## † 5

**The effect of tracheal surfactant (Exosurf or Survanta) installation on retinal (RBF) and choroidal (ChBF) blood flow.** Maria Aparicio, Jose Quero, Tom A. Stiris. Autonoma Univ. of Madrid, Hospital La Paz, Dep of Pediatrics and Surgical Res. Madrid, Spain.

**Introduction:** Synthetic (exosurf) and natural surfactant (Survanta) are used in the treatment of RDS. It has been shown that its administration may affect organ blood flow. However, it has been speculated that this effect is secondary to other hemodynamic changes i.e. blood gases, blood pressure. Little is known of surfactant's possible effect on ocular blood flow.

**Material and method:** 20 newborn piglets < 7 days old were used, divided into a Survanta (Su) group (n=6), an Exosurf group (Ex) (n=7) and a control group (n=7). Pulmonary lavage was done in all groups. Blood flow was measured using the radiolabelled microsphere technique at BL after the lung lavage and 5, 10 and 60 min after tracheal installation of either survanta or exosurf. The control group did not receive any installation

**Results:** Results are expressed as ml/min/100gr tissue (mean±SE).

| | BL | 5min | 10 min | 60min |
|---|---|---|---|---|
| RBF-Su | 55±7 | 53±5 | 65±9 | 59±6 |
| RBF-Ex | 57±8 | 55±5 | 70±5 | 60±6 |
| ChBF-Su | 1614±124 | 1862±256 | 2050±298 | 1987±403 |
| ChBF-ex | 2683±426 | 2805±571 | 3475±705 | 2754±600 |

No significant changes were found neither regarding RBF nor ChBF after installation of survanta or exosurf. The apparent increase at 10 min did not reach any significance. Also, the control group remained stable through out the study period.

**Conclusion:** Installation of surfactant (exosurf or survanta) did not affect RBF or ChBF. Thus, we believe that reported changes in blood flow are not due to a direct effect of surfactant.

## † 6

**INFLUENCE OF AN HYPOXIC-ISCHEMIC (HI) INSULT ON PROGRAMMED CELL DEATH (APOPTOSIS) IN THE IMMATURE RAT BRAIN.**

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**Background:** Excessive apoptosis is one suggested mechanism by which cells die following perinatal hypoxia-ischemia (HI). The complete removal of a cell undergoing apoptosis may happen within hours and counting apoptotic cells on one occasion does not reflect the relative importance of this process. In healthy 7 day old rats 0.12% of cells undergoing apoptosis is reported in the cortex. **Our aim** was to determine the time course and extent of apoptosis in the hippocampus after HI.

**Subjects:** Thirty two 7 day old rat pups were exposed to 2h of 8% hypoxia after left carotid ligation. Animals survived to 0, 1, 2, or 7 days after the insult. All neurons (healthy, necrotic and apoptotic) of both hippocampi in 5 H&E stained coronal brain sectionsper animal were counted by two observers and the number of apoptotic cells (classified after strict morphological criteria) was expressed as percentage of total. Mean(±SD) hippocampal cell count was 2550±680, a total of 860 000 cells were counted. Neuropathological damage was graded from 0.0; no necrotic cells to 4.0;>90-% necrotic cells on a 0.5 step scale.

**Results:** In the ligated hemisphere, the mean% apoptotic cells was 0,09 on day 0, significantly increasing to 0.26 after 1 day, 0.25 after 2 days and declining to 0.07 after 7 days survival. There was a strong corrrelation between percentage apoptosis and neuropathological damage on days 1,2 and 7; eg after 2 days mean % apoptosis was 0.13 in undamaged animals and in animals with >90% necrosis the percentage apoptotic cells was 0.49. The right (unligated) side of the brain never had necrotic cells and mean % apoptotic cells was was 0.14, 0.19, 0.12 and 0.03 on day 0, 1 ,2 and 7 respectively.

**Conclusion:** The maximum increase in apoptosis occured 24-48 h after after HI. There was a 4 fold increase in apoptosis which correlated with with the degree of brain necrosis.

## † 7

**DEXAMETHASONE-INDUCED LUNG MATURITY IN EXPERIMENTAL CONGENITAL DIAPHRAGMATIC HERNIA (CDH) IN FETAL RATS.**

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**Background**: The lungs of Nitrofen-induced CDH fetuses have an immaturity of the surfactant system. The posibility of farmacological induction of lung maturity in this model has been suggested. Previously, we had shown that the lungs of fetuses with CDH had a lower DSPC/DNA ratio (0.27±0.03) than both untreated controls (0.37±0.06) and Nitrofen-feed rats without hernia (0.34±0.04).

**Subjects**: 12 fetuses of Wistar rat with and without CDH.

**Interventions**: Two groups (n=6) were studied: fetuses with (CDHd) and without hernia (No-CDHd), born to dams previously exposed to Nitrofen (100mg) on day 9.5, and to 0.25 mg/Kg Dexamethasone (DEX) on days 18, and 19 of gestation. Fetuses were recovered at 21 days, and the lungs dissected and weighed. DNA, protein, total phospholipids and disaturated PC (DSPC) were measured. Statistical analysis by Mann-Whitney test was performed ($p<0.05$).

**Results**: At term, CDHd group had a similar DSPC/DNA ($\mu g/\mu g$) ratio (0.35±0.03) than both No-CDHd (0.38±0.04) and untreated controls (0.37±0.06).

**Conclusions**: In term rats with Nitrofen-induced CDH, prenatal expose to DEX increases DSPC/DNA ratio to those values found in normal fetal rats.

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## † 8

**LEARNING DIFFICULTIES: A LONGITUDINAL COHORT STUDY FOR RISK FACTORS**

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**Aim:** The investigation of any association between learning difficulties (L.D.) and pre- and post-natal factors in 7 years old Greek children.

**Subjects:** A cohort of 6594 infants, born in April 1983 throughout Greece, longitudinally studied up to 7 years. Children mentaly retarded and/or with severe sensory and motor deficits were excluded.

**Measurements:** School performance was evaluated as a whole and separately in 5 educational skills by teachers using the same predefined scale. Two hundred and fifty variables related to pregnancy, delivery and preschool period were modelled through series of logistic regressions.

**Results:** Severe L.D. were found in 10% of children. The following risk factors were identified:(Relative Risk in brackets). Sosial isolation (3.0), poorly educated mothers (3.0), attention deficit (2.0), history of eclampsia (1.7), chronic illness (1.6), not attending nursery (1.6), overcrowding (1.5), being teased by others (1.4), unhappiness (1.3), lack of self-dependancy (1.3), aggressiveness(1.3) and not socialized with peers (1.2).

**Conclusions:** Early identification of behavioural problems in childhood and appropriate intervention on personal and family level may reduse the prevelance and severity of L.D.

## † 9

**MR INVESTIGATIONS OF CEREBRAL DEVELOPMENT IN THE BEAGLE PUPPY : T2-WEIGHTED IMAGING AND PROTON LOCALIZED SPECTROSCOPY**

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**Background/aim** : The Biochemical changes accompanying the brain maturation are not available from MR images. The beagle puppy is a model for intraventricular hemorrhage of the preterm infant. The purpose of this study was to investigate the brain maturation of the beagle using quantitative analysis of MR imaging and spectroscopy.

**Subjects/interventions** : Three young beagles were followed from birth (d8) to 4 months. MR examinations were conducted once a week for each animal using T2 weighted images (2.5 tesla system) and proton localized spectroscopy.

**Results** : T2 values were observed to decrease from 45% from 15 days of age to 60 days of age. This decrease was correlated with an increase in the grey/white matter contrast and with the metabolites concentrations evaluation. The NAA/cho ratio which reflects neuronal maturation increases form 0.2 to 1.2 whereas the Cho/Cre ratio which reflects the myelination process rapidly decreases form 5 to 1.7 (8 to 16 days) ; Lactate pic was present until 3 weeks after birth.

**Conclusions** : Although faster, the brain development of the beagle puppy appears to be similar to the maturation of the child brain. Due to adaptative mechanisms (energy metabolism) the lactate pic of proton spectroscopy is a normal finding during the first weeks of life in immature brains. Combining T2 and metabolites concentrations measurements provides a new tool to investigate normal and abnormal brain development.

## ●10

**HUMAN GROWTH HORMONE(hGH) TREATMENT IN CHILDREN WITH ACHONDROPLASIA**

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**Background:** The efficacy and safety of hGH administration in children affected by achondroplasia was examined.

**Subjects:** 13 children with achondroplasia aged 4 to 11.8 years who were treated with hGH daily at a dose of 1IU/kg/week for 1 year.

**Measurements:** Stature,weight,sitting height(SH)and subischial leg length were measured 6 months before,at the beginning and after 6 and 12 months of GH therapy.Before initiating GH therapy,hypothalamic-pituitary and thyroid function were evaluation.Serum IGF-I and IGFBP.3 levels and GH response to provocative tests were also assessed.

**Results:** GH response in two stimulation tests was normal in all children except for two.During the first semester of GH treatment,a significant increase in height velocity(HV)was observed in all children(from 3.5±0.8 to 8.3±0.9cm/year).However,during the second semester,a relative decrease in growth rate was observed.By the end of the year,HV rose to 6.5±0.8cm/year(mean HV increase:3.0cm/year, ranging from 1.1 to 8cm/year)in 11 children and the change in their HSDS averaged 0.4 sds.Two children showed no increase in HV.SH% did not change throught GH therapy and no significant change in bone age was observed.

**Conclusion:** hGH increased the growth rate in achondroplasia and the improvement of HSDS was not at the expense of a disproportionate advance in skeletal maturity. A considerable variation in response to GH therapy within treated cases was observed.

## * 11

RECOVERY RATE, RESPONSE TIME AND PATIENT COMPATIBILITY OF FACE MASK, HEAD HOOD AND BODY CHAMBER FOR OPEN FLOW-THROUGH INDIRECT CALORIMETRY IN VLBW INFANTS.

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**Background.** Correct energy expenditure measurements by open flow-through indirect calorimetry require complete sampling of expired air. In VLBW infants masks, hoods and body chambers have been used to sample air, but their performance characteristics and patient compatibility were not tested. **Objective.** To implement standards for air sampling systems and to develope a simple method to evaluate their performance. **Methods.** With a self-built preterm size manikin simulating a $VO_2$ of 13.8 and a $VCO_2$ of 9.2 ml/min and a Deltatrac II (Datex Corp, Finland) we measured recovery rate and response time of a face mask, a head hood, and a body chamber in vitro. In 8 preterm infants we measured rectal temp., resp. rate, heart rate and activity with and without air sampling. **Results.** Each system needed a different flow to achieve 100% recovery, but then the three systems had the same response time. During in vivo measurements no system increased respiratory rate, heart rate or activity, but hood and body chamber increased rectal temperature by 0.3°C/h. **Conclusion.** Future studies with flow-through indirect calorimetry must include a detailed test of the air sampling system including flow for 100% recovery, response time and patient compatibility.

| | Mask | Hood | Body chamber |
|---|---|---|---|
| Capacity of sampling system (L) | 0.08 | 2.5 | 7.5 |
| Flow for 100% recovery (L/min) | 1.2 | 4.3 | 10.8 |
| Response time ((Min) | 4 | 4 | 4 |

## † 12

THE HYPOXIC NEONATE HAS A HIGH RISK TO ACCUMULATE LONG-CHAIN ACYL-CARNITINES IN THE MYOCARDIAL TISSUE

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Several reports have been published about accumulation of long-chain acylcarnitines (LC) in junctional sarcolemma during hypoxia. The protective role on the use of L- carnitine and short-chain acylcarnitine (SC), in conditions of acute hypoxia, have been also informed. In the present study, we researched if any difference exits in free and total carnitine (FC and TC), SC and LC transfer across the placenta, when a fetal acute acidosis takes place. **MATERIAL AND METHODS: Subjects:** A total of 100 "mother-infant" pairs (born at term) were studied divided into two groups, depending on the umbilical artery pH (pHua): G-I, (n:60): When pHua was equal or greater than 7.20 and G-II, (n:40): with pHua less than 7.20, (acute acidosis). **Biochemical analysis:** FC, LC, SC, and TC were measured using radioisotopic assay following McGARRY's method. **Stadistical Method:** ANOVA and correlation analysis were done. **Units:** nmol/ml. * = p < 0.001; $ = p < 0.01; #: p = NS. **RESULTS:** The FC, LC, SC and TC values in G-I were: 24.37(1.14) [mean(SEM)]-37.64(1.78),*; 2.07(0.14)-3.21(0.23),*; 4.93(0.58)-9.81(0.91),*; 32.58(1.43)-51.23(2.45),*, respectively; and the values in G-II were: 40.47(2.08)-33.99(2.34), $; 4.03(0.37)-3.43(0.27),#; 8.87(1.05)-8.37(1.07),#; 52.52(3.46)-45.22(2.57),$. G-II had the ratio LC/FC significantly hihger and the ratio SC/LC significantly lower than G-I. There are close lineal correlations between FC, LC and TC umbilical vein plasma levels and their mothers in G-II, but not in G-I. **DISCUSSION:** It has been demonstrated that electrophysiological darangements depend on the accumulation of endogenous LC in hipoxic neonatal myocites. Newborn infants that have suffered an acute acidosis at delivery, show a high risk to accumulate the potentially toxic LC in junctional sarcolemma. There is a low FC concentrations during acute hypoxia, which determine a decrease in the protective effect of cellular oxidative damage. We have demostrate low SC concentrations in G-II. A marked depression in the activity of piruvate dehydrogenase complex and in the mitochondrial respiratory function occur during hypoxia conditions. These phenomena could have negative effects on myocardial metabolism under ischemia conditions. **Sponsored by C.D.T.I. Proyect nº 920083, 1992-1996.*

## ● 13

PARENTERAL IRON INCREASES SERUM ERYTHROPOIETIN CONCENTRATION (s-iEpo) DURING THE EARLY ANAEMIA IN MICE.

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**Background:** There are several observations suggesting that regulation of erythropoiesis in the postnatal period differs from what observed in the adult mammal. Parenteral iron abolishes the early anaemia in all mammals tested, and the haematocrit reached by iron injections are higher than observed in the adult mammal.

The aim of the present study was to examine the effect of iron injections upon Epo concentration in young and adult iron deficient mice.

**Subjects:** Young BALB/CJ mice from 6 to 25 days of age, and adult (60-90 days old) mice, made iron deficient by low iron diet from the time of weaning.

**Interventions:** All mice were given one injection of iron subcutaenously (Iron Sorbitol, $Fe^{+++}$, 1mg/100g body weight). 20-24 hours later the animals were killed, and the blood tested for haematocrit and s-iEpo. Control mice were given saline injections.

**Results:** The injection of iron did not affect haematocrit in any of the groups. In young mice prior to weaning s-iEpo levels increased significantly following iron injection compared to the controls ($p < 0.001$). Similar increase in s-iEpo was not observed in the adult iron deficient mice given one dose of iron parenterally.

**Conclusion:** During the period of early anaemia iron increases s-iEpo levels, while in adult mice iron has no such effect. This suggests that iron at this age has additional effects in regulation of erythropoiesis, that are not observed in adult animals.

## 14

CEREBROSPINAL FLUID INFUSION OF ALGLUCERASE IN THE TREATMENT OF ACUTE NEURONOPATHIC GAUCHER'S DISEASE.

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**Backgraund:** Intravenous (i.v.) enzyme replacement therapy (ERT) with alglucerase has shown good results in non-neuronopathic form of Gaucher's disease (GD1). This approach hasn't shown efficacy in the treatment of acute neuronopathic form (GD2). We studied the effect of alglucerase infusions into cerebrospinal fluid (CSF) of one GD2 patient.

**Subject**: One 7 month-old male patient with symptomatic GD2.

**Interventions**: The patient received only i.v. ERT for 4 months at the dosage of 120-240 IU/kg/month of alglucerase. After this period CSF infusions were comenced at dosage of 10 IU every 2 weeks.

**Results**: After 7 months of CSF treatment clinical data showed the arrest of the progression of neurological symptoms. A clear improvement of auditory brain stem response was detected. Laboratory data showed a decrease of CSF glicolipids from 5.33 mcg/ml to 0.42 mcg/ml. Blood biochemical parameters increased and hepatosplenomegaly reduced.

**Conclusions**: direct ERT into CSF may be effective in the treatment of acute neuronopathic form of GD before the beginning of severe neurological involvement.

## * 15

THE ROLE OF "OCCULT" GASTROESOPHAGEAL REFLUX IN CHRONIC PULMONARY DISEASE IN CHILDREN

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**Background:** It has repeatedly been demonstrated that a correlation exists between gastroesophageal reflux and the presence of various "atypical" complaints, such as recurrent chest pain, apneic attacks in infants, and recurrent or chronic respiratory symptoms. Very recently it has been shown that gastroesophageal reflux is frequently associated with non-controlled asthma in children and that medical treatment for reflux can improve the further course of respiratory disease.

**Study design:** The aim of the present study was to study a possible cause-relationship between recurrent respiratory symptoms in children and the presence of gastroesophageal reflux disease, and to investigate the value of continuous 24-hour esophageal pH-monitoring in the diagnosis and management of these complaints in 62 children with chronic respiratory disease.

**Results:** Continuous 24-hour pH-monitoring was abnormal in 39/62 patients (62.9%). However, no statistically significant correlation could be detected between the presence of gastroesophageal reflux and various anamnestic parameters (parental smoking, pet in household, sibling with gastroesophageal reflux disease), or concomitant atopy.

All children that were found positive for gastroesophageal reflux (n=39) were started on an anti-reflux therapy (cisapride 0.2 mg/kg q.i.d.). This treatment resulted in an improvement of the symptoms in 84.6%.

**Conclusion:** We conclude that gastroesophageal reflux is an important (causative) factor in chronic recurrent respiratory disease. This entity is often resistant to "classical" respiratory treatment, but can be treated with an anti-reflux therapy. We, therefore, suggest to perform continuous 24-hour esophageal pH-monitorings as a standard procedure in all patients with recurrent respiratory complaints, independent of the severity of their symptoms.

## ● 16

THE VALUE OF SPECIFIC ANTIBODIES IN THE DIAGNOSIS OF *HELICOBACTER PYLORI* INFECTION.

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**Background:** Serology has previously been proposed as a valid screening technique for *Helicobacter pylori (H. pylori)* infection. Last generation serologic tests are easy to use and reasonably cheap, which is an important advantage when compared to the $^{13}$C-urea breath test (UBT), which is not only rather expensive but also rather complicated to analyze. To screen for *H. pylori* infection by means of serology, both, specific IgG and IgM titers can be determined.

**Study design:** In order to evaluate the value of specific IgG and IgM in the detection of *H. pylori* infection, sera from 36 *H. pylori* infected children (ages 1 to 15 years), as defined by a positive $^{13}$C-UBT, were examined by means of last generation serum ELISA tests (MALAKIT™ HELICOBACTER PYLORI series, Biolab, Limal, Belgium). A symptom-free $^{13}$C-UBT negative pediatric population served as control.

**Results:** All investigated children had positive levels for IgG antibodies. However, anti-*H. pylori* specific IgM could only be detected in 9/36 (25.0%). These findings reflect a sensitivity, specificity, positive predictive value, and negative predictive value of respectively 13.3%, 100%, 100%, and 72.9% for the serum ELISA test for the detection of *H. pylori* specific IgM vs. 100%, 95.6%, 100%, and 96%, respectively for the anti-*H. pylori* specific IgG.

**Conclusion:** We conclude that, while *H. pylori* specific IgG are a reliable indicator for an active infection with this bacteria, the determination of specific IgM against this bacteria does not seem to be of major diagnostic value in the detection of *H. pylori* infection.

## * 17

INFLUENCE OF NEONATAL DISEASES ON ACTIVITIES OF PANCREATIC ENZYMES IN DUODENAL ASPIRATES OF VERY LOW BIRTH WEIGHT (VLBW) INFANTS

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**Background:** We studied the effects of neonatal diseases on the activities of pancreatic lipase and trypsin in duodenal aspirates of VLBW infants .

**Study design:** During the 4th and 5th week of life, when normally the activities of both enzymes are stable, 16 VLBW infants with bacterial septicemia, 14 with severe intrauterine growth retardation (IUGR) and 10 infants with bronchopulmonary dysplasia (BPD) were enrolled in the study. The results were compared with those found in healthy VLBW infants of similar postnatal age as controls.

**Results:**

| | Controls | Sepsis | IUGR | BPD |
|---|---|---|---|---|
| N(m/f) | 16 | 13 | 14 | 10 |
| Trypsin (kU/l) | 8.6 ± 2.3 | 5.9 ± 3.2 | 6.8 ± 3.4 | 3.7 ± 2.1[a] |
| Lipase (kU/l) | 19.4 ± 6.8 | 5.7 ± 3.1[b] | 8.7 ± 5.2[b] | 4.4 ± 3.8[b] |

[a] p<0.05 vs. controls; [b] p<0.01 vs. controls

**Conclusion:** Neonatal diseases and intrauterine growth retardation can alter the postnatal development of exocrine pancreas. The activity of lipase is more affected than that of trypsin. Therefore, limited fat digestion should be considered when nutritional management is planned in these infants.

## † 18

EFFECTS OF APNEA ON NEONATAL CEREBRAL HAEMODYNAMICS

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**Background:** We investigated whether important alterations occur in cerebral blood volume (CBV) with different severe apnea and whether such alterations relate to bradycardia or hypoxia.

