal vascular endothelium. Our purpose was to determine whether plasma from the fetus of preeclamptic mother has the same effect on human umbilical endothelial cells as the plasma from their mothers. **Design/Methods :** Isolated and cultured human umbilical vein endothelial cells were exposed to preterm fetal and maternal plasma of preeclampsia (cord plasma n=5, maternal plasma n=5). Electrophoresis onto 10% SDS-PAGE at 150V and western immunoblotting with anti-caspase 3 rabbit polyclonal Ig G were done with cultured cells. Quantitative determination of sICAM-1 and sVCAM-1 were done with fetal and maternal plasma of preeclampsia(term cord n=10, term mother n=10, preterm cord n=10, preterm mother n=10) and compaired with normal controls(term cord n=10, term mother n=10, preterm cord n=10, preterm mother n=10). **Results :** 1) Caspase-3 activity in the endothelial cells was significantly higher were stimulated with preeclampsia maternal plasma than with preeclampsia fetal plasma. 2) Plasma ICAM-1 concentration was higher in preeclampsia maternal plasma than fetal plasma and control maternal plasma. 3) Preterm fetal groups showed higher plasma ICAM-1 concentration than term fetal groups and there were no significant differences in the plasma ICAM-1 concentration between preeclampsia fetus and control fetus. 4) Plasma VCAM-1 concentration showed no significant differences in the study groups. **Conclusions:** Plasma from the fetus of preeclamptic mothers has not the same effect on human umbilical endothelial cells as the plasma from their mothers. Our results suggest the presence of some factors in the fetal plasma that inhibit the endothelial cells to undergo apoptosis and inhibit the activity of cell injury mechanism

0443OTH

DO IL-6 AND TNF-A CROSS BLOOD-BRAIN-BARRIER? A STUDY IN ASPHYXIATED AND SEPTIC NEWBORNS

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Background: Evidence suggests that inflammatory cytokines contribute to pathogenesis of hypoxic-ischemic encephalopathy (HIE) and neonatal sepsis. **Objective:** Evaluate IL-6 and TNF-α plasma and CSF levels in term newborn infants with HIE, and in septic newborns comparing them with a control group. **Design/Methods:** The study included 3 groups of term newborn infants: 19 asphyxiated neonates characterized by Apgar scores ≤4 and ≤6 in the first and fifth minutes of life respectively,umbilical cord pH<7.20,and necessity of bag and mask ventilation for at least 2 minutes just after birth; 19 septic infants with no meningitis,with Apgar scores ≥9 in the first and fifth minutes of life; 20 normal control infants with Apgar scores ≥9 in the first and fifth minutes of life.Blood and CSF were collected within the first 48 hours of life to determine IL-6 and TNF-α levels. IL-6 and TNF-α were measured by enzyme-immunoassay. **Results:** The three groups were similar in gestational age, birth weight, proportion of AGA/SGA, mode of delivery, and mean time of blood and CSF collection.Median plasma levels of IL-6 were similar in asphyxiated and septic infants(44.3 pg/ml and 89.7 pg/ml respectively), significantly higher than in control infants (20.2 pg/ml)($p<0.0001$). Median plasma levels of TNF-α were similar in asphyxiated and control infants(5.2 pg/ml and 4.4 pg/ml respectively) , significantly lower than in septic infants(18.6 pg/ml)($p<0.00001$) . In asphyxiated newborns, median CSF IL-6 and TNF-α were significantly higher than in neonates with sepsis and controls . Median CSF IL-6 was significantly higher in newborn infants with sepsis than in controls, and median CSF TNF-α was similar in newborns with sepsis and controls. CSF/plasma ratio for IL-6 and TNF-α was similar in control and septic infants, lower than in asphyxiated infants($p<0.0002$ for IL-6,$p<0.00001$ for TNF-α). **Conclusions:** IL-6 plasma levels were equally high in asphyxiated and septic term neonates. TNF-α plasma levels were high in septic but not in asphyxiated newborn infants. Septic infants presented high IL-6 and low TNF-α levels in CSF. Term newborn infants with HIE presented high IL-6 and TNF-α CSF levels. High CSF/plasma ratios for IL-6 and TNF-α in asphyxiated infants suggest a local production of these cytokines inside of the CNS in term newborn infants with HIE. TNF-α levels in CSF of septic newborn infants were similar to those of control group suggesting that there is no transport across the blood-brain barrier. Normal IL-6 CSF/plasma ratio in septic infants suggests passage of IL-6 across blood-brain-barrier in newborn infants with sepsis and no meningitis.