**Subjects:** 11 preterm newborns, 27-34 week of gestation (median 29), were studied during 54 episodes of apnea.

**Interventions:** Changes in CBV were measured by near-infrared spectroscopy. The observed episodes of apnea were divided into three groups: I with a fall of $SatO_2$ to a value > 80% or bradycardia>80/min; II and III with a fall of SatO2 <80% and/or bradycardie <80/min. In addition to the criteria of group II, infants in group III needed tactil stimulation or extra oxygen for recovery.

**Results:**

| CBV changes ml/100 | mild apnea gr. I, n=22 | moderate apnea gr. II, n=20 | severe apnea gr. III, n=12 |
|---|---|---|---|
| median | 0,3 | 0,65 | 0,9 |
| range | 0,1-0,7 | 0,3-1,1 | 0,7-2,7 |

Fischer's exact test: group I to II p=0,000035* and I to III p=0,0006*, group II to III p=0,015
Significant correlation between changes of CBV heart rate, r=-0,4, p= 0,00295*.
Correlation between changes of CBV and $SatO_2$ not significant, r=-0,113, p=0,435.

**Conclusion:** In the neonate cardiac output strongly depends on heart rate. A fall in heart rate should therefore lead to a fall in cardiac output and thus cerebral blood volume. Our data suggest potential deleterios hypoxic-ischemic effects on the brain from apnea complicated by bradycardia with heart rate<80/min. Urgent intervention is indicated for episodes with moderate and severe apnea.

## * 19

REGIONAL CEREBRAL BLOOD FLOW IN NEONATAL SEIZURES.

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**Introduction:** In the neonatal period seizures are often related to brain damage. However, it remains unclear to what extent seizures affects cerebral metabolism and therefore, it remains unclarified how intensively neonatal seizures should be treated. Therefore, we have measured regional cerebral blood flow in infants with seizures in the neonatal period.

**Methods:** Regional cerebral blood flow was measured using SPECT (Tomomatic 248®) and $^{99m}$Tc-HMPAO.

**Patients:** 12 infants (median BW 3370g, GA 40 weeks) were examined during seizures. The etiology of the seizures was birth asphyxia (8), meningitis (1), cardiac surgery (1) and unknown (2). A reference material was made up of interictal studies made in 8 of them 1-3 days later supplemented with studies of further 11 mature infants 1-7 days after seizure.

**Results:** In 9 of 12 infants (75%) the ictal study showed a significantly increased side-to-side difference. In a paired analysis of the infants examined ictally and interictally all infants had hyperperfused areas in the ictal study. Four infants with clinically focal convulsions all showed a unilateral or predominantly unilateral hyperperfused area of the contralateral hemisphere.

**Conclusion:** We conclude, that also in the newborn with major brain damage, seizures are associated with a locally increased CBF and focal convulsions are associated with a localized increased cerebral blood flow in the contralateral hemisphere. This hyperperfusion may be due to an increased cerebral metabolism, but may also be due to a reflex vasodilatation without increased metabolism.

## † 20

CLINICAL & LABORATORY FINDINGS TO PREDICT BACTERIAL ETIOLOGY OF ACUTE DIARRHOEA IN CHILDREN

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BACKGROUND:A rapid preliminary diagnosis of acute bacterial diarrhoea (ABD)is of importance in many therapeutical and economical respects but clinical studies led to divergent results.AIM:To assess clinical and laboratory features predicting ABD in children.SUBJECTS:Two hundreds two children (median age 34m,range 1-170m), consecutively admitted because of acute diarrhoea .Group A included 89 children with positive stool cultures (SC) for Salmonella (80) or Campylobacter(9)spp;group B consisted of 53 children with stool specimens positive for rotavirus or adenovirus by specific enzyme linked immunosorbent assays and 60 children with negative stool specimens for bacterial & viral pathogens.METHODS:Presenting history,physical examination & screening laboratory tests in the two groups of children were compared and subsequently a logistic model developed.RESULTS:In univariate analysis duration of fever (sensitivity(SE)55%; specificity(SP)83%;area under ROC curve=0.733)had the best balance of diagnostic efficacy,followed by the absence of vomiting before the onset of diarrhoea(SE53%;SP80%;ROC=0.66),duration of diarrhoea (SE31%;SP78%;ROC=0.652)frequency of diarrhoeal stools(SE24%;SP 87% ROC=0.59)and headache(SE15%;SP97%;ROC=0.55).Presence of mucoid stools had SE63%;SP89%;ROC=0.70,gross blood stools SE36%;SP88%; ROC=0.622,C-reactive protein (CRP) >12 mg/L SE48%;SP84%;ROC=0.756 and ESR SE40%;SP83%;ROC=0.636.In subsequent multivariate analyses, the best fitted model included duration of diarrhoea, absence of vomiting,headache, presence of mucoid stools and CRP >12 mg/L (Log Likelihood=-89.86), SE 80%;SP 83%;positive and negative predictive values of 81% and 82% respectively;ROC=0.856.
CONCLUSIONS:we identified a cluster of variables that can serve to construct algorithms for clinical diagnosis & selective use of SC.

## * 21

LUNG PATHOLOGY IN SURFACTANT-TREATED PRETERM INFANTS WITH RESPIRATORY DISTRESS SYNDROME

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**Background:** Histological examination of the lungs of neonates dying of respiratory distress syndrome or related complications after surfactant therapy was performed.

**Subjects:** 10 surfactant-treated preterm infants. Controls: 30 infants who died before surfactant therapy could be begun.

**Interventions:** Complete autopsies were performed 6-12 hours after death. Paraffin sections representative of all lobes of the lungs were stained with hematoxylin-eosin and examined under the microscope. A few selected slides were also stained with PAS, Vierhoff-Van Gieson and Mallory trichrome.

**Results:** Hyaline membrane disease and bronchopulmonary dysplasia were observed in both groups. A higher incidence of intra-alveolar hemorrhage was detected in surfactant-treated babies than controls (8/10 vs 7/30; $\chi^2$ = 10.28, p = 0.001). Persistent acute alveolar damage with unresolved hyaline membrane disease was observed in 5 of the surfactant-treated infants who died at the ages of 5, 6, 10, 12 and 13 days. Histological evidence of acute bronchopulmonary dysplasia was found in two more of the surfactant-treated babies who died at 22 and 41 days of age.

**Conclusion:** Surfactant-treated infants who fail to respond to therapy show persistent alveolar damage and an increased incidence of intra-alveolar hemorrhage.

## * 22

CEREBRAL VASOREACTIVITY DURING HYPOXAEMIA IN NEWBORN PIGLETS.

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Dept. of Neonatology, Rigshospitalet, Copenhagen, Denmark[1]; PFI, Rikshospitalet, Norway[2]

**Background:** Hyperventilation of the sick preterm infant has been shown to be associated with later cerebral palsy. Normally an increase in oxygen extraction fraction (OEF) will compensate for the decreased cerebral blood flow(CBF). It has been suggested that hypoxaemia, however, may blunt the $pCO_2$-CBF-reactivity thereby protecting the brain's blood supply. This study examined cerebral OEF reactivity in a newborn piglet model during severe hypoxamia.

**Subjects:** 8 newborn piglets (age 1-5 days). In only six pigs a steady-state was possible for the last phase of the experiment (mean arterial blood pressure (MABP) dropped below 20mmHg).

**Interventions:** After being anesthesized piglets were catheterized in femoral arteries and veins as well as in the superior sagittal sinus. Piglets were then subjected to normal ventilation, hyperventilation, hypoxaemia, and hypoxaemia + hyperventilation.

**Results:** In each state the values obstained were (OEF is $SaO_2$-Sagittal sinus $SvO_2$) (±S.E.M):

| State: | Normal | $pCO_2\Downarrow$ | $pO_2\Downarrow$ | $pO_2\Downarrow$&$pCO_2\Downarrow$ |
|---|---|---|---|---|
| $pCO_2$(kPa) | 4.7±0.2 | 2.0±0.2 | 4.7±0.2 | 2.5±0.2 |
| $SaO_2$(%) | 89.3±1.1 | 92.5±0.6 | 49.0±3.0 | 52.6±3.5 |
| OEF(%) | 56.7±3.6 | 71.8±1.8 | 30.0±2.5 | 38.3±2.2 |
| MABP(mmHg) | 64.0±4.5 | 54.5±4.5 | 50.3±4.7 | 44.2±4.3 |

As seen all piglets responded to hyperventilation from the normal state. As can be seen there was a significant (p=0.02) mean rise in OEF.

**Conclusion:** A 27% rise in OEF was demonstrated as a response to hyperventilation, both during normoxaemia and hypoxaemia. This could be associated with increased risk of brain damage. However, it is not known whether the level of hypoxaemia induced is critical in newborn piglets or whether the results were influenced by the concurrent drop in MABP

## † 23

### NEAR-INFRARED TISSUE OXYGENATION INDEX ESTIMATES MEAN CEREBRAL TISSUE SATURATION IN NEWBORN PIGLETS.

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**Background:** A non-invasive second-to-second monitoring of tissue haemoglobin oxygen saturation would be a powerful tool for research as well as clinical care. Near-infrared spectrophotometry (NIRS) can monitor changes in concentrations of tissue oxy-(ΔHbO2) and deoxy(ΔHHb)-haemoglobin. This study sought to validate $\Delta HbO_2$-ΔHHb (Hbdiff) as such a measure against invasively measured arterial and superior sagittal sinus(SSS) values in newborn piglets .

**Subjects:**10 newborn piglets (age 1-5 days).

**Interventions:**Piglets were anaesthesized and catheterized in femoral arteries, veins and SSS. They were then ventilated through 8 physiological states:1)normal 2)hypocapnic 3)normal 4)hypercapnic 5)normal 6)hypoxaemic 7)hypoxaemic and hypocapnic 8)normal. Blood samples for $SaO_2$ and SSS-saturation ($SvO_2$) were drawn in each state and mean cerebral oxygen haemoglobin saturation($SmO_2=(SaO_2+SvO_2)/2$)was calculated. Hbdiff was recorded from a NIRS-prototype (Radiometer). Optodes were placed biparietally directly on the scull with a 3.5 cm separation.

**Results:** Hbdiff (change from start) and $SmO_2$-values (±S.E.M.) in each physiological state:

| State: | Normal | $pCO_2\Downarrow$ | Normal | $pCO_2\Uparrow$ | Normal | $pO_2\Downarrow$ | $pO_2\Downarrow$&$pCO_2\Downarrow$ | Normal |
|---|---|---|---|---|---|---|---|---|
| Hbdiff(μM) | **0**±1.6 | **-12.1**±2.2 | **3.1**±3.4 | **22.5**±4.9 | **-1.7**±2.4 | **-34.9**±2.4 | **-37.1**±3.2 | **4.6**±3.4 |
| $SmO_2$(%) | **60.8**±1.3 | **56.1**±1.1 | **64.5**±1.7 | **75.7**±2.4 | **61.4**±1.7 | **32.1**±2.4 | **31.9**±2.5 | **58.9**±3.6 |

**Conclusion:** Mean cerebral oxygen haemoglobin saturation can be estimated accurately with NIRS in newborn piglets in the range of 30-75%.

## † 24

### CHANGES IN CEREBRAL BLOOD VOLUME IN NEWBORN PIGLETS AS DETECTED BY NEAR-INFRARED SPECTROPHOTOMETRY.

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**Background:** Cerebral vascular reactivity is a relevant parameter to monitor in the prevention of perinatal brain damage. Near-infrared spectrophotometry (NIRS) offers continous non-invasive monitoring of total cerebral haemoglobin concentration changes(dtHb) as well as absolute measurement of cerebral erythrocyte and plasma volumes by the indicator dilution principle.. These measures were sought validated against measurements of cerebral erythrocyte volume(CEV) by $^{99m}$Tc-labelled erythrocytes.

**Subjects:** 6 newborn piglets (age 1-5days).

**Interventions:** Piglets were anaestesized and catherized in femoral arteries and veins. They were then ventilated through 8 physiological states:1)normal 2)hypocapnic 3)normal 4)hypercapnic 5)normal 6)hypoxic 7)hypoxic and hypocapnic 8)normal.

**Results:** In the normal states NIRS-CEV was 1.50±0.62(S.E.M.)ml/100g compared to CEV by $^{99m}$Tc: 0.91±0.26ml/100g. NIRS cerebral haematocrit was 0.50±0.18, compared to the peripheral haematocrit of 0.22±0.02. dtHb and CEV by $^{99m}$Tc correlated well exept for the hyperventilated state. Analysis of variance showed a higly significant relationship (ANOVA:p<0.0001). In each state the values for dtHb and CEV by $^{99m}$Tc were(±S.E.M. change from baseline):

| State: | Normal | $pCO_2\Downarrow$ | Normal | $pCO_2\Uparrow$ | Normal | $pO_2\Downarrow$ | $pO_2\Downarrow$&$pCO_2\Downarrow$ | Normal |
|---|---|---|---|---|---|---|---|---|
| dtHb(μM) | **0** | **-1.1**±1.5 | **5.6**±3.1 | **17.2**±4.3 | **0.3**±3.5 | **13.9**±4.6 | **14.9**±4.7 | **3.6**±3.5 |
| CEV by(μM) | **0** | **1.2**±1.6 | **0.7**±2.2 | **8.6**±3.8 | **1.7**±2.3 | **6.8**±4.6 | **3.2**±5.0 | **3.2**±4.1 |

The magnitude of the change, however, was different: NIRS appeared to overestimate the changes compaerd to the $^{99m}$Tc-method.

**Conclusion:** This study does not support NIRS as a reliable method for the measurement of cerebral blood volume.

## ● 25

### Collection and manufacturing of placental blood for autologous blood transfusion in neonatal intensiv care patients

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**Background:** Near by 80% of neonatal intensive care patients need blood transfusions during the first 6 weeks of live. Because of the special requests (CMV-negative, x-ray) the used blood components are rare and expensive. **Aim of the study:** In this study we examined the possibility to collect, manufacture and store sterile placental blood for a later autologous blood transfusion. **Subjects:** Directly after cord clamping placental blood of 98 patients was collected using a special placenta blood collection kit (Maco Pharma, France). Centrifugation was performed with 1900 rpm for 10 minutes. **Interventions:** Laboratory parameters were performed using standard methods. Each collection was examined for aerobe and anaerobe microbial contamination. Laboratory parameters of EK's were performed after 10 days storage.

**Results:** Results were given as mean value and standard deviation:

< 2000 gr Birthweight (n=3, 3 sections)

| BW: | Plac.-weight | Total Volume | Vol/Kg/BW | Gl | Erys | Hkt |
|---|---|---|---|---|---|---|
| 1260,00 | 270,00 | 24,67 | 20,47 | 34,00 | 3,91 | 50,20 |
| ±427,55 | ±131,05 | ±5,51 | ±4,45 | ±5,29 | ±0,33 | ±1,20 |

2000 gr - 3000 gr Birthweight (n=11, 5 sections)

| BW: | Plac.-weight | Total Volume | Vol/Kg/BW | Gl | Erys | Hkt |
|---|---|---|---|---|---|---|
| 2682,73 | 583,64 | 52,32 | 19,43 | 37,64 | 4,24 | 45,73 |
| ±267,81 | ±248,78 | ±17,13 | ±5,71 | ±1,80 | ±0,57 | ±7,58 |

3000 gr - 4000 gr. Birthweight (n=70, 10 sections)

| BW: | Plac.-weight | Total Volume | Vol/Kg/BW | Gl | Erys | Hkt |
|---|---|---|---|---|---|---|
| 3411,00 | 624,55 | 65,80 | 18,89 | 40,07 | 4,26 | 46,16 |
| ±254,24 | ±160,96 | ±26,73 | ±7,98 | ±1,56 | ±0,65 | ±7,05 |

> 4000 gr Birthweight (n=14, 4 sections):

| BW: | Plac.-weight | Total Volume | Vol/Kg/BW | Gl | Erys | Hkt |
|---|---|---|---|---|---|---|
| 4316,43 | 783,57 | 99,79 | 23,11 | 40,79 | 4,26 | 45,91 |
| ±262,17 | ±104,67 | ±25,37 | ±5,93 | ±0,80 | ±0,30 | ±3,93 |

No probe showed any signs of microbial contamination. Centrifugation with 1900 rpm for 10 minutes produced a mean amount of: 25 +/-11 ml red packed cells.. After 10 days of storage no significant lost of red cells by lysis could be detected (Blood counts after 10 days: Hct: 87,5 ±0,2; Erys: 8,1 ±0,5).

**Conclusion:** This study proofs the possibility to collect, manufacture and store placental blood for an autologous blood transfusion in neonatal patients.

## † 26

### IN VITRO COMPARISON OF ARTEFICIAL AND BOVINE SURFACTANT: IMMUNOLOGIC PROPERTIES

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**Background:** Surfactant, which is being applied into the lungs for treatment of respiratory distress syndrome, can reach the circulatory blood system by absorption. It influences local function of macrophages and lymphocytes and increases the accumulation of neutrophils into the lungs. The aim of this study was to compare the immunologic properties of natural and artificial surfactant in vitro. **Material and methods:** a) Measurement of TNF-a, Il-6, $LTB_4$ and thromboxane $B_2$-release in whole blood: Each of 1.5 ml heparinised blood of healthy adult volunteers was incubated for 2 hours with either 10 ug/ml LPS, 1 mg/ml bovine surfactant (Alveofact/Thomae), 1 mg/ml artificial surfactant (Exosurf/Wellcome), 10 ug LPS + 1 mg/ml bovine surfactant or 10 ug LPS + 1 mg/ml artificial surfactant. Heparinised blood without additions was used for controls. The concentration of cytokines and eicosanoids was measured semiquantitatively by ELISA or EIA (Dianova/Hamburg) after centrifugation. b) Measurement of platelet aggregation: Each of 1.5 ml heparinised blood of healthy adult volunteers was incubated for 2 hours with either 10 ug/ml LPS, 1 mg/ml bovine surfactant (Alveofact/Thomae), 1 mg/ml artificial surfactant (Exosurf/Wellcome), 10 ug LPS + 1 mg/ml bovine surfactant or 10 ug LPS + 1 mg/ml artificial surfactant. Platelet aggregation in whole blood was measured by impedance in the aggregometer (Sarstaedt). c) Measurement of the clotting activity: Citrated blood of healthy adult volunteers was mixed with different concentrations of bovine or artificial surfactant and then prothrombin times and partial thromboplastin times were measured. For measurement of the prokoagulation activity the reagent in the Quick test was replaced by surfactant. **Results:** Both surfactants stimulated the release of Il-6 but not of TNF-a in whole blood. There was no suppression of the LPS-induced cytokine-release. Both surfactants did not influence the extrinsic blood coagulation system, while both activated the intrinsic activity. Platelet aggregation was slightly stimulated by bovine surfactant and strongly inhibited by by artificial surfactant. In combination with LPS both factors showed no difference to LPS alone.The release of eicosanoides was stimulated more by artificial surfactant then by bovine surfactant with regard to the cyclooxygenase (thromboxane $B_2$) and the lipooxygenase (leucotriene $B_4$) pathways. **Conclusion:** We conclude: 1) Bovine as well as artefcial surfactant stimulate the cellular immune response. 2) Bovine as well as artefcial surfactant activate the intrinsic coagulation cascade. 3) Bovine surfactant stimulates platelet aggregation, artefcial surfactant inhibits platelet aggregation..

## † 27

### NUMBER AND ACTIVATION OF CIRCULATING NEUTROPHILS (N) AND PLATELETS (P) ARE ASSOCIATED WITH SEVERITY OF IDIOPATHIC RESPIRATORY DISTRESS SYNDROME(IRDS).

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**Background:** We studied the association between IRDS severity and number and activation of circulating N and P.
**Patients:**18 preterm infants with severe and 18 with mild/moderate IRDS.18 severe and 12 mild/mod.infants were ventilated.17 severe and 5 mild/mod.received surfactant.
**Measurements:** N and P counts (x $10^9$/L), elastase-α1-PI (E-α1-PI,ng/ml) and thromboxane B2 (TxB2. pg/ml) plasma concentrations, and E-α1-PI/N (ng/$10^6$) and TxB2/P(pg/$10^6$) ratios (to correct for N and P count).

| **Results:** | severe IRDS | | mild/mod.IRDS | |
|---|---|---|---|---|
| | day 1 | day 3 | day 1 | day 3 |
| PMN | 2.7(2.1-3.7) | 1.6(0.8-2.5)* | 3.6(1.4-6.5) | 2.6(2.2-3.7)## |
| E-a1-PI | 43 (34-60) | 61 (48-82)* | 48 (37-70) | 52 (38-71) |
| E-a1-PI/N | 17 (12-32) | 64 (40-80)* | 10 (8-31) | 22 (14-29)## |
| platelets | 168(132-128) | 115(64-183)* | 252(198-281)# | 237(205-248)## |
| TxB2 | 118(80-225) | 270(83-320)* | 95 (46-145) | 114(64-175) |
| TxB2/P | 0.8(0.6-1.2) | 2.6(0.9-11.6)* | 0.4(0.2-0.5) | 0.6(0.3-1.0)# |

Median values (25th-75th percentile) shown.*p < 0.05 for d 3 *versus* d 1; # p < 0.05 and ## p < 0.01 for mild/mod.*versus* severe IRDS

**Conclusion:**Severe IRDS is associated with lower number of circulating N and P and more release of elastase and thromboxane, indicating more activation of these cells.