0449OTH

REOXYGENATION INJURY INCREASES MYOCARDIAL MMP-2 ACTIVITY IN HYPOXIC NEWBORN PIGLETS

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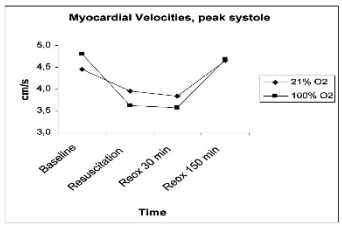
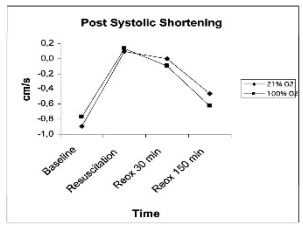
Background: Perinatal asphyxia may result in myocardial dysfunction secondary to global ischemia. During resuscitation it is important to avoid further damage due to reoxygenation injury. Whether resuscitation of the newborn should be performed with ambient air or 100%O_2 is still a controversy. **Aim:** In order to explore any differences in myocardial function between these two methods, we studied left ventricular (LV) function by Tissue Doppler Imaging (TDI) during global ischemia and subsequent reoxygenation with ambient air or 100%O_2. **Methods:** Newborn anesthetized piglets (12–36 h) were exposed to hypoxemia by ventilation with 8% O_2. When mean arterial blood pressure decreased to 15mmHg or base excess (BE) was ≤ -20mmol/L, the piglets were resuscitated with either 21% (n=10) or 100% O_2 (n=10) for 30 min, then ventilated with ambient air for 2h. Blood samples were analysed for CardiacTroponin I (CTnI). TDI was assessed from apical 4-chamber view at baseline, start resuscitation, and during reoxygenation. Myocardial velocities (Fig 1, 2) were measured at mitral annulus during peak systole and early diastole (post-systolic shortening (PSS)). **Results:** CTnI increased tenfold from baseline to endpoint 0.05 (±0.003) vs 0.34 (±0.1) μmol/L (mean (±SEM), $p< 0.001$), confirming a serious myocardial injury, although blood pressure, heart rate, BE, pulmonary artery pressure and CO/kg restored to baseline values. TDI verified LV dysfunction during systole in hypoxemia 3.70 (±0.2) cm/sec compared to baseline 4.63 (±0.3) cm/sec, $p<0.001$. During early diastole, TDI were predominantly negative at baseline, positive during hypoxemia and early reoxygenation, indicating PSS. LV function restored to baseline values at endpoint. There were no differences in LV function whether the piglets were resuscitated with ambient air or 100%O_2. **Conclusion:** Myocardial dysfunction evaluated by TDI, verified ischemic alterations during peak systole and pathological PSS. 100% oxygen during resuscitation offered no benefit compared to ambient air assessed by TDI.





0463OTH

HYPOXIC-ISCHEMIC BRAIN INJURY INDUCES SELECTIVE NEURAL DEATH

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Background/Aim: Hypoxic-ischemic injury represents one of the major causes of morbility in preterm neonates. To study early damage of hypoxic-ischemic injury in the brain. **Methods:** We have used an experimental model of perinatal disease in fetal lambs at 80–90% of gestation. Hypoxic-ischemic injury was performed by partial occlusion of umbilical flow during 60 minutes. We have evaluated the histopathological changes in the brain after 0 and 3 hours survival. Lambs were sacrificed and brains fixed by perfusion. Serial gross sections were performed and multiple blocks of the different brain territories selected. Samples from different areas were embedded in paraffin wax for light microscopy and in Epon for ultrastructural examination. Quantification of the severity, extension and distribution of damage were carried out in the following regions: cerebral cortex (frontal, parietal, temporal, occipital); basal nuclei; hypothalamus; thalamus; hippocampus; amygdaloid body; mesencephalon; pons; cerebellum (cortex and intracerebellar nuclei) and white matter. **Results:** In the two treated groups (mesencephalon, pons, intracerebellar nuclei) scattered great-size cells, whose cytoplasm has lost detail and acquired a homogeneous, eosinophylic appearance. Nuclei showed a loss of chromatin pattern. In the ultrastructural study, these cells were dense, with well-defined contours although under greater magnification the cells had a generalized faded appearance. Thus, the cells showed karyolysis, with nucleoli preserved but with loss of nuclear envelope. In none of the experimental groups, areas of necrosis, hemorrhage or increase in cellularity were observed. **Conclusion:** In our model of perinatal asphyxia by partial occlusion of umbilical cord, early brain injury can be assessed as brief as 3 hours after hipoxia-ischemia event. This work has been supported by two grants from the Fondo Investigaciones Sanitarias of the Ministerio de Sanidad (FIS01/0110–1 and FIS01/0110–2) and a grant from the University of the Basque Country (1/UPV075.327-E-14885/2002).

0464OTH

APOPTOSIS IN OLIGODENDROCYTE-LIKE LINEAGE AFTER HYPOXIC-ISCHEMIC INJURY

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Background/Aim: We set forth the utilisation of an experimental model of perinatal disease in premature a lamb, that allows us to study early damage of hypoxic-ischemic injury in the brain. **Methods:** 15 fetal lambs at 80–90% of gestation (124–133 days of developmental age; at term: 145 days). 60 min or 180 min after hypoxic-ischemic injury, lambs were killed and brains fixed by perfusion. Serial gross sections were performed and multiple blocks of the different brain territories included to apoptotic quantitation. Apoptotic nuclei were identified by modified TUNEL method first proposed by Gravieli et al. (1992). One-factor ANOVA was performed ($p<0.05$). **Results:** Apoptotic figures correspond with small and round cells located both in white and gray matter but also in gray matter. In some cases these cells were located in the neighbouring neurons. The number of TUNEL positive cells was increased at 3 hours post-injury with respect to both control and 0 hours hypoxic-ischemic event. An increase ($p<0.005$) in number of apoptotic was observed in the cerebral cortex, cerebellum and as well as mesencephalon and pons. **Conclusion:** In summary, our results show an increase in the number of apoptotic cells after hypoxic-ischemic injury and suggest that the positive-TUNEL cells could correspond to oligodendrocyte lineage. This work has been supported by two grants from the Fondo Investigaciones Sanitarias of the Ministerio de Sanidad (FIS01/0110–1 and FIS01/0110–2) and a grant from the University of the Basque Country (1/UPV075.327-E-14885/2002). Gravieli Y., Y. Sherman, S. Ben: Identification of programmed cell death in situ via specific labelling of nuclear DNA fragmentation. J. Cell Biol. 119: 493–501, 1992.