## † 28

### Impact of central, obstructive and mixed apnea on cerebral haemodynamics in preterm infants

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**Objectives:** To study the effect of central, obstructive and mixed apnea on cerebral total haemoglobin concentration (tHb), which is analogous to cerebral blood volume, and to investigate whether systemic haemodynamic changes correlate with tHb alterations.

**Methods:** Measurements were carried out on 17 preterm infants with frequent apneic events. Near infrared spectrophotometry (NIRS) was used to quantify changes in tHb. Respiration was monitored by chest movements using impedance pneumography and by nasal airflow using a thermistor. In addition, heart rate, arterial oxygen saturation in each infant and esophageal pressure in three babies were continuously recorded.

**Results:** 130 apneic episodes of > 10 seconds duration showed four different patterns of tHb alterations: 1) no change in tHb (28%), 2) isolated decrease (35%), 3) isolated increase (12%), or 4) both combined, an initial decrease followed by an increase over the previous baseline level (25%). Obstructive apneic episodes were associated with a significantly greater maximum fall in tHb (median 11.5, 90% CI 0.95 to 30.5 μmol/l,) compared to mixed (4.9, 90% CI 0.0 to 26.4 μmol/l) and central events (3.0, 90% CI 0.0 to14.0 μmol/l). Changes in tHb correlated with heart rate only in purely central apnea and were not reflected in arterial oxygen saturation in any type of apnea.

**Conclusion:** Obstructive apnea was observed to have the strongest impact on tHb. As these tHb alterations may exacerbate or cause intracranial haemorrhage, efforts must be made to prevent obstruction of upper airways and to focus monitoring on cerebral perfusion.

## † 29

### HYPOXIC ISCHEMIC BRAIN DAMAGE IN NEONATAL RATS MONITORED BY $^{31}$P MAGNETIC RESONANCE SPECTROSCOPY (MRS)

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**Background:** The neonatal rat is a valuable model for investigation of cerebral high energy metabolism following hypoxia-ischemia (HI). Although local cerebral perfusion is temporarily reduced following unilateral common carotid artery (CCA) ligation, collateral vascularisation subsequently recompensates.
**Aim:** We studied the influence of the time delay between surgery (unilateral CCA ligation) and exposure to hypoxia on the energy breakdown in the brain of rat pups during HI and on the subsequent metabolic recovery, using $^{31}$P-MRS.
**Interventions:** 7-day old rats were kept inside the magnet system (2.35 and 4.7 Tesla) under constant normal temperature and exposed to 8% O2 for 1h, with a time delay of 1/2h (Gr. A) and 3h (Gr. B) after surgery. The phosphorylation potential (PCr/Pi) and ATP/EPP* were monitored in the affected brain region during HI and subsequent recovery, respectively.
(*EPP = exchangable phosphate pool.)
**Results:** During hypoxia, PCr/Pi decreased exponentially ($\sim e^{-\alpha t}$) with $\alpha$ of 5% (Gr A) and 0.5% (Gr B) per min, respectively. Following hypoxia, PCr/Pi increased exponentially ($\sim 1\text{-}e^{-\alpha t}$) with $\alpha$ of 10% per min in both groups. 24h after hypoxia, a marked secondary energy failure leading to a 40% fall of PCr/Pi was found in Gr A) but not in Gr B).
**Conclusion:** $^{31}$P-MRS allowed to monitor the changes of the cerebral high energy metabolism in rat pups during HI. Gr A showed a slower energy breakdown during hypoxia and a less pronounced secondary energy failure during the recovery period than Gr B, probably due to a more complete collateral perfusion.

## † 30

### SOLUBLE L-SELECTIN (sCD62L) PLASMA LEVELS INCREASE DURING FETAL MATURATION

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**Background:** Soluble L-selectin (sCD62L) interferes with leukocyte extravasation into areas of inflammation. Decreased levels of plasma sCD62L have been reported in severely neutropenic patients and in trauma patients who subsequently developed acute respiratory distress syndrome. Sepsis in newborns is associated with decreased levels of cell-bound CD62L while neonatal sCD62L plasma levels had not been investigated yet.
**Subjects and measurements:** A luminescence-based sandwich ELISA (sensitivity 0.017 pmol/ml) was developed to determine sCD62L umbilical cord plasma levels of 255 term and preterm newborns with a gestational age of 23 to 43 weeks.
**Results:** Cord plasma sCD62L levels (10-90 percentile range 3.8 - 10.4 pmol/ml, median 7.2) showed strong independent correlations with gestational age ($r$ = 0.71, $p$ < 0.001) and absolute neutrophil counts ($r$ = 0.62, $p$ < 0.001). Multiple gestation was independently associated with decreased sCD62L levels while acute bacterial infection had no impact on sCD62L levels. Cord vein plasma sCD62L levels of term singletons (10-90 percentile range 6.4 - 10.8 pmol/ml, median 8.3) were significantly ($p$ < 0.001) lower than sCD62L levels in adult cubital vein plasma (10-90 percentile range 9.2 - 14.5 pmol/ml, median 11.8).
**Conclusion:** Plasma sCD62L levels display a strong increase during fetal maturation. The low sCD62L plasma levels of preterm newborn infants may be associated with their increased susceptibility to disseminated inflammatory lung disease.

## † 31

### IS THERE A PHYSIOLOGIC HYPOSELENEMIA AT HUMAN EARLY AGE?

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**Background:** Our aim have been to assess if there is any difference in serum Se (SSe)levels in placental cords and healthy infants from birth to four months who were fed by maternal (MM)or non-Se-supplemented formula milk(NSFM).
**Subjects:** The SSe levels of 146 samples of blood corresponding to 61 cords and 85 infants were measured fluorometrically.
**Interventions:** The infants were divided in five groups of age and regarding their type of feeding. Mean daily intakes of Se were determined knowing that in our area, Se content of mature MM is 11.7 +/- 4.2 $\mu$g/L and NSFM´ 5.0 +/- 1.6 $\mu$/L(own data).
**Results:** Se intakes with NSFM ranged from 0.3 to 1.3 and with MM from 0.6 to 1.9$\mu$g/Kg/d.

Serum Selenium ($\mu$g/L)

| Age(days) | No | mean +/- SD | Age(days) | Feeding group NSFM/MM |
|---|---|---|---|---|
| <7 | 24 | 38.3 +/- 18.8 | 1 - 30 | 28.9 +/- 8.9*/ 42.4 +/- 20.7* |
| >7-14 | 19 | 37.6 +/- 14.1 | 30-120 | 35.9 +/- 20.9/ 44.5 +/- 15.6 |
| >14-30 | 19 | 35.5 +/- 10.6 | | * p<0.001 |
| >30-60 | 16 | 34.9 +/- 16.7 | | |
| >60 | 7 | 41.7 +/- 20.0 | | |
| cord | 61 | 39.3 +/- 11.5 | | |

differences between cord and amongts age´s groups p>0.05(Wilcoxon´s test)
**Conclusion:** The SSe levels and Se intakes are among the lowest reported in western world, and infants MM-fed showed greater levels than those who were fed with NSFM. We did not find any fall in SSe levels shortly after neonatal period or "physiologic hyposelenemia" as some studies have pointed out.

## † 32

### TIME CLOSURE OF THE DUCTUS VENOSUS IN THE NEWBORN

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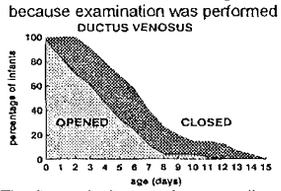
**Objetive:** To prove if the time of closure of the ductus venosus Arantii is brief after birth as it is widely assumed or longer as some reports suggest.
**Subjects:** 45 healthy newborn delivered by caesarean section, selected because they stayed at hospital long time.
**Interventions:** Two-dimensional real-time sonography, colour flow imaging and pulsed doppler velocimetry. The infants were examined within three days after birth and then every three or four days until closure of the ductus venosus.
**Results:** The rate of infants with open ductus venosus decreased gradually within 15 days after birth as it is shown in figure. The time closure is shown by means of the dark area because examination was performed by interval of some days.




| examination | n | Flow velocity (m/sec) mean | range |
|---|---|---|---|
| 1st | 44 | 0.41 | 0.20 - 0.79 |
| 2nd | 36 | 0.36 | 0.06 - 0.86 |
| 3rd | 12 | 0.39 | 0.09 - 0.75 |
| 4th | 2 | 0.24 | 0.18 - 0.31 |

Length, mean (range): 17.5 (12 - 20) mm.

The flow velocity waveform was diverse and variable, sometimes it was pulsatile as in the fetus sometimes continuous as venous flow.
**Conclusions:** The ductus venosus Arantii remains opened within 15 days after birth, although with decreased rate in relation to age. Flow velocity does not decrease in relation to age.

## † 33

### 9 YEAR OLD CHILDREN WHO WERE THIN AT BIRTH HAVE RAISED ADRENAL STEROID EXCRETION AND AN INCREASED WAIST TO HIP RATIO

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**Background:** We postulated that an adverse fetal environment might programme permanent changes in adrenal steroid metabolism. We therefore examined steroid excretion in relation to birth and current size in a group of healthy children.
**Subjects:** 171 children aged 9 to 10 years (89 M, 102 F) from a population sample born in and still living near Salisbury, UK.
**Methods/Intervention:** The children were measured, and urine was collected over 24 hours at home. Steroid metabolites were analyzed by gas chromatography.
**Results:** Mean (SD) birth weight was 3.38 (0.47) kg and birth length 51.1 (2.4) cm. Total cortisol metabolites ranged from 320 to 6420 and adrenal androgens from 20 to 1220 $\mu$g/day. All statistical analyses included adjustment for sex and weight at 9 years. For a given birth length a 1 kg decrease in birth weight predicted an increase in adrenal androgens of 63.4% (19.7 to 123.0%; p=0.002) and a 0.017 (0.001 to 0.034; p=0.03) increase in WHR. For a given length the highest cortisol metabolite excretion was found in those children who had been lightest at birth, though the relationship across the range of birth weights was U shaped (test for quadratic term p=0.006).
**Conclusion:** This study shows that the thin baby has increased adrenal androgen excretion and an increased WHR in childhood. These findings may represent an earlier onset of adrenarche in thin babies, and may also be important as the thin baby is known to be at increased risk of cardiovascular disease in adult life.

## † 34

Paediatric surveillance as a tool for the evaluation of National Immunisation Programmes (NIP), particularly of immunisation against invasive infections by *Haemophilus influenzae* type b (Hib).

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*Background*: Clinical surveillance of invasive Hib infections through paediatricians can contribute to th evaluation of Hib vaccination which has been introduced in several European countries recently.
*Study design*: Active surveillance of invasive Hib disease / vaccine failures by national paediatric surveillance centres in the United Kingdom, Germany and the Netherlands.
*Methods:* Monthly reporting of meningitis, epiglottitis, bacteraemia, osteomyelitis and arthritis with isolation of *Haemophilus influenzae* (type b) from a normally sterile site in vaccinated children in the United Kingdom (vaccine failure study), and irrespective of immunisation history in Germany and the Netherlands (continuous surveillance).
*Results*:

| | United Kingdom | Germany | the Netherlands |
|---|---|---|---|
| period | Sept '92-Jan'95 | July'92-Dec'94 | Oct'93-Aug'94 |
| number of reports concerning children up to 10 years | 141 | '92 70<br>'93 121<br>'94 65 | <br>'93 144<br>'94 21 |
| true vaccine failures | 32 | 15 | 0 |
| possible failures | 3 | 48 | 1 (strain not typed) |

*Conclusions*: Paediatric surveillance has shown a reduction of Hib infections since the introduction of vaccination and is of added value for the evaluation of the effect of Hib vaccination. Accurate typing of isolated strains of *Haemophilus influenzae* is essential.

## * 35

Formula Feeding Preterm Infants After Hospital Discharge: 1. Effects on Nutrient Intake, Growth, and Weaning.
Cooke RJ, Griffin I, J Wells, Smith J, Robinson S, Leighton M. University of Newcastle-Upon-Tyne, England.

Hypothesis: infants fed a 'preterm' formula will grow better and wean later than those fed a 'term' formula.
Subjects: preterm infants (BWT ≤ 1750 g, GEST ≤ 34 weeks)
Intervention: infants were fed a 'preterm' (discharge-4 months corrected age; gp A) or a 'term' (discharge-4 mths; gp B), or both ('preterm' from discharge-term, 'term' from term-4 mths; gp C) infant formulas at hospital discharge.
Measurements: intake, anthropometry, and serum chemistries every two weeks between discharge-term and monthly to 4 m.
RESULTS: Were analysed using ANOVA and viewed significant at $p < .01$. At enrollment the groups were similar. Volume of intake was less (A = 144 > B = 169, C = 160 mls/kg/d) but energy intake (A = 115, B =112, C = 111 cals/kg/d) was similar in the groups. Protein intake was greater (A = 3.2 > B = 2.4, C = 2.6 g/kg/d) and related to a higher BUN, increased weight ( A = 6073 > B = 5730, C = 5708 g) and head circumference (A = 42.3 > B = 41.5, C = 41.6 cms). Infant in gp B weaned 3 weeks earlier than those in A.
CONCLUSIONS: The type of formula fed signficantly altered protein energy status, growth, and the time of weaning in these infants

## * 36

### NON-INVASIVE MEASUREMENT OF ABSOLUTE DEOXY-HAEMOGLOBIN CONCENTRATION IN THE NEONATAL BRAIN

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**Background**: Near-infrared spectroscopy (NIRS) currently measures *changes* in cerebral haemoglobin concentration in the neonatal brain. Novel multiwavelength spectrometers can measure *absolute* concentrations of chromophores by ratioing second differential spectral features to those of a fixed chromophore (tissue water).
**Subjects:** 19 healthy newborn infants (median gestational + postnatal age = 37 weeks); 19 neonatal pigs (age < 24 hours), anaesthetised with 1-2% isoflurane and ventilated with an oxygen/nitrous oxide mixture.
**Interventions:** The absolute deoxyhaemoglobin concentration [Hb] was determined by ratioing the second differential peak at 760 nm to those of water at 730 nm and 830 nm, assuming a mean cerebral water content of 85%. In the piglets, reducing the inspired $[O_2]$ to zero fixed the oxyhaemoglobin concentration $[HbO_2]$ at zero and allowed the absolute calculation of [Hb], [Hb] + $[HbO_2]$ (cerebral haemoglobin concentration, CHC) and $S_{mc}O_2$ (cerebral mean haemoglobin saturation).
**Results:** (mean ± SD)

| Subject | Hb μM (n) | CHC μM (n) | $S_{mc}O_2$ % (n) |
|---|---|---|---|
| Human Infant | 14.6 ± 4.0 (19) | ND | ND |
| Neonatal Pig | 14.8 ± 2.5 (19) | 44.2 ± 11.2 (6) | 67.9 ± 6.7 (6) |

**Conclusion:** NIRS can measures absolute Hb concentrations rapidly and non-invasively. The neonatal pig and human have identical cerebral deoxyhaemoglobin concentrations ; the neonatal CHC is about half that of an adult, consistent with a smaller cerebral blood volume in the neonate.

## † 37

THE CONTRIBUTION OF BIRTH ASPHYXIA TO CEREBRAL PALSY IN A DEVELOPING COUNTRY
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**Background:** Current estimates in developed countries suggest that birth asphyxia (BA) accounts for cerebral palsy (CP) in only 1-2/10000 deliveries, but this figure is likely to be higher in developing countries.
**Study design:** Prospective, observational survey of all term asphyxiated neonates over a one year period at Baragwanath Hospital (tertiary care centre) and satellite Soweto clinics (total 30000 deliveries) who subsequently developed hypoxic ischaemic encephalopathy (HIE).
**Results:** 101 term infants with BA and subsequent HIE were enrolled and 53 were evaluated at 1 year as shown below.

| HIE grade | No. enrolled | Died | Lost | CP |
|---|---|---|---|---|
| I | 25 | 0 | 8 | 0 |
| II | 55 | 10 | 11 | 21 |
| III | 21 | 19 | 0 | 2 |

Thus 23 infants developed CP that could reasonably be ascribed to BA (Freeman & Nelson criteria used).
**Conclusions:** The rate of 7,7/10000 cases of CP due to BA is substantially higher than that for developed countries. Prospective intervention drug studies (magnesium, allopurinol, etc) are currently being planned.

## † 38

HEMOLYTIC CRISIS IN A G6PD DEFICIENT FEMALE NEWBORN INFANT WHOSE MOTHER INGESTED FAVA BEANS BEFORE DELIVERY
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**Background:** Cases of favism have been reported in G6PD deficient breast-fed infants when mothers had eaten fava beans. We report here the first documented case of favic crisis occurred in utero and whose clinical signs were evident at birth.
**Subject:** A baby girl born at 37 weeks gestation by cesarean section for initial fetal distress with diffuse pallor, yellow sclerae and enlarged liver and spleen.
**Measurements:** Standard hematological determinations and urinalysis; G6PD activity and 2dG6P utilization rate were measured on erythrocytes purified by cellulose column filtration and in mononuclear cells, respectively.
**Results:** At birth Hb 7.3 g/dl, Htc 23%, erythroblasts 10%, reticulocytes 9%, Heinz bodies 5.4%, bilirubin 174 μmol/l, blood group O Rh+ (mother O Rh+), Coombs' test negative, TORCH antibodies absent, presence of hemoglobinuria. Both mother and infant were heterozygote for G6PD deficiency, and the mother had ingested fava beans 5 days before delivery. The anemia was treated with blood transfusion; the highest bilirubin value (326 μmol/l) was reached on day 4th; the hemoglobinuria disappeared on day 5th.
**Conclusions:** The risk of favism extends into the intrauterine life, with possible threaten for the fetus' life. Women in high prevalence areas should avoid the ingestion of fava beans and the exposure to oxidizing substances during pregnancy.

## † 39

PROSPECTIVE STUDIES OF VITAMIN K DEFICIENCY BLEEDING (VKDB) IN VARIOUS COUNTRIES
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**Background:** Concern about potential carcinogenic effect of parenteral vitamin K prophylaxis has prompted several countries to introduce different oral prophylaxis schemes. Are these as effective as parenteral prophylaxis and which is the most effective sheme?
**Methods:** Active surveillance programs for VKDB are presently run in Germany, British Isles, Switzerland, Australia and Holland. Uniformity in case-definition allows international comparison of the incidence of VKDB and the efficacy of different prophylaxis regimes.
**Results:** In Germany, British Isles, Switzerland and Australia two or three repeated oral doses of 0.5-2 mg vitamin K are recommended. The incidence of late VKDB was calculated to be about 2-5/100,000. In Holland, however, the incidence seems to be lower than 1/100,000. In Holland a daily dose of 25 μg vitamin K is recommended for breastfed infants between 1 and 13 weeks of age.
**Conclusion:** Comparison of international data on the incidence of VKDB will show which regime of oral vitamin K prophylaxis is most effective.

## * 40

COLLAGEN MARKERS AND GROWTH IN PRETERM INFANTS WITH BRONCHOPULMONARY DYSPLASIA TREATED WITH DEXAMETHASONE
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BACKGROUND : High-dose dexamethasone (DXM) is commonly used to treat bronchopulmonary dysplasia (BPD) in preterm infants, but there are concerns about its side effects on bone and growth.
STUDY DESIGN : A prospective longitudinal study in a neonatal intensive care unit.
SUBJECTS & INTERVENTIONS : Thirty-four preterm infants (birthweight <1500g, 23-33 weeks gestation) were studied over the first 15 weeks of life. Twelve babies who developed severe BPD received DXM (500μg/kg/d for 3 days, followed by gradually decreasing doses for various periods).
MEASUREMENTS : Plasma procollagen Type I C-terminal propeptide (PICP), the cross-linked telopeptide of Type I collagen (ICTP), procollagen Type III N-terminal propeptide (P3NP), weight velocity (WV) and lower leg length velocity (LLLV, by knemometry), all at intervals of ≤1week.
RESULTS : In the non-DXM-treated babies, PICP, P3NP, LLLV & WV increased rapidly to a plateau, while ICTP decreased (ANOVA, $P < 0.01$). Mean LLLV and WV correlated positively with mean PICP ($r = 0.74$ and 0.94 respectively) but negatively with mean ICTP ($r = -0.76$ and $-0.71$). DXM treatment resulted in rapid marked decreases in all markers compared to pre-treatment values: -39±5%, -69±4%, -43±9% (mean ± SE) for PICP, ICTP & P3NP respectively (paired t tests, $P < 0.002$). Maximum decreases in daily LLLV and WV in response to DXM were -230±40% and -262±35% ($P < 0.0001$). As the DXM dose was gradually reduced, the markers, LLLV and WV all returned to or exceeded the expected levels for postnatal age.
CONCLUSIONS : Growth in preterm infants was strongly related to markers of bone collagen turnover. High-dose DXM treatment resulted in dramatic decreases in all collagen markers and in growth, with evidence of a dose-dependent effect. Collagen markers may be used to determine the optimum dose of DXM that will avoid deleterious effects on bone turnover and growth.

## † 41

BIOCHEMICAL MARKERS OF BONE AND SOFT TISSUE TURNOVER DURING CHEMOTHERAPY IN CHILDREN WITH ACUTE LYMPHOBLASTIC LEUKAEMIA

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BACKGROUND: Intensive chemotherapy may have a detrimental effect on growth, but the precise timing, extent and aetiology of any growth deficit and/or catch-up growth are unknown.
SUBJECTS, STUDY DESIGN & INTERVENTIONS: Five children (1.2-5.4years) with acute lymphoblastic leukaemia and enrolled in UKALL(XI) were studied longitudinally from diagnosis to week 23 of chemotherapy. None of the children received cranial irradiation.
MEASUREMENTS: Procollagen Type I C-terminal propeptide, the cross-linked carboxy-terminal telopeptide of Type I collagen, procollagen Type III N-terminal propeptide and bone alkaline phosphatase (BALP) were measured at frequent intervals in all children. In the two oldest children, weekly knemometry allowed calculation of lower leg length velocity (LLLV).
RESULTS: BALP and all three collagen markers were suppressed during induction and first intensification, then increased dramatically after completion of first intensification, often to supra-normal levels (paired t-tests, P<0.05). A second decrease in the markers occurred during second intensification, followed by a second post-intensification increase (P<0.05). Individual children showed some variation within this overall pattern: sudden decreases in the markers could be ascribed to clinical events such as ileus and septicaemia. In the two children who underwent knemometry, LLLV parallelled the changes in biochemical markers.
CONCLUSIONS: Marked changes in biochemical markers of bone and soft tissue turnover were seen during the first 6 months of chemotherapy in this small cohort of children. Following suppression of all markers during induction and intensification, a catch-up response was then observed. There is preliminary evidence that these marked biochemical changes reflected equally marked short-term fluctuations in growth. The study continues.

## † 42

**Transcutaneous oxygen (tcpO2) levels preceeding retinopathy of prematurity (ROP)**

Steve Cunningham Brian Fleck Robert Elton Neil McIntosh

**Background** ROP continues to cause major morbidity in preterm infants. Questions still exist as to the role of oxygen in its development

**Study Design** Retrospective comparative analysis
**Setting** Tertiary neonatal intensive care unit
**Subjects** 31 infants with grade 3 ROP matched for birthweight and gestation to 38 infants with ROP grade 0,1 or 2

**Measurement** TcPO2 was routinely collected at 1 minute intervals to a computerised cot monitoring system. TcpO2 data was assessed in 6 hour time periods from birth for the first 21 days. For each time period the mean, sd, maximum and minimum values were calculated and the number of minutes with a tcpO2 >12kPa, >10kPa and <5kPa were measured. 22 other factors were considered from casenotes. Chi-squared (+Yates), Wilcoxon rank sum and multiple logistic regression were used for analysis.

**Results** ROP was associated with maximum intra-ventricular haemorrhage (IVH) grade ($p<0.01$), number of blood transfusions ($p<0.01$), average volume of colloid given per kg per day over 21 days ($p<0.01$), average number of blood gases taken per day over 21 days ($p<0.05$), and number of days of ventilation ($p<0.01$) and supplemental oxygen ($p<0.001$). When adjusted for birthweight and gestation only IVH ($p<0.01$) continued to be significant. When adjusted for birhtweight, gestation and IVH, babies with grade 3 ROP showed an increased sd of tcPO2 ($p<0.05$) and greater maximum tcpO2 ($p<0.05$) over the first 21 days of life. Duration of high tcpO2 was not associated in our study. The sd of tcpO2 gave a stronger independent prediction of ROP in the first week ($p<0.01$), than the second ($p<0.05$) or third (NS) weeks.

**Conclusion** TcpO2 variability in the first week of life is a significant predictor of severe ROP. Increased sensitivity of the preterm infant to variable oxygen may be responsible for the development of ROP.

## † 43

EVOLUTION OF STRIATAL DOPAMINE RECEPTORS AFTER A NEONATAL HYPOXIC-ISCHEMIC INJURY IN THE RAT.

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**Background/aims**: Cerebral hypoxia-ischemia (H/I) occurring during the neonatal period in humans often induced damages to the striatum. Scintigraphic exploration (SPECT) of the brain is actually the most valuable atraumatic method to study the neuronal function. We hypothesized that exploration of striatal dopamine receptors would be a valuable reflect of neuronal dysfunction induced by a neonatal H/I.
**Subjects**: 8-day-old Wistar rats.
**Interventions**: They were submitted to unilateral ligation of the common carotid followed by 2h of hypoxia (8% O2). Dopamine D1 and D2 receptors were studied 1, 2 and 11 weeks after H/I using an ex vivo autoradiographic method with iodinated ligands suitable for SPECT, TISCH for D1 and IBZM for D2 receptors.
**Results**: In brains devoid of visible anatomic lesion, we observed with IBZM a bilateral decrease in the ex vivo binding of 20% and 40% respectively 1 and 2 weeks after H/I. However, no modification compared to control rats was obtained 11 weeks after H/I. With TISCH, no modification in the ex vivo binding was observed at 1, 2 and 11 weeks afetr H/I.
**Conclusions**: Results showed that a transitory dysfunction in dopaminergic transmission consecutive to a neonatal H/I can be detected without visible loss of cerebral volume. Dopamine D2 receptors were more vulnerable than D1 in this developmental period. This may be related to different time-course in the maturation of each type of receptors. It can be assumed that SPECT exploration of dopamine D2 receptors in human neonates suffering from asphyxia would be valuable for the diagnosis and follow up of striatal dysfunction.

## † 44

**ERYTHROPOIETIN IN RHESUS HEMOLYTIC DISEASE DURING PREGNANCY AND IN THE FIRST TRIMENON**

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Aim of this study was to investigate the relationship between Erythropoietin (EPO) and hemoglobin in fetuses and newborns suffering from Rhesus hemolytic disease (RHD).
**Patients and methods:** We measured EPO in 28 fetuses during the $19^{th}$ and $37^{th}$ week of gestation, in cord blood at birth and postpartally during the first 12 weeks in 35 newborns. All 429 blood samples were taken before or after an intervall of more than 6 days beyond a transfusion to exclude a relevant suppression of endogenous EPO synthesis.
**Results:** In spite of decreased hemoglobin levels intrauterine EPO was low during the $19^{th}$ to $28^{th}$ week (Hb $\bar{x}$= 8.1 g/dl, EPO $\bar{x}$= 11.6 mU/ml). Later on intrauterine EPO increased significantly with gestational age ($r = 0.71$; $p < 0.001$). These EPO levels were also significantly elevated in comparison to EPO in healthy fetuses ($p < 0.05$). Independently from gestational age we found extremly elevated EPO if hemoglobin (≤ 5 g/dl) was extremly decreased. At birth mean EPO concentration was significantly higher (171 mU/ml) in RHD than in a control group of 54 healthy term newborns ($p < 0.001$). Neonatal EPO decreased to low values; a minimum of 6.5 mU/ml was reached at the $14^{th}$ day. At this time we found relatively high, hemolytically relevant anti-D-antibody-titers ($\bar{x}$= 1:64 - 1:128). In the $6^{th}$ week EPO values increased up to 50 mU/ml.
**Conclusions**: After the $28^{th}$ week of gestational age a significant increase of fetal EPO synthesis is possible in order to correct fetal anemia. The course of EPO in newborns with erythroblastosis resembles the physiological changes of preterm newborns in the first two weeks and shows similar dynamics. Late anemia in RHD seems to be caused by a prolonged hemolysis and an inadequate EPO synthesis.

## * 45

**BODY COMPOSITION IN BREAST-FED (BF) AND FORMULA-FED (FF) INFANTS: DIFFERENT EFFECTS OF FEEDING MODE IN BOYS AND GIRLS - A 12 MONTHS FOLLOW-UP.**

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Background: FF infants grow faster than BF infants. In baboons sex-related differences in growth and composition of weight gain which were dependent upon feeding mode (FMo), have been observed [1]. We report an influence of sex and FMo on human infant growth and body composition.
Subjects / study type: Longitudinal study in 46 non-hospitalized, healthy, Caucasian infants.
Interventions: Infants were either BF (n=23,♂:♀=9:14) or FF (n=23, ♂:♀=15:8). Solid foods were introduced > 4 months of age. Gain in body fat (BF), fat-free mass (FFM) (from TOBEC® measurements), weight (W) and length (L) was measured between 1, 2, 4, 8 and 12 months of age.
Results: The Table shows differences in gain between sexes (Δsex) for each FMo, and between FMo (ΔFMo) for each sex, as calculated for W (g/d), L(mm/d), BF(g/d) and FFM(g/d).

| | | Δsex | | | | | | ΔFMo | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| age | FMo | W | L | BF | FFM | age | sex | W | L | BF | FFM |
| 1-2 | BF | 6.5* | 0.10 | 4.2# | 2.4 | 1-2 | m | -2.3 | 0 | -2.7 | 0.4 |
| | FF | 0.9 | 0.12 | -2.3 | 3.2 | | f | 3.4 | -0.02 | 3.8* | -0.4 |
| 2-4 | BF | 5.7** | 0.18** | 0.8 | 4.9** | 2-4 | m | -1.7 | -0.11 | -0.1 | -1.6 |
| | FF | -2.4 | 0.05 | -1.8 | -0.6 | | f | 6.4** | 0.02 | 2.6* | 3.8** |
| 4-8 | BF | -0.1 | -0.01 | 0.8 | -0.8 | 4-8 | m | -0.5 | 0.04 | -0.5 | 0 |
| | FF | -0.4 | -0.04 | 0.2 | -0.5 | | f | -0.2 | 0.06 | 0.1 | -0.3 |
| 8-12 | BF | 0.3 | -0.03 | 0.4 | -0.1 | 8-12 | m | 1.3 | -0.01 | -0.8 | 2.1 |
| | FF | 1.9 | 0.01 | -0.6 | 2.5 | | f | -0.3 | -0.06 | 0.2 | -0.6 |

*f=female, m=male. BOLD: *p< 0.05, ** p< 0.01 (# p=0.07) by one-way ANOVA*

Conclusions: 1) In the period of exclusive BF or FF, gain in length and weight as well as composition of weight gain depend upon feeding mode and sex (Δsex only significant in BF, ΔFMo only significant in girls). Feeding-[2] or gender-related hormonal differences (e.g. high androgen levels found in young male infants) may explain these phenomena. 2) Beyond 4 months of age (after the introduction of solid foods) no effect of previous feeding mode or gender on W-, L-, BF- and FFM-gain was found.

[1] *Lewis et al. J Nutr 1984; 114:2021-6,* [2] *Lucas A et al. Lancet i, 1980:1267-8*

## † 46

**ENERGY AND MACRONUTRIENT INTAKE IN BREAST-FED AND FORMULA-FED INFANTS: A 12 MONTHS FOLLOW-UP.**

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Background: It has been reported that BF infants consume less energy ($kg^{-1}d^{-1}$) than FF infants. Whether the difference in energy intake (EI) and/or in macronutrient intake persist beyond the period of exclusive BF or FF has not yet been widely explored on a longitudinal basis.
Subjects / study type: Longitudinal study in 46 non-hospitalized, healthy, Caucasian infants.
Interventions: Infants were either BF (n=23,♂:♀=9:14) or FF (n=23, ♂:♀=15:8). Solid foods were introduced > 4 mo of age. Food intake was measured by 5-day test weighing (at 1, 2, 4 and 8 mo of age) or by the 'double-portion' method for 3 consecutive days (12 mo of age) and body weight was recorded. EI was calculated from fat (F), protein (P) and carbohydrate (C) composition of the foods'. Effects of gender and feeding mode on intake were assessed by standard two-way ANOVA.
Results: No significant difference between boys and girls was found on any test variable. Total intake ($g^{-1}kg^{-1}d^{-1}$) was not different between feeding groups, except at 2 mo of age (FF=156 $g^{-1}kg^{-1}d^{-1}$, BF=139 $g^{-1}kg^{-1}d^{-1}$, $p< 0.001$). Significant higher EI were found for FF vs BF infants aged 1 mo (115 vs. 102 $kcal^{-1}kg^{-1}d^{-1}$, $p=0.043$), 2 mo (109 vs. 87 $kcal^{-1}kg^{-1}d^{-1}$, $p<0.001$) and 4 mo (90 vs. 76 $kcal^{-1}kg^{-1}d^{-1}$, $p<0.001$). These differences were caused by significant higher intakes in FF infants of F and P, but not of C. No significant differences were found beyond 4 months of age.
Conclusion: 1. Significant differences in energy intake (kcal/kg/d) (FF>BF) during the first 4 months of life are due to different intakes of fat and protein, but not of carbohydrate. Differences in intake disappear beyond the period of exclusive FF or FF. 2. Although sex-related differences in growth clearly exist, intake of energy and macronutrients did not differ between sexes in this study. The effect must be due to differences in digestibility and/or utilization of metabolizable energy intake.

*Garza C et al. In: Jensen RG, Neville MC, eds. Human lactation. New York: Plenum Press. 1985:121-6*

## † 47

**ligh frequency ventilation (hfv) of rabbits with three types of ventilators.**

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**Aim:** Evaluation of three different high frequency ventilators, 2 true oscillators Dufour OHF-1, SensorMedics 3100A-SM) and 1 hybrid ventilator (Dräger Babylog 8000 hfv-BBL), in animals with severe respiratory failure.

**Subjects:** Anaesthetized, tracheotomized and ventilated New Zealand rabbits n=7) with respiratory failure induced by repeated whole-lung lavage.

**nterventions:** With $pO_2 < 80$ mmHg on standard ventilation (P26/6; $FiO_2 = 1.0$) nimals were switched to hfv ($FiO_2 = 1.0$; frequency 10Hz in BBL +SM, 15Hz n OHF). Mean airway pressure (MAP) was increased till $pO_2 > 450$ mmHg, vich means lungs were open (=high MAP) and then decreased to keep $O_2 > 450$ mmHg (=low MAP). Peak-peak pressure (p-p) was adjusted to naintain $pCO_2$ 35-45mmHg. MAP (high and low) and p-p were recorded at the roximal endotracheal tube connection with an independent pressure monitor.

**tesults:**

| | MAP ($cmH_2O$) | | $pO_2$ (mmHg) | | p-p ($cmH_2O$) | | $pCO_2$ (mmHg) | |
|---|---|---|---|---|---|---|---|---|
| ean ±SD | high | low | high | low | high | low | high | low |
| BL | 17.4 ±2.8 | 13.6 ±1.6 | 498 ±20 | 489 ±20 | 18 ±2 | 18 ±4 | 39.0 ±5.4 | 39.1 ±5.3 |
| HF | 18.2 ±2.8 | 12.3 ±3.3 | 452 ±53 | 469 ±27 | 26 ±5.5 | 26 ±8 | 39.0 ±3.2 | 39.6 ±4.8 |
| M | 18.7 ±2.3 | 13.8 ±3.0 | 475 ±36 | 479 ±32 | 26 ±6 | 24 ±9 | 35.9 ±4.5 | 33.3 ±3.4 |

Ieart rate and blood pressure were not influenced by the type of ventilator.

**Conclusions:** Adequate gas exchange could be achieved in all animals with the )HF and SM, and in animals up to 3.1 kg with the BBL. Ventilatory arameters were not significantly different between the three hfv devices.

## † 48

hG-CSF IN SEVERE CHRONIC NEUTROPENIA: SUCCESSFUL INTERMITTENT REATMENT IN 3 INFANTS.

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ackground: rhG-CSF appeared to be effective for treatment of atients with diagnosis of idiopathic, cyclic and congenital forms f neutropenia; we describe our long-term experience in 3 infants ith chronic idiopathic neutropenia.

ubjects: three infants (1M; 2 F) aged between 6 and 15 months ith an absolute neutrophil count (ANC) $< 0.5 \times 10^9$/l lasting for ore than 6 weeks, with severe repeated infections.

nterventions: patients received, after informed consent, rhG-CSF t a starting dosage of 3-10 μg/Kg/d s.c. until ANC $> 1 \times 10^9$/l and han 3-10 μg/Kg/d s.c. every 3-7 days.

esults: ANC were $> 1 \times 10^9$/l after 3-7 days of treatment and they ould have been mantained at those mean levels with a single dministration every 3-7 days. Follow-up: patients received etween 4 and 10 months of treatment obtaining a reduction of nfections and no notable side effect.

onclusion: intermittent administration of rhG-CSF is safe and ffective in infants with severe chronic neutropenia.

upported by a grant from MURST (40%).

## * 49

**:ONTINUOUS GASTRIC INFUSION OF GLUCOSE (CGG) IN THE 'REVENTION OF HYPOGLYCAEMIA IN LBW INFANTS.**

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**Background.** Continuous gastric infusion of glucose (CGG) is routinely sed in our Unit in the first 12 hours of life in order to prevent the ccurrence of hypoglyceaemia in moderately LBW infants. A shorter eriod of CGG, if equally effective, has been advocated for promoting arly sucking and breast feeding.

**ubjects.** 243 newborns weighing 1800-2499g. at birth were randomly llocated to a short or long (standard) CGG regime from the first hour .

**nterventions.** *Short CGG*: 8% glucose 15ml/Kg/4 hours followed by uman milk or formula 80ml/Kg/20 hours orally or by gavage. *Long CGG*: % glucose 45ml/Kg/12 hours then same as other group 50ml/Kg/12 ours. Blood glucose was measured at 2-6-12-18-24 hours of life.

**esults.** The relative risk of hypoglycaemia (<30mg/dl) in the short CGG roup was *1.4* (95%C.I.= 0.7-2.8) at T2 (both groups on CGG), *5.1* )5%C.I.= 1.5-17.5) at T6-12 (on different feeding regimes) and *0.7* )5%C.I.= 0.2-2.7) at T18-24 (both groups on oral/gavage feeding).

**onclusions.** CGG is more effective than intermittent oral or gavage eeding in preventing the occurrence of hypoglycaemia in moderately low irth weight infants and should not be shorter than 12 hours.

## ● 50

**ANTIOXIDANTS IN HEALTHY, FULLTERM INFANTS FED FORMULA ENRICHED WITH LONG-CHAIN POLYUNSATURATES (LCP)**

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**Background:** It is not known whether enrichment of infant formula with LCP may alter the availability of fat- and/or water-soluble antioxidants in fullterm infants (FTI).

**Subjects:** FTI fed formula without (F, n=10) or with LCP (LCP-F, n=12).

**Interventions:** Plasma concentrations of α-tocopherol (α-TOCO), cholesterol (C), triglyceride (TG) and urate were measured on Day 5, 30, 60 and 90 of life.

**Results:** Neither α-TOCO values, nor α-TOCO/(C+TG) ratios differed (table). Urate values were significantly lower on Day 30 with LCP-F, later no differences were seen.

**Table: Antioxidants in healthy, fullterm infants fed formula without (F, n=10) or with long-chain polyunsaturates (LCP-F, n=12)[mean (SEM), *P=0.01].**

| Age | | Day 5 | Day 30 | Day 60 | Day 90 |
|---|---|---|---|---|---|
| α-tocopherol | F: | 5.1 (2.1) | 8.7 (1.5) | 11.5 (0.9) | 11.5 (1.0) |
| (μg/ml) | LCP-F: | 5.0 (1.2) | 7.6 (1.2) | 10.7 (1.7) | 11.5 (2.4) |
| α-tocopherol | F: | 0.9 (0.3) | 2.5 (0.5) | 2.6 (0.3) | 2.7 (0.2) |
| C+TG (g/mol) | LCP-F: | 1.1 (0.3) | 2.1 (0.3) | 2.5 (0.2) | 3.0 (0.4) |
| Urate | F: | 222 ( 21) | 181 ( 10)* | 191 ( 23) | 178 ( 18) |
| (μmol/l) | LCP-F: | 206 ( 24) | 127 ( 9)* | 157 ( 14) | 204 ( 37) |

**Conclusion:** Enrichment of formula with LCP did not influence the availability of α-tocopherol in FTI, but was accompanied with transient decrease of plasma urate.

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**LONG-CHAIN POLYUNSATURATES (LCP) IN MALNOURISHED CHILDREN WITH HUMAN IMMUNODEFICIENCY VIRUS-1 (HIV) INFECTION**

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**Background:** ω-3 LCP have been suggested as coadjuvant treatment in HIV disease in adults. We are unaware of data on the LCP status of HIV-seropositive children.

**Subjects:** 35 severely malnourished children (MC) [age: 29 (7) months, BW: 9.2 (2.1) kg, median (IQR)] were studied. They were either HIV-seronegative (P0, n=16) or suffered from asymptomatic (P1, n=12) or symptomatic (P2, n=7) HIV-infection.

**Method:** Plasma phospholipid fatty acids were determined by chromatography.

**Results:** BW of MC did not correlate with linoleic (C18:2n-6, LA) and alpha-linolenic (C18:3n-3, ALA) acid values (r= -0.02 and 0.07), but were significantly correlated to values of arachidonic (C20:4n-6, AA) and docosahexaenoic acids (C22:6n-3, DHA) (r = 0.40 and 0.63, P<0.0001). LA and ALA did not differ between P0, P1 and P2.