0465OTH

REGULATION OF CEREBRAL NITRIC OXIDE, L-ARGININE AND L-CITRULLINE DURING HYPOXEMIA IN NEWBORN PIGS

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Background: It is proposed that an intercellular citrulline-nitric oxide (NO) cycle is operating in brain with astrocytes storing arginine for the benefit of neighbouring cells in need of the amino acid for a proper synthesis of NO. The aim of the study was to determine whether L-arginine availability declines during cerebral hypoxemia, which could contribute to a decreased nitric oxide (NO) production that are features of cerebral perfusion. **Methods:** We examined alterations in cerebral NO, extracellular L-arginine and L-citrulline concentrations during hypoxemia in 25 newborn pigs. Another five normoxemic animals served as controls. L-arginine annd L-citrulline were analysed from cerebral microdialysate and NO concentration was measured electrochemically. Cerebral blood flow was measured with locally implanted laser Doppler probes. Hypoxemia was terminated when pH was < 7.0, base excess < -20 mmol/l or MABP < 15 mmHg. **Results:** The total duration of hypoxia was 69 ± 3 min. Cerebral NO concentration decreased from 1.05 ± 0.19 to 0.82 ± 0.07 ($p<0.05$) arbitrary units, L-arginine decreased from $1,62 \pm 0.66$ to 1.14 ± 0.05 ($p<0.05$) and L-citrulline from 1.52 ± 0.76 to 1.29 ± 0.09 μmol/l ($p<0.05$). Laser Doppler flow signals increased to a steady state 44 % above baseline values ($p<0.0001$). **Conclusion:** Substantial amounts of substrate and co-product of NO synthesis were not found to be released in the brain of hypoxemic pigs. We speculate that cerebral blood flow regulations during hypoxemia are not associated with disordered NO production.

0466OTH

RESUSCITATION WITH 21% OXYGEN IS AS EFFICIENT AS 100% IN REVERSING THE HYPOXAEMIA-INDUCED CARDIOVASCULAR EFFECTS IN NEWBORN PIGS

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Background- There is an ongoing debate whether room air is as efficient as 100% oxygen in reversing the hypoxaemia-induced cardio-vascular effects after a global hypoxic-ischaemic insult. **Aim-**To assess by Doppler echocardiography and serum Cardiac Troponin I (CTnI) the consequences on the myocardium and the pulmonary artery pressure during global ischaemia and reoxygenation with 21% and 100% O_2 in newborn pigs. **Methods-**Twenty newborn anaesthetised and instrumented pigs (aged 12–36 hrs) were subjected to a hypoxic-ischaemic insult by ventilation with 8% O_2 in nitrogen. When mean arterial blood pressure had fallen to 15 mm Hg or arterial base deficit ≤ -20 mmol/L, the animals were resuscitated with either 21% O_2 ($n=10$) or 100% O_2 ($n=10$) for 30 min, then ventilated with ambient air for 120 min. Blood was analysed for CTnI. Ultrasonographic studies were performed at baseline (H0), during hypoxia (H30), at start of reoxygenation (R0) and during reoxygenation (R30, R90, R150). Cardiac output (CO) was measured from aortic flow. Pulmonary artery pressure was estimated from the peak tricuspid regurgitation velocity (TR). **Results-** CTnI increased tenfold from baseline to endpoint (0.05 ± 0.003 vs 0.34 ± 0.100 μmol/L (mean $\pm$SEM), $p<0.001$), confirming a serious myocardial injury, but with no differences between the 21% and 100% O_2 group ($p=0.120$). TR increased in all pigs during the insult (H0 2.38 ± 0.193 vs R0 2.91 ± 0.13 m/sec), then returned towards baseline values during reoxygenation, but with no differences between the groups ($p=0.831$), or between CTnI level ($p=0.310$). An inverse relationship was found with increasing age of the pigs and the TR during hypoxia ($p=0.034$). CO/kg increased during the early phase of hypoxia (H0 0.31 ± 0.02 vs H30 0.42 ± 0.02 L/min/kg), but then decreased. The changes in CO were mainly due to changes in heart rate and not stroke volume, and there were no differences between the two groups during reoxygenation ($p=0.298$). **Conclusion-** A global hypoxic-ischaemic insult affects the myocardium and the pulmonary vascular resistance. Reoxygenation with 100% O_2 showed no benefits compared to ambient air in normalising the myocardial function and the pulmonary vascular resistance.