**Table: Major LCP in plasma phospholipids** [mg/l; $^{a,b}$ = P<0.05, $^{c,d}$ = P<0.005].

| | C20:3n-6 | C20:4n-6 | C20:5n-3 | C22:6n-3 |
|---|---|---|---|---|
| Stage P0 | 25.98 (6.37)$^a$ | 61.46 (10.1)$^a$ | 2.51 (0.64)$^a$ | 9.62 (1.75)$^c$ |
| Stage P1 | 32.39 (3.10)$^b$ | 57.73 (7.70) | 2.53 (0.47)$^b$ | 7.91 (1.42)$^d$ |
| Stage P2 | 21.02 (8.88)$^{a,b}$ | 46.10 (14.5)$^a$ | 1.41 (0.62)$^{a,b}$ | 4.78 (1.51)$^{c,d}$ |

**Conclusions**: 1. MC exhibited deficiency of both AA and DHA directly proportional to the degree of malnutrition. 2. Children with stage P2 HIV-disease had more severe depletion of both ω-3 and ω-6 LCP than children with stage P0 or stage P1.

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**Differences in the aminogram in children with severe hepatic disease, according to the different pathogeny.**

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**Background:** This work evaluates the plasma aminogram of children with severe hepatic disease. **Subjects:** A prospective study was done in 26 pediatric patients included in a hepatic transplant program. The patients were divided into two groups -cholestasis and cellular damage- to evaluate if there were any differences in the aminogram according to the clinical diagnosis. **Interventions:** 24 aa. and 5 aa. groups -total, essential, non-essential, branched and aromatic- were analyzed and the Fisher index used. **Results:** Our results coincide with the alterations described in adults, with a significant increase of the AAA phenylalanine($p<0.04$) and tyrosine($p<0.0003$) and a decrease of the BCAA isoleucine($p<0.00001$), leucine($p<0.00001$) and valine($p<0.00001$), and in the BCAA/AAA($p<0.00001$) ratio. We also found a significant increase in glutamic acid($p<0.0009$), ornithine($p<0.03$) and citrulline($p<0.03$) and a significant decrease in glutamine($p<0.00001$),cysteine($p<0.03$),taurine($p<0.005$),tryptophan($p<0.05$), serine($p<0.008$), threonine($p<0.00001$), TAA($p<0.002$) and EAA($p<0.00001$), that seem to express a greater metabolic affectation. Our two different physiopathological groups have specific differentiating characteristics: the cholestasis group has very low values of taurine($p<0.0003$) while we found clearer increases of tyrosine($p<0.01$), phenylalanine and hydroxyproline($p<0.01$) in the cellular damage group. **Conclusions:** These findings clarify the complex mechanisms of the different hepatic diseases. The low levels of taurine found allow us to recommend that this aa. be supplemented in the alimentation of the child with severe hepatopathy, especially if it has a cholestatic basis.

## † 53

METABOLIC AND HORMONAL EFFECTS OF PROPOFOL IN CHILDREN: IS IT A SAFE TREATMENT ?

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**Background:** The safety of propofol infusion in children has recently been challenged by the demonstration of unexplained metabolic acidosis[1]. We therefore examined the metabolic effects of propofol in critically ill children receiving this agent for sedation.
**Patients:** 8 critically ill children {age, median(range)= 7(3-12) years}
**Interventions:** The median and total dose of propofol ranged from 2.6-11.4 mg/kg/h, and 590-24178 mg respectively, with median (range) duration of use 68.5 (15.3-166.4) h.
**Measurements:** We measured the acid-base status and the concentrations of intermediary metabolites and stress hormones prior to and daily after the institution of propofol.
**Results:** None of these children became acidotic during propofol infusion. Their mean lactate, ß-hydroxybutyrate, non-esterified fatty acid and cortisol concentrations ranged from 0.9 to 1.75 (mean, 1.28) mmol/l, 0.06 to 0.68 (mean,0.16) mmol/l, 0.52 to 1.13 (mean 0.72) mmol/l, and 260 to 1613 (mean 606) nmol/l, respectively. These data did not differ significantly from the stress responses of head injured children sedated with other agents, or those undergoing major surgery.
**Conclusion:** Although we found no adverse metabolic effects, this does not prove the safety of propofol in a larger population, and the precise cause of propofol related acidosis remains uncertain. Propofol should be used cautiously and as a part of an evaluative programme in larger number of children.

1. Parke TJ, Stevens JE, Rice ASC, et al. Metabolic acidosis and fatal myocardial failure after propofol infusion in children: five case reports. Br Med J 1992; 305: 613-6.

## † 54

DELIVERY OF METERED DOSE INHALER AEROSOLS TO PARALYSED AND NON-PARALYSED VENTILATED RABBITS. T.F.Fok, M.Al-Essa, S. Monkman, M.Dolovich, L. Girard, G. Coates, H. Kirpalani. Depts. Peds, Med, Nucl.Med., McMaster University, Hamilton, Ontario, Canada.

Background: Effects of spontaneous respiration on pulmonary deposition of aerosol, technetium-$^{99m}$labelled salbutamol have not been studied. Subjects and Design: Aerosol delivery to sedated and ventilated rabbits was administered via a MDI (Ventolin, Glaxo,UK) and spacer (MV15 Aerochamber, Trudell,Canada); inserted between the ETT and the ventilator circuit. Group 1 rabbits (n=7, weight [mean±sem] 2681±83g) were paralysed (Pancuronium 100$\mu$g/kg) and ventilated with a rate of 30/min. Group 2 rabbits (n=6, weight 2743±75g) were not paralysed, but spontaneously breathing at 40-50/min. Ventilator settings were the same as those in Group 1 except for a slower rate (10/min). Each animal was given 5 puffs (100$\mu$g/puff) of the MDI aerosol actuated at 1 min intervals. Deposition was measured by radioactivity counts in dissected lung. Results: Values for lungs and airway distal to the ETT were (mean±sem) 0.08±0.23% of the actuated dose in Group 1 and 1.10±0.21% in Group 2 (p=0.344). Deposition as a % of the actuated dose, in the lung tissues beyond the carina was Grp 1 0.23±0.05% vs Grp 2 0.51±0.08% (p=0.009). Deposition in the ventilator circuit, ETT and trachea did not differ significantly between the two groups. There was no significant difference in aerosol distribution among lobes and between lung regions in either groups. Conclusion: In aerosol delivery to ventilated neonates, pulmonary deposition may be significantly greater in those breathing spontaneously on slow intermittent mandatory ventilation that in infants that are ventilated but paralysed.

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GROWTH FACTORS IN PERINATAL PERIOD

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**Background:** We studied the role played by GH, IGF-1 and IGFBP-3 on the neonatal growth and if their blood levels would be influenced by the type of lactation
**Subjects**: Full term and preterm newborns ,with 1 and 3 weeks of postnatal life (n = 83 and 34 respectively)
**Measurements:** Serum levels of GH, IGF-1 and IGFBP-3 and 24 hours urine levels of GH and anthropometric variables were measured.
**Results:** At third week of life serum and urinary GH levels were significantly higher in preterm SGA type I than SGA type II (GHs: 28.0±4.4 vs 11.0±7.21 µ UI/ml p<0.05; GHu: 3.6±0.5 vs 0.5±0.1 ng/kg/24 h p<0.02); serum levels of IGF-1 and IGFBP-3 in preterms showed a significant increase with reference to values obtained at first week (IGF-1: 9.6±5.7 vs 50.3±30.6 ng/ml p<0.0l; IGFBP-3: 389.5±233.2 vs 726.4±318.5 ng/ml p<0.02). Preterms infants feeding with maternal milk supplemented with formula showed significantly higher IGF-1 levels than those who received exclusively a formula (48.1±30.0 vs 26.0±18.7 ng/ml p<0.05). The postconceptional age had a direct relationship with IGF-1 (p<0.0l) and an inverse one with urinary GH ( p<0.001). The intake of human milk had a direct relationship with the levels of IGF-1 ( p<0.001)
**Conclusions:** GH does not contribute to neonatal growth, which is influenced by IFG-1, IGFBP-3, energy and protein intake and the type of lactation.

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NEURODEVELOPMENTAL PROGNOSTIC SIGNIFICANCE OF EARLY CRY ANALYSIS IN PRETERM INFANTS. G.P.Donzelli, G.Rapisardi, M.Moroni, F.Scarano, A.Ismaelli*, P.Bruscaglioni*. Dept of Paediatrics, NICU - *Dept of Physics - University of Florence, Italy.

**Background:** a new transportable device for computerised infant cry analysis which uses digital signal processing techniques and allows quick and complete evaluation of the most important parameters of infant cry, is now in use within the NICU of A.Meyer Children's Hospital, as an aid in neurodevelopmental diagnosis and prognosis in infants affected by CNS diseases. We developed a new method of qualitative evaluation of computerised infant cry analysis based on visual assessment of the quasi-three dimensional graphic output ('Infant Cry Modulation Assessment Scale').
**Subjects:** 25 high risk preterm infants. Based on CNS clinical status and commonly performed diagnostic tecniques (mainly EEG, US) at 6months of age, infants were divided in: normal (n=13); suspect or abnormal (n=12). The 2 groups did not differ for mean GA (31.2±3.8 vs 30.7±3.7 wks), mean BW (1465±503 vs 1435±524g) and mean postconceptional age when the cry was recorded (32.5±3.1 vs 31.9±3 wks).
**Measurements:** the cry was recorded and analysed during the first 2 weeks of life.
**Results:** infants with normal neurological outcome had higher mean energy of the cry and 'ICMAS' score, which indicate a better quality of the cry ($p < 0.05$).
**Conclusion:** our data support the hypothesis that our methodology of infant cry analysis can be used as a non invasive functional method of early CNS assessment in high risk preterm infants. (Sponsored by CNR. Contract No. 92.00083.PF41)

## † 57

EFFICIENCY OF BLUE-GREEN FLUORESCENT LAMP IN THE MANAGEMENT OF NEONATAL HYPERBILIRUBINEMIA.

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**Background:** phototherapy (PT) for neonatal jaundice is based on the photoconversion of bilirubin (ZZ-BR) into the more excretable isomer lumirubin (LR), with maximal formation rate at 480 nm. The configurational photoisomer (ZE-BR) is formed at much higher rates than LR, but it is less excreted, and quickly reaches high, stationary values in serum.
**Hypothesis**: increase of PT efficiency with a blue-green (BG) lamp (for the combined effects of : increase from blue to green of the quantum yield of LR and corresponding decrease of the ZE-BR quantum yield; filtering of the skin, which attenuates more blue than green light).
**Subjects and interventions:** 40 low birthweight infants randomly assigned to receive either BG PT (spectrum peaked at 480nm, 40nm wide) or Special Blue PT (Philips F20T12/BB).
**Results**

| Study groups | BW (g) | GA (wks) | Age at PT onset (hrs) | BR (mg/dL) PT onset: T0 | T 24 hrs |
|---|---|---|---|---|---|
| SB (n = 20) | 1534± 87.4 | 31.2±0.5 | 73±3.8 | 13.6±0.2 | 10.5±0.4 |
| BG (n = 20) | 1517±144.0 | 31.0±0.7 | 77±5.2 | 14.3±0.3 | 7.5±0.5 |

After the first 24 hours of light exposure, the mean percentage decrements in serum BR concentrations were 46.4 ± 2.6 for the BG group and 22.6 ± 3.0 for the SB group ($p < 0.0001$). At 24 hrs 18 subjects of the BG group terminated PT, while 10 subjects of the SB group still needed light treatment. ($p< 0.01$).
**Conclusions**: this study shows a high PT efficiency of this new BG fluorescent lamp, allowing only 1 day of PT in the management of hyperbilirubinemia in preterm infants.

## ● 58

**Evaluation of indirect calorimetry in critically ill children**

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**Background:** Indirect calorimetry was performed to evaluate the energy metabolism in stressed children with different severe pathologies. **Subjects:** Forty children, admitted to the PICU, after extracorporeal cardiac surgery ( group 1 n=14) orthotopic liver transplantation (OLT) (group2 n=15), septic shock ( group 3 n=5) and others (group 4 n=6). **Interventions:** VO2, VCO2, REE, RQ were measured before surgery, at admission, and every 24 h untill day 7. Severity of illness (PRIMS score ) was assessed daily .**Results:** REE differs in +4.2% to -17,1% from calculated basal metabolic rate . Patients showed a significant decrease from admission to day 1 in VO2(7,83 ± 1,97 VS 6,64 ± 1,69 ml/min/kg) p< 0,05, VCO2(6,84 ± 1,94 VS 5,68 ± 1,50 ml/min/kg) p<0,05, and REE (54,4 ± 13,3 VS 47,1 ± 13,4 Kcal/day/kg.. Differences between groups are reflected in table 1:

| | VO2(ml/min/kg)* | VCO2(ml/min/kg)* | REE(Kcal/kg/day)$ |
|---|---|---|---|
| Group 1 | 8,73 ± 2,28 | 7,59 ± 2,50 | 60,3 ± 15,2 |
| Group 2 | 7,26 ± 1,64 | 6,38 ± 1,38 | 50,5 ± 11,3 |

* p<0,001 $ p<0,05

A correlation was found between VO2, REE and PRIMS .**Conclusions:** Indirect calorimetry can be safely performed in the PICU, metabolic parameters may be used to assess general condition in critically ill children.

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**THE EFFECT OF N-ω-NITRO-L-ARGININE (NLA) TREATMENT ON POST HYPOXIC-ISCHEMIC BRAIN INJURY** CA Dorrepaal, M Shadid, P Steendijk, ET van der Velde, JH Meinesz, M van de Bor, J Baan, F van Bel. Dept. of Peds., Univ. Hosp. Leiden, The Netherlands.

**Background:** Post hypoxic-ischemic (HI) brain injury is characterized by an initial cerebral hyperperfusion, followed by cerebral hypoperfusion, decreased cerebral $O_2$-consumption ($CMRO_2$) and decreased electrocortical brain activity (ECBA). Excessive nitric oxide (NO) production upon reoxygenation and reperfusion may play an important role in this post-HI reperfusion injury (e.g. NO-mediated glutamate neurotoxicity).
**Subjects:** 18 newborn lambs, subjected to severe HI
**Interventions:** Changes from pre-HI values were measured for brain blood flow (carotid flow [ml/min]; Qcar), (relative) $CMRO_2$ and ECBA [μV] at 15, 60, 120 and 180 min after HI. Immediately after completion of HI, 6 received a placebo (CONT), 6 a low dose NLA (10mg/kg/iv; NLA-10), and 6 a high dose NLA (40 mg/kg/iv; NLA-40).
**Results:** In contrast to NLA-10 and NLA-40, CONT showed a clear initial hyperperfusion. From 1h after HI, cerebral perfusion was about 80% of the original cerebral perfusion in all 3 groups. In contrast to NLA-10 and NLA-40, $CMRO_2$ was significantly decreased after HI in CONT. ECBA decreased in all lambs, but only recovered to pre-HI-values in NLA-10 at 180 min after HI. Convulsions (ECBA) were detected in 4/6 CONT, 0/6 NLA-10 and 2/6 NLA-40. Brain to body weight ratio was 15.4 ± 1.8 (CONT), 12.5 ± 2.6 (NLA-10) and 11.3 ± 2.2 in NLA-40 (p=0.0086), suggesting less cerebral edema in NLA-treated lambs.
**Conclusion:** Preservation of $CMRO_2$, recovery of ECBA, and the absence of convulsive activity in NLA-10, suggests that a low, rather than a high dose NLA may reduce post-HI-brain injury.

## † 60

IN VIVO EFFECT OF rhG-CSF ON NEUTROPHIL NUMBER AND FUNCTION OF SEPTIC NEONATES
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**Background/Aim:** In vitro and experimental studies have shown that rhG-CSF has a favorite effect on the number and function of neutrophils. The aim of this study was to evaluate the in vivo effect of rhG-CSF on the number and respiratory burst activity (RBA) of neutrophils in septic neonates.
**Subjects:** 1) 42 preterm neonates with proven sepsis (GA=32±5wk). 19/42 were treated with rhG-CSF and 23/42 were not. 2) 25 healthy preterm neonates (GA=32±4wk).
**Intervention:** rhG-CSF was administered subcutaneously at doses of 5 μg/kg (n=7) and 10 μg/kg (n=12), for 3 consecutive days. Measurement of absolute neutrophil count (ANC) and assessment of neutrophil RBA utilizing a flow cytometric microassay with dihydrorodamine 123 were performed before initiation of treatment (time 0) and at 4 subsequent time intervals (24, 48, 72 and 96 hours). Serum levels of G-CSF were measured at time 0 and at 2, 24 and 120 hours thereafter, using ELISA. In healthy neonates, the same measurements were performed only once, during the first week of life.
**Results:** Levels of G-CSF in septic neonates at time 0 (400±380pg/mL, range 98-1074pg/mL) were significantly higher than those found in healthy neonates (108±16pg/mL, range 91-132pg/mL, p <0.05). Administration of rhG-CSF resulted in an impressive elevation (>5000pg/mL) of G-CSF in serum that was maintained for at least 48 hours after the last dose. ANC was found significantly increased at 24 h following administration of 10 μg/kg but not 5 μg/kg of G-CSF. Neutrophil RBA in septic neonates at time 0 (44±24%) was significantly lower than in healthy neonates (69±15%, p<0.001). The RBA in treated neonates showed a progressive increase from 39% at time 0 to 52% at 72 h following administration of rhG-CSF. At the same time, septic neonates not treated with rhG-CSF did not exhibit any increase of RBA.
**Conclusions:** Preliminary results of this study indicate that rhG-CSF administered in septic neonates induces the number of neutrophils and enchances their RBA.

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ASSESSMENT OF NEUTROPHIL RESPIRATORY BURST ACTIVITY (NRBA) IN HEALTHY AND SEPTIC NEONATES USING A WHOLE BLOOD FLOW CYTOMETRIC MICROASSAY
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**Background/Aim:** Conventional methods for measurement of NRBA are difficult to be used in neonates because of the required large volumes of blood. The aim of this study was to apply a "whole blood" microassay to assess NRBA in healthy and septic neonates.
**Subjects:** 103 healthy term neonates aged 1 (n=46), 4 (n=42 and 7 (n=15) days, 28 healthy preterm neonates aged 1 (n=15) and 7 (n=13) days, 29 septic preterm neonates and 17 healthy adults.
**Methods:** A flow cytometric microassay was used for assessing the NRBA with dihydrorodamine 123 (DHR). The required volume of whole blood was 100μL per measurement. The precision of the DHR microassay was examined by performing triplicate assays in 40 samples and the optimun time for testing was determined in 9 samples tested after staying at ambient tempreture for 1,2, 4, 8, 12 and 24 hours.
**Results:** The coefficient of variation of the microassay ranged from 0.5% - 5 %. Optimum DHR activity (92%) occured at hours 1 and 2, slightly declining (to 85 %) at hour 12; values droped to 54 % at 24 hours. DHR activity in healthy term neonates (83±11%) was comparable to that in adults (89±9%), whereas DHR activity in healthy preterm neonates (73±12%) was significantly lower than that in term neonates and in adults (p<0.001). No significant difference was found between the 1st and 7th days of life. Septic preterm neonates had significantly lower DHR values (39±25%) compared to healthy preterm neonates (p<0.001).
**Conclusions:** The DHR microassay used in this study is highly reproducible and requires minimal volumes of blood, so that wide application of NRBA assessment in neonates becomes practicable. Our results indicate that NRBA is diminished in preterm neonates, and further decline during sepsis. These findings would justify administration of hemopoietic growth factors in septic neonates in an attempt to enhance their phagocytic capacity.

## † 62

**UNDESIRABLE EFFECTS OF DIETARY CALCIUM RESTRICTION IN IDIOPATHIC HYPERCALCIURIA (IH)**
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**Background:** In spite of calcium diet restriction is often recomended in children with IH, no studies focused on studying nutrient and mineral intake in patients on this diet are available. Likewise, the effect of diet calcium restriction on calcium stone promoting factors of urine of IH children is not known
**Subjects:** 10 children with IH diagnosed by urine calcium excretion greater than 4 mg/kg/day in two 24-hour urine samples. Subjects were normocalcemic and other metabolic and renal diseases were ruled out
**Interventions:** Four-day diet records while patients receiving a free diet (at diagnosis) and after one week on calcium restricted diet obtained by suppressing dairy products. 48-hour urine samples were collected at the end of both periods. Two-tailed Student t test for paired data were used for statistical analysis
**Results:** After dairy product suppression, calcium, phosphorus, and fat intakes (X±SD) were 32±8% (p<0.0001), 60±23% (p<0.004), and 82±22% (p<0.01) of those found on free diet, respectively. Restricted diet resulted in intakes of calcium and carbohydrates equal to 34±10% and 67±25% of recommended dietary allowances (RDA)
Calcium diet restriction induced no significant modifications in calciuria (5.9±2.5 vs 5.0±1.4 mg/kg/day) whereas brought about elevations of urinary oxalate (20±8 vs 21±5 mg/l, p<0.04), urine uric acid concentration (36±15 vs 46±16 mg/dl, p<0.03), and oxalate/citrate ratio (0.17±0.10 vs 0.19±0.08 mg:mg, p<0.03)
**Conclusion:** In short-term, dietary suppression of milk and dairy products results in severely depressed calcium intake without apparent benefits on urine composition of IH children

## ● 63

**EXPRESSION OF THE PHAGOCYTE RECEPTOR CD64 (FcγRI) ON GRANULOCYTES DURING INFECTION.**
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**Background:** The phagocyte receptor CD64 (FcγRI) is normally expressed on the surface of monocytes, but not on granulocytes. However, after stimulation with cytokines like G-CSF and γ-interferon, in vitro and in vivo, even granulocytes express CD64. The aim of this study was to investigate if this could be the case during the course of infections.
**Subjects:** Blood samples were taken from 15 children (8 newborn infants born after 24 - 42 w and 7 older children, 10m - 6y) with diagnosed or probable bacterial infections. From 9 subjects a second blood sample was available after recovery.
**Methods:** After fixation and incubation with a monoclonal antibody against CD64, the granulocytes were analysed by flow cytometry.
**Results:**

| | CD64 positive granulocytes (%) | |
|---|---|---|
| | Preterm, term neonates | Infants, children |
| During infection (n): | 78 ± 14 (8) | 79 ± 21 (7) |
| After infection (n): | 13 ± 5 (7) | 10 (2) |

**Conclusion:** During the course of bacterial infections, granulocytes from preterm and term newborn infants and older children do express the high affinity Fcγ-receptor, CD64. This might contribute to an increased capacity for phagocytosis, and it has the potential of a diagnostic aid.

## * 64

NEONATAL NUTRITION IN EXTREMELY LOW BIRTHWEIGHT INFANTS(ELBW) AND INTELLIGENT QUOTIENT/ VISUAL ACUITY AT 6-8 YEARS
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Hypothesis: Is there any association between the quantity and/or quality of feeding during the neonatal period and the intelligent quotient and visual acuity at 6-8 years in ELBW?
Study type/Setting: Retrospective study of infants <1000g cared for in a regional NICU between 1981-86.
Subjects: 76 children among 157 ELBW survivors of NICU were recruited for study at 6-8 years of age.
Measurements: WISC-R was assessed in a standard manner by six examiners. Visual acuity was assessed by an ophthalmologist.
Results: Children of IQ<85 were fed significantly less with EBM for 8wks(p<0.01) compared with children of IQ≥85. No differences were noted in the energy intake between groups, gestational age(27.0±2.2 vs 27.4±1.9) and birthweight(800gm±158 vs 879gm±152) between groups. No correlation was found between the visual acuity and the neonatal nutrition.
Conclusion: There was a favorable trend in IQ at 6-8 years for those fed with EBM during the first two months after birth. Visual acuity did not correlate with neonatal nutrition.

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DIAGNOSTIC VALUE OF COW'S MILK PROTEIN ANTIBODIES (IgG and IgA) IN COW'S MILK PROTEIN INTOLERANCE

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Background: We investigated the diagnostic value of serum IgG and IgA against casein, α-lactalbumin and ß-lactoglobulin, mesured with an ELISA method.
Subjects: Three groups of infants younger than 12 months were studied: 68 normal controls, 37 infants with cow's milk protein intolerance (CMPI) and 55 sick controls with various other gastro intestinal disorders.
Results: Statiscally significant difference is found for IgG between the normal control group and the patient group ($p<0,01$). However the wide range of results in each group causes large overlap. There is no difference between the sick control group and the patient group. IgA levels were low in all three group, with no diference between groups.
Conclusion: We conclude that the determination of IgG and IgA antibodies to casein, α-lactalbumin en ß-lactoglobulin is neither a sensitive nor a specific diagnostic tool for the diagnosis of CMPI in infants presenting with gastro intestinal symptoms.

## † 66

PROGNOSTIC VALUE OF CSF NEURON SPECIFIC ENOLASE (NSE) IN COMATOSE TERM INFANTS WITH SEVERE HYPOXIC-ISCHEMIC BRAIN INJURY.

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We questioned the relationship of CSF-NSE to the outcome and to the extent and severity of histologic brain damage in comatose term neonates after a hypoxic-ischemic event. **Methods.** Coma was defined as the absence of arousal after repeated noxious stimulation. Comatose consecutive term infants were included. CSF samples were obtained at 12 and 72 hours by LP. NSE was meassured by enzyme immunoassay. Neurologic follow-up (24±5 months) was performed in all survivors. On necropsy, neuronal necrosis was assessed semiquantitatively in 15 regions from the cerebrum, brainstem and cerebellum. **Results.** 22 infants were studied: 15 with severe perinatal HIE and 7 who had cardio-pulmonary arrest. Of them, 19 had adverse outcome: 13 died and 6 had cerebral palsy. 3 infants had normal outcome. Patients with adverse outcome had NSE levels significantly higher in both determinations ($p<0.0001$) than infants with normal outcome, whose NSE levels were within the reference range.[1] Infants who died had higher NSE levels than infants with cerebral palsy at 72 hours (413±112 vs 184±15 ng/ml, $p<0.05$). NSE increased in both subgrups with adverse outcome from 12 to 72 hours, but differences were significant only in infants who died ($p<0.05$). Necropsy was performed in 9 infants; in all, neuronal necrosis was found in every region examined. NSE level above 230 ng/mL was invariably associated with severe necrosis in frontal cortex, thalamus, corpus estriatum and hipocampus. **Conclusion.** CSF-NSE is a reliable marker of adverse outcome in comatose infants after a hypoxic-ischemic event, and relates to the extent of brain damage. 1. García-Alix A et al. Pediatrics 1994; 93:234-240.

## ● 67

NEWBORN PIGLET MODELS TO STUDY PERINATAL BRAIN DAMAGE

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Hypoxic insult is used as the main model to study asphyxia in piglets. We hypothesized that Hypoxic-ischemic insult could be a better model than Hypoxia alone to mimic human perinatal brain injury. Both models were compared by means of CSF-NSE levels and hystologic examination. **Methods.** Piglets (<7 days) were asigned to (H) hypoxic group (n=8) or (HI) hypoxic-ischemic group (n=8). In both, temporary oclusion of the carotid arteries followed by 10% $FiO_2$ during 30 min was made. Hemorrhagic hypotension (BP at aprox. 50% of control levels) was made after 15 min of hypoxia in goup HI. Serial CSF samples were obtained by cisternal punction. NSE levels were meassured by EIA. Cerebral hystologic examination was performed; neuronal necrosis was assessed in 15 regions of the brain.

| **Results:** | NSE base line (n) | | NSE at 3 h. | (n) | NSE at 12 h | (n) | NSE at 48 h | (n) |
|---|---|---|---|---|---|---|---|---|
| Sam | 7.1±3.0 | (3) | 2.15±0.75 | (2) | 4.2±2.6 | (2) | 7.3 | (1) |
| Hypoxic | 5.1±0.77 | (5) | 15.0±3.05 | (5) | 24.8±8.12 | (3) | 56 | (1) |
| Ischemic | 6.5±1.2 | (7) | 51.27±14 * | (3) | 112.8±15.3* | (4) | 154±66 | (2) |

NSE in H group vs HI group: * = $p<0.05$. Values expresed as Mean±SE. CSF-NSE in ng/mL

Significant increase in NSE levels at 3 and 12 hours were found in group H ($p<0.05$) and group HI ($p< 0.005$). No brain damage was found in any of the sections examined in group H. In contrast, severe damage was found in 6 of the 8 (80%) animals from group HI, mainly in cortex, thalamus, basal ganglia and hippocampus (Fisher, $p<0.001$).

**Conclusion.** Severe brain damage in newborn piglets (similar to that observed in human neonates) is produced by hypoxic-ischemic insult better than hypoxia alone, asessed by both biochemical and hystological methods. Supported by grant from the FIS # 930782.

## † 68

URINARY CYTOKINES IN CHILDREN WITH ACUTE PYELONEPHRITIS. M. García-Fuentes, J. Rodríguez-Soriano, A. Vallo, J. A. Amado, M. T. G. Unzueta, L. Alvarez-Granda, J. Quintela. Hospital Valdecilla, Cantabria University, Santander/Hospital de Cruces, Basque Country University, Bilbao (Spain )

Urinary cytokines, and especially IL-6 and IL-8, have been found to be increased in the urine of children with urinary track infection (UTI). The purpose of the present investigation was to determine whether such changes were specific for kidney inflammation and if they correlated with clinical or biochemical parameters.

We studied urinary excretion of IL-1b, IL-6 and IL-8 in 30 children clinically diagnosed of acute pyelonephritis (AP) (6.9±3.7 y.) and values were compared to those obtained in 7 febrile children (5.5±4.0 y.) and in 5 controls (9.5±1.8 y.). In children with AP the study was performed at admission and after completion of antibiotic therapy. Median values for cytokine excretion were similary increased in AP (IL-1b, 6.0; IL-6, 51.0; IL-8, 272.0 pg/mg Cr.), as in febrile children (IL-1b, 8.0; IL-6, 29.0; IL-8, 280.0 pg/mg Cr.) and significantly higher than values in controls. In AP, urinary values for IL-6 and IL-8 tended to be higher according to the presence of back pain, dysuria, and leucocituria. However, no differences were observed when children with normal or abnormal ultrasound, or with or without vesico-ureteral reflux were compared. Surprisingly, 8 children with normal DMSA, performed a few days after admission, had significantly higher values for IL-8 excretion, than 22 children with abnormal DMSA (688 vs. 294 pg/mg Cr. $p<0.05$). In AP poor correlations were observed between cytokine excretion and biological signs of acute inflammation. Only C-reactive protein related significantly with IL-8 ($r=0.34$, $p<0.05$) and percentage of neutrophiles in leucocyte count correlated significantly with IL-6 ($r=0.40$, $p<0.05$) and IL-1b ($r=0.43$, $p<0.05$).

These findings sugest that increased cytokine excretion is not specific of UTI and only reflects a state of acute infection. However, more studies are needed to definitely establish its value in the evaluation of children with UTI.

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## † 69

EFFECTS OF NITRIC OXIDE (NO) IN PULMONARY HYPERTENSION (PH) INDUCED BY EXPERIMENTAL MECONIUM ASPIRATION SYNDROME (EMAS) IN NEWBORN LAMBS. E. Gastiasoro, FJ. Alvarez, A. Arnaiz, B. Fernandez, L. Alfonso, I. López-Heredia, A. Valls-i-Soler. Dpt. Pediatrics, Hospital Cruces, Univ. Basque Country, Bilbao, Spain.

**Aim:** To study the effects of inhaled NO on pulmonary pressure, gas exchange, mechanics, and functional residual capacity (FRC) in lambs with EMAS.
**Subjects:** Fifteen newborn lambs <7 days, on mechanical ventilation (IMV).
**Intervention:** Lambs were randomly assigned to 3 groups (n=5); **Control:** on IMV without further intervention; **EMAS:** PH induced by tracheal instillation of meconium; **NO:** PH exposed to inhaled NO (20ppm). Colored microspheres were injected in the trachea and pulmonary artery to study lung ventilation/perfusion ratio.
**Measurements:** Catheters were placed in the trachea, femoral and pulmonary arteries and right ventricle. Blood gases, systemic (SAP) and pulmonary pressure (PAP), cardiac output (CO), pulmonary vascular resistance (PVR), mechanics and FRC were measured. Microspheres distribution in lung tissue was studied.
**Results:** EMAS lambs had severe hypoxemia ($paO_2$ <80mmHg), low compliance ($C_{rs}$ =0.33±0.017mL/cm$H_2O$/Kg), FRC (15±2mL/Kg), and high PAP (27±1.1mmHg). NO inhalation produced an increase in $paO_2$ (59.85±5.05 vs. 101±26.9mmHg), and a decrease in PAP (32.5±0.5 vs. 24.5±1.5mmHg), without changes in $C_{rs}$ (0.37±0.039mL/cm$H_2O$/Kg) and FRC (14±3mL/Kg).
**Conclusion and Speculation:** In EMAS, NO inhalation improves $paO_2$ and decreases PAP while CO is mantained. Since NO tends to distribute to better areated lung units, an adequate FRC should increase lung exchange surface area for better NO effects. Grant FIS 95/1348.

## * 70

MUTATIONS IN CLASSICAL AND DUARTE$_2$ GALACTOSEMIA

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**Aim:** To analyze the mutations in the galactose-1-P uridyltransferase (GALT) gene in patients with classical and Duarte$_2$ galactosemia.
**Subjects:** 29 families with classical galactosemia, 5 families with the Duarte$_2$ variant, 25 healthy controls.
**Methods:** Denaturing gradient gel electrophoresis (DGGE) followed by sequencing of affected exons.
**Results:** DGGE detected 57 of 58 classical galactosemia alleles. 60% carried the mutation Q188R, 28% the mutation K285N. Seven novel missense and one nonsense mutation were found. All Duarte$_2$ patients (mean GALT activity 24% of normal) were compound heterozygous for one allele carrying N314D in cis with G1104C (intron 4) and G1391A (intron 5) and one classical galactosemia allele. G1104C flanks a possible binding site of the erythroid specific transcription factor GATA-1. A second distinct N314D allele, not found in Duarte$_2$ patients, carried N314D in cis with a neutral mutation (C1721T) and did not decrease GALT activity.
**Conclusion:** DGGE detects almost all mutations in the GALT gene. Duarte$_2$ galactosemia may not be due to the N314D polymorphism but to a regulatory mutation.

## * 71

**PREVENTION OF HYPOXIA-INDUCED MODIFICATION OF THE NMDA RECEPTOR BY INHIBITION OF CEREBRAL NITRIC OXIDE SYNTHASE IN NEWBORN PIGLETS.** Floris Groenendaal, David J.Hoffman, Om P. Mishra, Jane E. McGowan, and Maria Delivoria-Papadopoulos. Dept of Physiol, Univ of Pennsylvania Sch of Med, Philadelphia, USA and Wilhelmina Children's Hospital, Utrecht, NL.
**Background**: The present study tests the hypothesis that inhibition of nitric oxide synthase (NOS) by i.v. $N^G$-nitro-L-arginine (NNLA) reduces hypoxia-induced modification of the NMDA receptor in cortical tissue of newborn piglets. **Subjects and interventions**: Studies were performed in 4 groups of anesthetized, ventilated newborn piglets (Nx: normoxia, n=5; Hx: hypoxia, n=5; NxNNLA: normoxia and NNLA, n=6; HxNNLA: hypoxia and NNLA, n=7). NOS was inhibited >60% by NNLA (25-50 mg/kg in 30 min i.v.). Hypoxia was induced in the HxNNLA group by lowering the $FiO_2$ to 0.05-0.07, and was maintained for one hour. $^3$H-MK-801 binding was measured as an index of NMDA receptor modification in the presence of glutamate and glycine as activators. **Results**: Receptor numbers (Bmax) in the Nx, Hx, NxNNLA and HxNNLA groups were 1.12 ± 0.18, 0.68 ± 0.23, 1.14 ± 0.28 and 1.07 ± 0.15 pmol/mg protein. Bmax in Hx were significantly lower than Bmax in the other 3 groups ($P<0.05$, Student-Newman-Keuls). Dissociation constants (Kd) were 10.0 ± 2.3, 4.9 ± 1.4, 9.4 ± 1.9 and 8.2 ± 2.1 nM in groups Nx, Hx, NxNNLA and HxNNLA, respectively. Kd values were lower (increased receptor affinity) in Hx than in the other groups ($P<0.05$). **Conclusion**: Inhibition of NOS during hypoxia did prevent hypoxia-induced modification of the NMDA receptor. As membrane lipid peroxidation is not prevented by inhibition of NOS (data not shown), we speculate that the hypoxia-induced modification of the NMDA receptor is produced by a direct effect of nitric oxide on the NMDA receptor.
*Funded by NIH #HD-20337, and Ter Meulen Fund, the Netherlands.*

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**HYPOXIA-INDUCED BRAIN CELL MEMBRANE LIPID PEROXIDATION AFTER INHIBITION OF CEREBRAL NITRIC OXIDE SYNTHASE IN NEWBORN PIGLETS.** Floris Groenendaal, Om P. Mishra, Anli Zhu, Jane E. McGowan, and Maria Delivoria-Papadopoulos. Dept of Physiol., Univ. of Pennsylvania Sch.of Med, Philadelphia, USA and Wilhelmina Children's Hosp., Utrecht, Netherlands.
**Background**: The present study tests the hypothesis that inhibition of nitric oxide synthase (NOS) by administration of i.v. $N^G$-nitro-L-arginine (NNLA) reduces cell membrane lipid peroxidation during hypoxia in cortical tissue of newborn piglets. **Subjects and interventions**: Studies were performed in 4 groups of anesthetized, ventilated newborn piglets (Nx: normoxia, n=6; Hx: hypoxia, n=5; NxNNLA: normoxia and NNLA, n=6; HxNNLA: hypoxia and NNLA, n=7). NOS was inhibited >60% in the NxNNLA and HxNNLA groups by NNLA (25-50 mg/kg in 30 min i.v.). Hypoxia was induced in the Hx and HxNNLA groups by lowering the $FiO_2$ to 0.05-0.07, and was maintained for one hour. Fluorescent compounds (FC) and conjugated dienes (CD) were measured as indices of membrane lipid peroxidation in cerebral cortical tissue. **Results**: FC in groups Nx, Hx, NxNNLA and HxNNLA were 0.75 ± 0.21, 0.96 ± 0.37, 0.88 ± 0.26, 0.90 ± 0.47 (relative fluorescence per g brain). For Nx vs. Hx results were just significant ($P=0.05$), other differences were not significant. CD were 0, 0.09 ± 0.07, 0.03 ± 0.03, 0.10 ± 0.10 μmol/g brain in groups Nx, Hx, NxNNLA and HxNNLA, respectively. CD in NxNNLA were lower than in Hx and HxNNLA ($P<0.02$), but higher than in controls. CD in Hx and HxNNLA were similar. **Conclusion**: Inhibition of NOS during hypoxia did not prevent peroxidation of brain cell membranes. We speculate that an overwhelming production of free radicals from pathways other than NO synthesis causes membrane lipid peroxidation during hypoxia in brain cell membranes of newborn piglets.
*Funded by NIH #HD-20337, and Ter Meulen Fund, the Netherlands.*

## † 73

**DEXAMETHASONE DECREASES SOLUBLE ICAM-1 CONCENTRATIONS IN TRACHEOBRONCHIAL ASPIRATE FLUID (TAF) OF INFANTS AT RISK FOR BRONCHOPULMONARY DYSPLASIA.**
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**Hypothesis:** Dexamethasone (Dxm) has been shown to reduce neutrophil influx into the airways of infants at risk for BPD by decreasing chemotactic activity of TAF (Groneck et al., J Pediatr 1993;122:938-44). We hypothesized that steroid treatment would affect pulmonary neutrophil adhesion as well in these infants.
**Setting:** Tertiary neonatal intensive care service.
**Patients:** 12 preterm infants (877 ±191 g, gestational age 27.1 ± 1.7 weeks, mean ±SD) at risk for BPD ($FiO_2 \geq 0.3$ and/or peak inspiratory pressure $\geq 16 cmH_2O$ after day 10 of postnatal age).
**Interventions:** All infants received Dxm at a median of 13 days.
**Measurements:** Concentrations of sICAM-1 were analyzed in TAF and serum on day 3-5 of postnatal age, before Dxm-reatment (day 10-14), and after steroid therapy (day 15-20). Levels of sICAM-1 were determined by ELISA.
**Results:** Levels of sICAM-1 in TAF increased from 724 (418) ng/ml (mean (SD)) on day 3-5 to 1411 (404) on day 10-14 ($p<0.05$) Following treatment with Dxm sICAM1 concentrations in TAF significantly decreased (day 15-20: 619 (460) ng/ml, $p<0.05$). Levels of sICAM-1 in serum were lower than TAF-values during the first 14 days of life. In contrast to TAF-levels, serum concentrations of sICAM-1 did not decrease after Dxm treatment; day 3-5: 357(165) ng/ml, day 10-14,before Dxm: 478 (195) ng/ml, day 15-20,after Dxm: 740 (204) ng/ml.
**Conclusion:** Infants at risk for BPD had higher levels of sICAM-1 in TAF than in serum. Dxm significantly decreases sICAM-1 levels in TAF, indicating a downregulation of pulmonary neutrophil adhesion.

## † 74

**INFLAMMATORY MEDIATORS IN TRACHEAL ASPIRATES OF PRETERM INFANTS WITH BRONCHOPULMONARY DYSPLASIA (BPD) AND WITH MICROBIAL COLONIZATION OF THE AIRWAYS.**
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Dept. of Neonatology, University Children's Hospital, Tübingen, Germany.
**Background:** We studied concentrations of inflammatory mediators in tracheal aspirate fluid in different clinical situations with bronchopulmonary inflammation: 1) development of BPD without microbial colonization 2) airway colonization with Ureaplasma urealyticum (Uu), Mykoplasma hominis (Myh), and Chlamydia trachomatis (Cht), and 3) airway colonization with bacteria.
**Study type, setting:** prospective cohort study; tertiary neonatal service; 28 preterm infants with 35 episodes of mechanical ventilation; mean (SD) birthweight 906 (191) g.
**Measurements:** Concentrations of interleukin-1(IL-1), interleukin-8 (IL-8), tumor necrosis factor (TNF), elastase $\alpha_1$-proteinase inhibitor were determined by ELISA. Free elastase was determined by enzymatic digestion of a peptide substrate. Repeated tracheal cultures were done for bacteria (quantitative assessment), Uu, Myh, and Cht. Significant airway inflammation was defined by IL-1 levels >100 pg/ml, IL-8 >10 ng/ml, detection of TNF, or presence of free Elastase (at least 2 of 4 items).

| **Results:** (No. of infants with BPD in parenthesis). | BPD present no colonization | Uu/ Myh/ Cht | bacterial colonization | no BPD no colonization | total |
|---|---|---|---|---|---|
| sign. airway inflammation | 4 (4) | 5 (1) | 4 (1) | 0 | 13 |
| no sign. airway inflammation | 0 | 0 | 5 (1) | 17 (0) | 22 |

**Conclusion:** Significant bronchopulmonary inflammation was detected both during development of BPD and during airway colonization with microorganisms.

## ● 75

**POLIMERASE CHAIN REANTION, VIRUS ISOLATION AND ANTIGEN ASSAY IN DIAGNOSTIC FOR VERTICALLY TRANSMITTED HIV-1 INFECTION.**
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OBJETIVE: To compare polymerase chain reaction (PCR), virus culture (VC) and antigen detection (AG) assays can be used for the early diagnostic of vertically transmitted HIV-1 infection in infants under 15 months of age, when a diagnosis cannot be based on seropositivity because of maternal antibody persistence.
METHODS: Thirty-nine children born to HIV-1-seropositive mothers were evaluated by the three techniques. The children were then followed up to the age of, at least, 18 months. P24 antigen was measured in plasma, and HIV proviral DNA was determined in peripheral blood mononuclear cells after amplification by PCR. Primer pairs from three different regions of the proviral genome were used for the PCR test.
RESULTS: In the first evaluation fifteen (100%) of the children who later developed clinical symptoms were positive by PCR analysis, 14 (93.3%) by the initial VC assay and only 8 (53.3%) by the p24 antigen assay.
CONCLUSIONS: PCR and VC assays were found to have higher sensitivity than p24-antigen assay for the diagnosis of HIV-1 infection. P24 antigenaemia was shown to be a useful pronóstic marker of disease onset. This study shows that the PCR test represents a more reliable and faster alternative to viral culture for the diagnosis of pediatric HIV infection.

## † 76

**ADVERSE EFFECTS OF HYPOTHERMIA FOLLOWING HYPOXIA IN NEWBORN PIGLETS** K. Haaland[1], E.M. Løberg[2], M. Thoresen[1]
(spn. by O.D. Saugstad) [1]Dept. of Surgical and Pediatric Research, The National Hospital, University of Oslo [2]Dept of Pathology, Ullevål Hospital, Oslo, Norway
**Background:** It has been shown in some animal models that hypothermia after a hypoxic and/or ischemic insult may ameliorate brain damage. Before mild hypothermia can be considered as a treatment for asphyxiated human newborns, possible adverse effects of hypothermia combined with hypoxia need to be investigated.
**Method:** Newborn piglets, 12-72h old, were anaesthetised with halothane and intubated. They underwent 45 min of whole body hypoxia followed by 3 h normothermia (38.5-39.4°C) (n=13) or mild hypothermia (34.5-35.4°C) (n=12). The piglets were observed for 3 d before autopsy. Microscopic evaluation was performed by a pathologist blinded to the mode of treatment.

| **Results:** | Hypoxia | Hypoxia + hypothermia |
|---|---|---|
| Intestine | 1 necrotic lesions (NL) | 4 NL, 1 peritonitis |
| Heart | None | 1 large and 3 small infarcts |
| Kidney | None | 2 small infarcts |
| Liver | 2 subcapsular haematomas | 2 subcapsular haematomas |
| | 1 small focal infarct | 1 parenchymal haemorrhage |

Piglets with NL in the intestines had small amounts of loose stool and a distended abdomen (NEC?). The other histopathological findings had no obvious clinical correlates. Base deficit at the end of hypoxia was 17.8±3.6 (mean±SD). Five normo- and 11 hypothermic animals needed dopamine to maintain blood pressure > 42 mmHg
**Conclusion:** Pathological changes in the intestines, heart and kidneys were commoner in hypoxic animals treated with hypothermia than in those kept normothermic.

## † 77

**ACCUMULATION OF CALPAIN DEGRADATION PRODUCTS IN CNS WHITE MATTER AFTER HYPOXIC-ISCHEMIA IN NEWBORN RATS.**

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**Background:** White matter of the immature brain is selectively vulnerable to hypoxic-ischemia. The activity of calcium-activated non-lysosomal proteases, calpains, is high in the white matter of the developing CNS and may be important in the neurochemical cascade leading to brain injury.

**Aim:** To provide regional and temporal information on the accumulation of calpain degradation products (fodrin) after hypoxic-ischemia in newborn rats.

**Methods:** 7-days-old rats were subjected to hypoxic-ischemia (unilateral carotid ligation + 7.7% oxygen during 2h) and sacrificed 2h, 1, 2 or 14 days after the insult. The frozen brains were either sectioned and stained with antibodies against α-fodrin and microtubule associated protein (MAP-2; marker of dendrities/cellbodies) or tissue specimens were subjected to Western blotting using the fodrin antibody.

**Results:** Western blots revealed a 3-fold increase of fodrin in the hypoxic-ischemic hemisphere 2h to 2 days after the insult ($p<0.001$). Areas that underwent injury displayed a reciprocal staining pattern: accumulation of fodrin and loss of MAP-2. In the striatum the fodrin accumulation was most pronounced in the white matter (negative to MAP-2).

**Conclusion:** Calpains may be involved in the pathological process leading to irreversible injury in the white matter. Further studies are warranted.

## * 78

**PULMONARY ARTERY PRESSURE (PAP) CHANGES IN RESPIRATORY DISTRESS SYNDROME (RDS) WITH 3 TYPES OF SURFACTANT.**

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Background: Doppler echocardiography was used to changes in PAP in preterm infants who were treated with Exosurf, ALEC or Survanta.

Subjects: Ventilated neonates with RDS.

Interventions: The ratio of acceleration time to right ventricular ejection time (AT: RVET) was determined in 83 infants (51 Exosurf (29 >1 kg and 22 <1 kg), 21 ALEC and 11 Survanta) prior to and 1, 6 and 12 hours after the 1st and 2nd dose of surfactant.

Results: The median AT:RVET ratio increased (indicating lowered PAP) significantly an hour after the 1st dose of Exosurf, ALEC and Survanta from 0.33, 0.35 and 0.307 respectively to 0.38, 0.399 and 0.351, and an hour after the 2nd dose from 0.426, 0.432 and 0.413 to 0.440, 0.457 and 0.449. Comparing Exosurf infants <1 kg with Survanta infants, and Exosurf infants >1 kg with ALEC revealed no difference in the median AT:RVET during the first 24 hours. The median FiO2 requirement at 16 and 20 hours was lower after the 1st dose Survanta than after Exosurf.

Conclusions: There was no difference in the rate of lowering of PAP between the 3 surfactants.

## † 79

**PERSISTENCE OF CEREBRAL LACTATE AFTER BIRTH ASPHYXIA**

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**Background:** Cerebral lactate may be elevated soon after birth asphyxia but it is not known how long this abnormality persists.

**Subjects and Methods:** $^1$H magnetic resonance spectroscopy (MRS) was repeated at 6-10 weeks of age in eight infants with clinical evidence of birth asphyxia and who had elevated cerebral lactate in the two weeks after birth. Three healthy infants were also studied for comparison. The ratio of lactate to creatine + phosphocreatine (Lac/Cr) in the basal ganglia was measured.

**Results:** Lactate was observed in all asphyxiated infants at the initial study (Lac/Cr:median,range, 0.52, 0.05-1.42). Lactate signals were subsequently present in three of these infants (Lac/Cr:0.35,0.60,0.67). One of the infants was studied further at 6 and 12 weeks of age and the Lac/Cr ratio reduced from 0.35 to 0.05. Lactate was not detected in the control infants.

**Discussion:** This preliminary study suggests that the metabolic abnormalities noted soon after birth asphyxia may persist for several weeks.

## † 80

**BILIRUBIN (B) IS OXIDIZED BY A CRUDE MITOCHONDRIAL FRACTION (CMF) FROM RABBIT PUP BRAIN.** Thor W.R. Hansen, Jeffrey W.Allen, Neonatal Critical Care, Dept Anesth & Crit Care Med, University of Pittsburgh, Children's Hospital of Pittsburgh, Pittsburgh, PA.

**Background:** Oxidation of B by brain tissue might contribute to clearance of B from brain. We recently showed that B was oxidized by CMFs from young adult rat brains, with differences between brain regions. The purpose of this study was to reexamine this phenomenon in a different species.

**Materials and methods:** A CMF ("P2") was prepared in 0.32 M sucrose from whole adult rabbitt brains. The CMF was washed once with 0.32 M sucrose before resuspension in aqua dest and sonification. 200 µL P2 was added to 2.5 mL of a 10 µM B solution, and the decay in optical density at 440 nm was measured over 60 min (OD measured in supernatant following centrifugation of aliquots at 20000G for 2 min ). The oxidizing activity had a temperature peak of ≈35°C, and a pH maximum of ≈9. Subsequent studies were done at 37.5°C in 0.1M pH 8.2 barbital buffer containing 500 U/mL catalase. Rabbit pups (7-9 d old, n=8) were killed by injection of pentobarbital i.p., and the brain vasculature was *flushed in situ*. Brains were dissected into 7 regions, and CMF suspensions were prepared from each region. The protein concentration of the CMF suspension was measured with the BioRad DC Protein assay. The rate of oxidation of B was measured as described, and calculated per mg protein per min for each of the brain regions. Statistical *analysis was performed with the Kruskal-Wallis nonparametric* ANOVA test. **Results:** B oxidizing activity was present in CMFs from adult as well as neonatal rabbit brain. The results from brain regions are shown in the table as pmol B oxidized/min/mg protein (mean value [95% confidence interval]). There was no significant difference between brain regions (KW=11.2, p=0.08). **Conclusion:** *Mitochondrial membranes from adult as well as neonatal rabbit* brains are able to oxidize B. B-oxidizing activity at the levels demonstrated here may contribute significantly to the clearance of B from brain. However, differences in B oxidizing activity between brain regions cannot explain the kernicterus staining phenomenon.

| Brain region | B oxidation |
|---|---|
| Cortex | 98 [ 82-114] |
| Hippocampus | 93 [ 84-102] |
| Striatum | 112 [102-121] |
| Midbrain | 89 [ 83- 96] |
| Hypothalamus | 107 [ 80-135] |
| Cerebellum | 89 [ 83- 94] |
| Medulla | 96 [ 69-123] |

## † 81

**THE BILIRUBIN (B) OXIDIZING ABILITY OF MITOCHONDRIAL MEMBRANES FROM A PURE NEURONAL SOURCE (SM) IS SIGNIFICANTLY LESS THAN THAT OF MITOCHONDRIAL MEMBRANES FROM A MIXED GLIAL/NEURONAL SOURCE ( MM).**

Thor W.R. Hansen, Jeffrey W.Allen, Neonatal Critical Care, Department of Anesthesia & Critical Care Medicine, University of Pittsburgh, Children's Hospital of Pittsburgh, Pittsburgh, PA.

**Background:** Oxidation of B by brain tissue may contribute to clearance from as well as detoxification of B in brain. We recently showed that B was oxidized by crude mitochondrial fractions from rat and rabbit brains. Neurons are more vulnerable than glial cells to B toxicity. We hypothesized that SM would oxidize B at a lower rate than MM. **Materials and methods:** Whole brains from adult rats (n=10) were homogenized with a glass-Teflon homogenizer in 0.32 M sucrose. The P2 was subjected to high speed centrifugation in a sucrose gradient (1.2/0.8/0.32 M) using the method of Whitaker and Barker. The mitochondrial pellet and the synaptosomal layer were washed in 0.32 M sucrose and pelleted. The mitochondrial pellet was then resuspended in distilled water, sonicated at high setting for 2x10 s, and immediately frozen at -70°C. These mitochondria are derived both from neurons and glial cells (MM). The synaptosomal pellet was resuspended in distilled water, vigorously squirted up and down in a glass pipette in order to rupture the synaptosomes, resuspended in 0.32 M sucrose, and layered onto 1.2 M sucrose, followed by high speed centrifugation to pellet the synaptosomal mitochondria. This mitochondrial pellet was also resuspended in distilled water, then sonicated and frozen as described above. The synaptosomal mitochondria are from a quite pure neuronal source (SM). To assay B oxidation, MM and SM suspensions were diluted to a standard protein concentration (0.5 mg/ml), 200 µL of the each suspension was added to 2.5 mL of a 10 µM B solution (pH 8.2), and the decay in optical density at 440 nm was measured over 60 min at 37.5°C (OD measured in the supernatant following centrifugation of aliquots at 20000G for 2 min). Each fraction was assayed in triplicate, and the rate of B oxidation calculated. Statistical analysis was performed with paired t-test. **Results:** The rate of B oxidation by SM was significantly less than by MM (57.8±29.8 [mean±SD] vs 74.6±26.7 pmol/min/mg protein, paired t = 3.9, p=0.0036) **Conclusion:** Mitochondrial membranes from a pure neuronal source oxidize B at a significantly lower rate than mitochondrial membranes from a mixed glial/neuronal source. **Speculation:** The increased vulnerability to B toxicity of neurons relative to glia may be associated with a lower ability of neurons to detoxify B locally.

## † 82

**CEREBRAL HEMODYNAMIC AND EEG EFFECTS OF TREATMENT WITH NATURAL *VERSUS SYNTHETIC SURFACTANT.*** J-M Hascoët, M André, F Didier, I Le Courtois, M Dalati, MC Buchweiller, INSERM 272,Univ of NANCY and Wellcome SA, ISSY LES MOULINEAUX-F.

**Background**: No difference in long term outcome has been found between surfactants despite a trend to short term respiratory benefit for natural surfactant. Brain disorders may explain this discrepancy since hemodynamic and EEG disturbances have been shown after natural surfactant.

**Subjects**: 27 newborns, 26 to 30 wk. gestational age (GA) with HMD requiring surfactant.

**Interventions**: *randomization to 2.5ml/kg of Curosurf® (gr C) in bolus, or 5ml/kg of Exosurf® (gr* E) over 10 mn. Mean cerebral blood flow velocity (MCBFV) and Resistance Index (RI) were measured by pulsed Doppler before, 1 min after the onset of instillation, then every 5 mn for 31 mn. The primary measure of outcome was the incidence of more than 30% variation from baseline MCBFV. EEG, mean arterial blood pressure (MABP), tcPO2 and tcPCO2 were continuously recorded throughout the study. Head ultrasound (HUS) was done before and 7 days after treatment.

**Results**: The 2 groups were similar for sex distribution, GA (28.1±1.3 vs 28.5±0.9 wk.) and BW.

83% (10/12) of the infants in gr C vs 43 % (6/14) in gr E [p=0.05] had more than 30% variation in MCBFV, with more at higher variability (>40%) in gr C: 67 vs 14% [p=0.014]. 41% in gr C vs 0 in gr E had also more than 30% variation from baseline RI [p=0.012]. There was no difference for MABP, tcPCO2 or aAO2 ratio at any time of the study between the infants within each group.

69% (9/13) of the infants in gr C vs 28% (4/14) in gr E [p=0.035] showed a depression of the background activity and/or slow or polymorphic sharp waves at EEG.

After treatment, HUS showed 2 grade III-IVH and 2 periventricular echodensities (PVED) in gr C; 1 grade III-IVH and 2 PVED in gr E. The infants with PVED in gr E and all infants with brain lesions in group C had more than 30% variation of MCBFV. 3 infants died in group C (2 from brain lesions) vs 1 in group E; all of them had had more than 30% variation of MCBFV plus EEG anomalies. Respiratory outcome at day 7 showed no difference between the 2 groups.

**Conclusion**: These data suggest that more infants maintain a stable cerebral status when treated by E. This study raises the question of cerebral tolerance to surfactant which is an important issue to be considered in addition to pulmonary efficacy. (funded by Wellcome SA)

## * 83

**EURO GROWTH STUDY - INFLUENCE OF BREAST-FEEDING ON SMOKING HABITS OF EUROPEAN MOTHERS**

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**Background:** In the past, little Europeanwide information has been available on the prevalence of maternal smoking before and during pregnancy and the influence of breast-feeding on maternal smoking cessation. One of the objectives of the Euro-Growth project, which started in 1991, was to study the interactions between nutrition and factors which are of major public health concern for European infants, such as exposure to maternal smoking.

**Subjects, Procedures:** 17 European study centers from 12 countries participated in this part of the pure longitudinal, observational cohort study. 1636 mothers provided data on smoking habits immediately before, during, and the first year after pregnancy. Maternal age, years of maternal education, mother's work outside home after pregnancy, smoking habits of the infant's father, and duration of breast feeding were studied as the possible factors with influence on maternal smoking habits.

**Results:** 34, 18, and 26 % of the mothers smoked immediately before, during, and after pregnancy, respectively. 76 % of the mothers who had smoked before pregnancy (n= 549) restarted smoking during the first 12 months after delivery. Equations for prediction of reintroduction of smoking at 12 months after pregnancy in the subsample of mothers who smoked before pregnancy were derived by logistic regression analysis after correction for center. Duration of breast feeding ($T= -6{,}982$; $p < 0.0001$) and smoking by the father ($T= +3{,}603$; $p < 0.0003$) were the only significant predictors of smoking reintroduction in this model.

**Conclusion:** Promotion of breast feeding is an important factor to prevent European infants from exposure to maternal smoking.

## † 84

DECREASED PHOSPHOCREATINE / FREE PHOSPHATE (PCr/Pi) RATIO OF SKELETAL MUSCLE IN PATIENTS WITH GYRATE ATROPHY OF THE CHOROID AND RETINA WITH HYPERORNITHINEMIA (GA). A MAGNETIC RESONANCE SPECTROSCOPY (MRS) STUDY.

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**Background:** GA is an autosomal recessive disorder with characteristic chorioretinal degeneration; atrophy and tubular aggregates in type II muscle fibres; 10 to 20 -fold increase in ornithine concentration in body fluids; and deficient activity of ornithine-delta-aminotransferase.

**Patients:** 20 patients ( 9 women, range 5 - 73 years ) with clinically and biochemically confirmed GA were included in the study. 11 healthy volunteers were studied as reference.

**Method:** Phosphorus-31 ($^{31}P$) in vivo magnetic resonance spectroscopy (MRS) was performed with a 1,5 T MR imager (Magnetom 63SP, Siemens, Germany) using a 10 cm diameter surface coil. Repetition time (TR) of 5000 ms was used. Spectra were obtained from the thigh muscle.

**Results:** GA patients with no treatment had clearly decreased skeletal muscle PCr/Pi-ratios compared to healthy volunteers ( 4,46 vs. 9,08 , $p<0{,}001$).

**Conclusion:** Patients with GA have decreased PCr / Pi ratios in skeletal muscles suggesting that creatine synthesis in GA patients is impaired. We also present phosphorus MRS as a valuable method for analysis of high-energy phosphate compounds in inborn errors of energy metabolism.

## * 85

**Changes in the Fatty Acid Composition in Human Milk and Plasma when Lactating Mothers are supplemented with Cod Liver Oil.**

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Background: Docosahexaenoic acid (DHA, 22:6 n-3) a derivative of the essential fatty acid alpha-linolenic acid (18:3 n-3), is an important lipid component of the brain and retina. The human foetus and neonate accumulate DHA in the central nervous system in particular, during the last trimester of pregnancy and the first months of life. Several studies have demonstrated that the content of DHA in blood of human infants depends on its concentration in the diet and that the intake of DHA correlates with visual acuity and visual evoked potentials. The amount of DHA in human milk depends on the mothers' diet.

Subjects: We examined therefore how the fatty acid pattern in human milk changed when 23 lactating mothers were supplied with different amounts of cod liver oil for 14 days.

Interventions: The women were divided into four groups receiving 0, 2,5 5 or 10 mL cod liver oil. The oil contained total n-3 fatty acids 20 g/100 mL, DHA 10 g/100 mL and EPA (20:5 n-3) 8 g/100 mL. The vitamin content was adjusted so that all the supplied women received the same amounts of vitamin A and vitamin D, and the vitamin E content was 112 mg/100 mL. The cod liver oil was taken every morning.

Results: Supplements of 10 mL cod liver oil daily promoted a significant increase in the concentration of DHA in mothers' plasma (45 to 63 ug/mL) and in breast milk (0.6 to 1.3 wt %). There was a significant correlation between the levels of DHA in breast milk and plasma. The amount of EPA also increased, in the mothers' plasma (from 16 to 26 ug/mL) as well as in breast milk (from 0.2 to 0.5 wt %). The level of arachidonic acid (20:4 n-6) was unchanged, both in human milk and plasma. There was no significant change in the concentration of alpha-tocopherol in breast milk or plasma during the supplementation with cod liver oil.

Conclusion: When lactating women are supplied with cod liver oil, the concentration of DHA and EPA in plasma and human milk increases, whereas the level of arachidonic acid and alpha-tocopherol in plasma and human milk remains unchanged.

## † 86

**PAEDIATRIC MENINGITIS IN THE WESTERN CAPE PROVINCE OF SOUTH AFRICA**

**BACKGROUND:** Bacterial meningitis has a high mortality and morbidity in developing countries. Children with meningitis were prospectively reviewed over a 9 year period at a tertiary centre. **SUBJECTS:** Cerebrospinal fluid (CSF) specimens from children under 13 years of age were reviewed daily. Meningitis was defined as the presence of $> 10 \times 10^6$/l leucocytes and $> 30 \times 10^6$/l leucocytes in children greater than and less than 3 months, respectively. All positive CSF cultures were included. Antibiotic sensitivity was evaluated. **RESULTS:** There were 2920 cases of meningitis identified. The commonest causes of bacterial meningitis were Tuberculosis (TB) (282), N.meningitidis (220), H.influenzae (156), and S.pneumoniae (106). Of the 118 cases of neonatal bacterial meningitis causes included group B ß haemolytic streptococcus (27), E.coli (21), klebsiella species (11), serratia marcescens (9) and candida species (15). Ampicillin and chloramphenicol resistance occurred in 11% and 3% of H.influenzae isolates; penicillin and chloramphenicol resistance in 4% and 2% of S.pneumoniae isolates and sulphonamide resistance in 30% of N.meningitidis isolates. Meningococcal meningitis occurred predominantly in winter, H.influenzae late autumn and early winter and TBM late winter with a second peak in summer. Of the 396 cases of viral meningitis the commonest viruses isolated were mumps, enterovirus, coxsackie and echovirus. **CONCLUSIONS:** 1) TB meningitis was the commonest form of bacterial meningitis 2) Followed by N.meningitidis, H.influenzae and Strep. pneumoniae. 3) Antibiotic resistance was lower than in other parts of the country. 4) Seasonal effects were noted for TBM, H.influenzae and N.meningitidis. 5) Recommendations are made for implementation of vaccination.

## † 87

**FETAL LUNG FIBROBLAST PROLIFERATION IS STIMULATED BY UREAPLASMA UREALYTICUM VIA MACROPHAGES.**

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**Background:** Despite the frequent clinical association between colonization with Ureaplasma urealyticum (Uu) and chronic lung disease in preterm infants remains the pathogenic role of Uu unknown.

**Subjects:** We investigated the influence of heat-inactivated Uu (hiUu) on the proliferation of human fetal lung fibroblasts (HFL) in vitro.

**Interventions:** Fibroblasts - cultured in 1% v/v fetal calf serum (FCS) - were stimulated with $10^{-2}$ - $10^6$ colour change units (ccu) hiUu/ml or with supernatants of monocyte-derived macrophages (mdm) incubated with hiUu. The effect of hiUu was compared to that of 0,1-10µg/ml lipopolysaccharide (E.coli).

**Measurements:** Proliferation of fibroblasts: Methylene-blue staining

**Results:** HiUu does not directly alter the proliferation of HFL. However supernatants of mdm stimulated with hiUu enhance HFL growth compared to supernatants of unstimulated mdm ($p<0.05$). The effect of hiUu is dosedependent. Medium hiUu concentrations ($10^4$ccu/ml) have a stronger growth enhancing effect than low ($10^0$ccu/ml) and high ($10^6$ccu/ml) concentrations ($p<0.05$). Supernatants of mdm incubated with $10^4$ccu/ml hiUu stimulate slowly growing fibroblasts (1%FCS) to 70% of the growth promotion gained by culturing HFL in 10%FCS (v/v). HiUu induces fibroblast growth as strongly as optimal concentrations of lipopolysaccharide.

**Conclusion:** Ureaplasma urealyticum induces fibroblast proliferation in vitro. Uu may play a role in the lung fibrosis of bronchopulmonary dysplasia.

## † 88

**CROSSED EYE HAND DOMINANCE AS A PREDICTOR OF FAILURE TO LEARN TO READ AND SUBSEQUENT SCHOOL DROP OUT**

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**Background:** Is crossed eye hand dominance as identified in a lateral dominance examination a predictor of failure learn to read and subsequent school drop out?

Crossed sectional study in a psychological and social services agency.

**Subjects:** 403 children from a "marginal" communities who had dropped out from school (Mean age 11.01 years, s.d. 2.26 years) and 201 children from the same socio-economic status, who had successfully remained in school (Mean age 10.60 years, s.d. 2.26 years).

**Interventions:** Assessment of reading ability by means of an informal reading inventory and lateral dominance by means of eye and hand preference and dominance measures.

**Results:** 89.67% of the children in the group that had dropped out of school were determined to be functional illiterates. Measures or eye dominance (ABC Vision Test) did not reveal significant differences between the groups (50.24% vs. 54.46 vs. 87.62% right hand preferent). Measures of hand dominance, including tapping, copying, and writting tasks revealed that the drop out group had significantly greater incidence of non-preferred (left hand) dominance than the group that successfully remained in school.

**Conclusion:** The results of the present study revealed that the neuropsychological assessment of a child who has dropped out of school should include measures of eye and hand dominance, and that the presence of crossed eye hand dominance, whit a typical pattern of right hand dominance and left eye dominance may be used as a predictor of failure to learn to read and a contributing factor to school drop out. The results are framed by the authors in terms of a neurodevelopmental perspective.

## † 89

### VENTILATORY INSUFFICIENCY IN HEALTHY PRETERM INFANTS

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**Background:** Development of pulmonary acini progresses over the full gestation. The efficiency of gas mixing is dependent, among others, of lung structure and it is of importance to set the stage for gas diffusion.
**Hypothesis:** Gas mixing is less efficient in preterm infants compared to fullterms.
**Subjects:** 24 preterm and 12 fullterm, healthy infants were studied.
**Intervention:** A modified nitrogen wash-out technique was used to determine functional residual capacity (FRC), variables of ventilation, and gas mixing efficiency in terms of nitrogen clearance (NC), effective breath fraction (EBF), and functional dead space (VD).
**Results:** FRC/kg, breathing frequency, and alveolar ventilation/kg did not differ between the groups. However, total ventilation was higher in preterm infants (375+/– 88 *vs* 236 +/– 60 ml/kg,min; p<0.001), and so were nitrogen clearance (6.7 +/– 1.6 *vs* 4.8 +/– 0.4; p<0.001) and functional dead space (4.3 +/– 1.1 *vs* 1.9 +/– 0.6 ml/kg; p<0.001). EBF was 43 +/– 12 % in term and 60 +/– 7% in preterm infants (p<0.001).
**Conclusion:** Preterm infants have higher total minute ventilation than term infants. This can be attributed to an impaired gas mixing efficiency. This aspect of lung function appears as an important cause of inefficient ventilation in immature infants.

## * 90

### Prevention of Disease in Glutaryl-CoA Dehydrogenase Deficiency (GDD)

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Depts. of Pediat., Marburg[1], Freiburg[2], München[3], F.R.G., Padova[4], Italy, Utrecht[5], Rotterdam[6], The Netherlands, Institute of Child Health[7] London, Great Britain, Graz[8], Austria, Copenhagen[9], Denmark.

Background: GDD is an important, most likely widely underdiagnosed neurometabolic disease. It is unknown, whether the severe neurological disease can be prevented by early diagnosis and therapy.
Subjects: In the last years 16 patients with GDD could be diagnosed by our groups before the onset of acute encephalopathic crises, which occur on average at the age of 14 months.
Results: After diagnosis and initiation of treatment all children continued to develop normally up to report (mean age 6.3 years; range 2.7 to 14 years). In older patients the neuroradiological changes, present in infancy, gradually diminished and even disappeared.
Conclusions: The onset or progression of neurological disease in GDD appears to be preventable by vigorous intervention during illnesses together with carnitine supplementation ± a diet low in protein or even a strict reduction of the intake of lysine supplemented with a lysine free amino acid mixture. Diagnosis must be achieved before the onset of the dystonic-dyskinetic movement disorder.

## ● 91

### RETINOL DEFICIENCY ASSESSED BY CONJUNCTIVAL IMPRESSION CYTOLOGY (CIC) IN PRETERM INFANTS

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Background: Preterm infants are known to be deficient in retinol. This may predispose to the development of chronic lung disease. We have used CIC to assess retinol status and aimed to determine the significance of abnormal findings on CIC.
Subjects: Eighty-nine preterm infants at a median age of 36 post menstrual weeks.
Interventions: CIC was successfully performed in 74 infants. Abnormalities were correlated with the presence of intraventricular haemorrhage, retinopathy of prematurity, chronic lung disease and days of oxygen requirement.
Results: Thirteen CIC specimens were abnormal, 61 were borderline normal or normal. Birth weight was significantly lower in the abnormal group. There was no significant difference in the incidence of intraventricular haemorrhage, chronic lung disease or days of oxygen requirement in each group. There was an increased risk of retinopathy of prematurity requiring treatment in the abnormal group (relative risk = 9, 95% conference intervals 2-40, p<0.01).
Conclusions: Retinol deficiency as assessed by CIC is associated with retinopathy of prematurity requiring treatment. It may be possible to perform CIC immediately after birth to identify an at risk group who may benefit from extra vitamin A supplementation.

## * 92

### ANALYSIS OF P16 $^{INK4}$ GENE IN RHABDOMYOSARCOMA (RMS).

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*Background*. The human 9p21 region is frequently involved in chromosomal inversions, deletions and LOH in a large variety of solid tumors. The p16 protein is encoded by a gene (named MTS1 , CDK4i or p16$^{INK4}$) localized on chromosome 9p21. P16 is a controller of the cell cycle: normal progression through G1 is promoted by the activity of the cyclin dependent protein kinases CDK4 and CDK6, which are inhbited by the protein p16 $^{INK4}$. For these reasons p16 could be considered a potential tumor suppressor gene. Moreover some recent data showed that p16 homozygous deletion is present in 10-85% of primary solid tumors and cell lines (Nobori et al.,1994; Kamb et al ,1994; Spruck et al. 1994).
*Subjects and Methods*. To establish the role of p16 in soft tissue sarcoma, we looked for homozygous deletions and point mutations of the p16$^{INK4}$ gene. We examined 12 RMS samples taken from pediatric subjects aged between 26 and 188 months (6 aveolar and 6 embryonal). p16 gene was amplified in the three constitutive exons. The presence of homozygous deletions were estimated by means of the coamplification of a single copy gene (β-actin or β-globin). Analysis of point mutations was performed by means of PCR-SSCP of the three amplified fragments by means of a non-radiactive approach previously described (Iolascon et al. 1994).
*Results and Conclusion*. Homozygous deletion of the p16 gene was seen in 3 of the 12 (25%) analyzed RMSs. In one case we found a point mutation in exon 2. Our data suggested that p16 inactivation is a common event in RMS accounting 33% of cases.
**This work is supported by grants from: AIRC,MURST 40% and Sp11 CNR/ACRO, Italy**

## † 93

### ATRIAL NATRIURETIC PEPTIDE (ANP) DURING HIGH FREQUENCY OSCILLATORY VENTILATION (HFOV) IN PRETERM INFANTS.

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Background: HFOV is a new mode of artificial ventilation for IRDS characterized by relatively high mean airway pressures (MAP) and superimposed oscillations. High MAP may lead to increased right ventricular afterload and distension of right atrium. HFOV is often complicated by generalized edema. We studied ANP secretion and its possible role in fluid homeostasis.
Setting: Prospective clinical study in 7 HFOV vs 7 conventionally treated preterm infants.
Interventions: MAP, fluidintake (FI), urineproduction (UP), fractional sodiumexcretion (FeNa), NT-proANP serum levels and edema were determined on ventilator days 1,2,3,5 and 3 days after extubation.
Results: The HFOV group showed significantly higher MAP on days 2, 5; reduced UP on days 2, 3; higher ANP levels on day 5; and edema on day 3, 5; (t-test, chi-square respectively; p<0.05). ANP levels were not correlated with MAP, UP, or FeNa.
Conclusions: A high MAP-HFOV strategy may lead to impaired lung perfusion, distension of right atrium and increased production of ANP. Elevated ANP levels during HFOV did not induce UP or FeNa but may have contributed to the formation of generalized edema by increasing vascular permeability.

## † 94

### EVALUATION OF SPONTANEOUS SPEECH AT 6½ YEARS OF AGE IN CHILDREN WHO HAVE REQUIRED NEONATAL INTENSIVE CARE (NIC).

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Aim: To study different aspects of spontaneous speech in children who needed NIC and in a control group.
Subjects: A cohort of 284 children born in 1980-1985 who needed NIC. Group 1: GA 23-31w, n=81, subgr.1A: GA 23-27 w, n=27, subgr.1B: GA 28-31w, n=54. Gr.2: GA 32-36w, n=132. Gr.3: GA ≥37w, n=71. Controls(C): GA ≥37w, n=40.
Measurements: During a 10-15 min conversation eight functional variables of spontaneous speech were evaluated: Ability to inform(A1), articulatory motor function(A2), sound pattern(A3), word finding(A4), word selection(A5), sentence structure(A6), conversational interaction(A7), interaction motivation(A8), 0-5(good ability). (Ups J Med Sci 1991, 97: 229-250).
Result: 25 children (8.8%) had a handicap in spontaneous speech (one of A1-A8 ≤2). (Gr.1A 3.7%, gr.1B 11.1%, gr.2 6.8%, gr.3 12.7%, C 0%). ANOVA showed significant difference in all scales. Tukey's HSD indicated significant difference between C and gr.3 in A1-A8, between C and gr.2 in A3-A6 and between C and gr.1 in A3 and A6 only.
Conclusion: Most children who needed NIC have a normal spontaneous speech at 6½ years of age. A speech handicap is more frequently found in moderately preterm and term infants than in very preterm infants.

## ● 95

### DIAGNOSIS OF FOOD ALLERGY IN ATOPIC ECZEMA: OPEN OR BLINDED?

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**Background:** The diagnosis of food allergy in practice is based on history, skin prick test or serum specific IgE. Objective diagnosis should be based on a formal elimination-challenge, the practicability of which was the subject of this study.
**Subjects:** Children with atopic eczema, mean age 14 months (range 2 to 36), and the parents of altogether 450 children. Attending pediatric residents.
**Interventions:** Randomly open, or double-blind placebo controlled food elimination-challenge, with follow-up visits at 7, 14 and 30 days post-challenge. Parents and residents were interviewed with a questionnaire on the procedures.
**Results:** Both challenge types resulted in a diagnosis of food allergy in 54% of patients. Half of all patients showed acute onset reactions (itching, hives,. exanthema) and the other half delayed reactions (eczema). The cumulative dose evoking delayed reactions was significantly greater than that evoking acute reactions, mean 250ml (200 to 300) vs. 21ml (10 to 33); figures were not different with open challenge. Preliminary results indicate that residents preferred the blinded challenge, while the preference was not so clear cut from parents' point of view.
**Conclusions:** When carefully executed, with appropriate follow up, open and double blind challenges seem equally accurate in the diagnosis of food allergy for practical purposes.

## † 96

### PREDICTION OF DISABLING IMPAIRMENT IN VERY PRETERM INFANTS BY LINEAR ARRAY AND SECTOR ULTRASOUND SCANNING.

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**Background:** The earliest reports predicting neurodevelopmental outcome used linear array ultrasound apparatus. Mechanical sector scanning is thought to give better resolution, particularly of periventricular white matter lesions.
**Study design:** Prospective cohort study in a tertiary referral centre.
**Subjects:** 215 very preterm infants who had linear array ultrasound scanning born between 1979-1982 and 888 who had sector scanning born between 1983-1991.
**Measurements:** ultrasound images were reported as favourable or unfavourable and neurodevelopmental assessments were classified on the presence or absence of disabling impairments, according to previous protocol (1). Predictions were based on the hypothesis that unfavourable ultrasound scans at discharge (any loss of brain tissue , or ventricular dilatation) will be associated with disabling impairment at one year.

| Results: | Sensitivity | Specificity | predictive value | Accuracy | Prevalence |
|---|---|---|---|---|---|
| Linear array | 74% | 87% | 40% | 85% | 11% |
| Sector scanning | 71% | 22% | 29% | 78% | 11% |

**Conclusion:** The introduction of mechanical sector scanning did not lead to improved prediction of neurodevelopmental outcome at 12 months of age. This may be because only the most obvious lesions carry a bad prognosis.

1. Stewart et al. Dev Med & Child Neurol 1987;29:3-11

## † 97

### ACELLULAR PERTUSSIS VACCINE (DTPa) VS. WHOLE-CELL PERTUSSIS VACCINE (DTPw) VS. NATURAL INFECTION: COMPARISON OF SPECIFIC CELL-MEDIATED IMMUNE RESPONSE

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**Background:** The course of pertussis is determined by pharmacological effects mediated by various toxins. Currently, there is little understanding of the importance of toxins and the immunological mechanisms relevant for protection from the disease. The aim of this study was to investigate the specific, cellular immunity (CMI) after vaccination with DTPa and DTPw and compare these data to immunity after natural infection.
**Methods:** Peripheral blood T-lymphocytes were isolated and their capacity to respond to the pertussis related antigens pertussis-toxin (PT), filamentous hemagglutinin (FHA) and 69kDa-protein was analysed in children before and after vaccination with DTPa or DTPw and 4-6 weeks after natural infection. CMI was investigated by measurement of antigen-specific proliferation, lymphocyte phenotype, cytokine pattern and expression of activation markers (CD25, HLADR).
**Results:** Vaccination with DTPa created a specific T-cellular response to PT, FHA and 69kDa that was shown increase continually, depending on the progress of the vaccination schedeule. The presence of a definite PT-specific response was proven by testing a non-mitogenic recombinant PT. Phenotype analysis revealed a predominant activation of T-helper-cells. Cytokine pattern demonstrated a predominant T-helper-1-type response. CMI responses after DTPa were superior to responses after DTPw and similar to those after natural infection.
**Conclusion:** Our data indicate that DTPa-vaccination induces a potent immune response to PT, FHA and 69kDa that is superior to CMI after DTPw and equivalent to the specific CMI after natural infection. The findings of a preferential T-helper-1 activation suggest a role of IFN-γ-activated macrophages in protective immune responses.

## † 98

### EFFECTS OF LOW, NORMAL AND ELEVATED PLASMA VITAMIN E (E) LEVELS ON OXIDATIVE MODIFICATION OF LDL AND LEUKOTRIENE $E_4$ ($LTE_4$) EXCRETION IN GENETIC VITAMIN E DEFICIENCY

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**Background**: Genetic E deficiency is caused by a defective α-tocopherol binding protein [Traber et al., J Lipid Res 34:201,1993]. The first patient described [Burck et al., Neuropediatrics 12:267,1981] was followed for 13 years. For most of this time he received daily oral E supplements of 1.8 g and maintained E plasma levels in the range of 20-50 µmol/L (controls: 10-35). Interruption of supplements caused very low plasma E concentrations within 3 days [Kohlschütter et al., J Inher Metab Dis 11Suppl2:149,1988].
**Interventions**: On two occasions the patient was studied at a "low" (after 4 days without supplements, plasma E <4µM), "regular" (1.8 g E per day for 2 days, plasma E 20-50µM) and "high" E status (3.6 g E per day for 2 days, plasma E 80-90µM). Isolated plasma LDL (1.0 µM) from the patient and two controls was oxidized in vitro by $Cu^{++}$ (7.5µM). During oxidation, degradation of polyunsaturated fatty acids (PUFA) and accumulation of conjugated dienes were studied. **Results**: PUFA in native and oxidized patient LDL at the low E status were comparable to those of control LDL. PUFA after oxidation of patient LDL at the regular and high E status were above those of control LDL. Dienes in oxidized patient LDL were highest at the low E status and lowest at the high status. Urinary $LTE_4$ was increased at the low E status (90 nmol/mol creatinine), decreased during regular supplements (62, 22, 20 nmol/mol) and was low at the high E status (9 and 11 nmol/mol). **Conclusions**: (1) Native patient LDL did not appear oxidized even at a very low E status, but was protected from oxidation in vitro at higher E status. (2) The $LTE_4$ results suggest that E modulates 5-lipoxygenase activity in vivo. Genetic E deficiency offers unique possibilities to study effects of E in humans. (Supported in part by DFG/Ma 1314/2-1.)

## † 99

### CENTRAL DYSREGULATION OF GONADOTROPIC AXIS IN CASTRATE RATS DURING UREMIA

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**Background/aim:** Chronic renal failure may result in delayed puberty and fertility disorders. We observed a reduction of hypothalamic gonadotropin-releasing hormone (GnRH) secretion in castrate uremic rats. The aim of this study was to reveal the changes in the regulation of GnRH secretion by catecholaminergic and serotoninergic neurons in medial preoptic area (MPOA) during uremia.
**Subjects:** Three groups of adult male Sprague-Dawley rats (300 g) were included.
**Interventions:** The animals were orchidectomized on day 1 and divided into the following groups: Group 1, subtotal (5/6) nephrectomized uremic rats; Group 2, sham-operated control rats fed *ad libitum*; and Group 3, sham-operated pair-fed control rats (malnutrition control). Guide cannula was implanted into the MPOA of each animal on day 12, and a microdialysis probe (CMA/12, Carnegie Medicine) was inserted on day 16. After a 2 h equilibration period, dialysate samples were collected every 10 min for 4 h. Norepinephrine (NE), 3,4-dihydroxyphenylglycol (DOPEG), 3,4-dyhydroxyphenylacetic acid (DOPAC) and 5-hydroxyindolacetic acid (5-HIAA) concentration was measured by HPLC with electrochemical detection in each sample. Statistical analysis was performed using the analysis of variance followed by Duncan's test.
**Results:** NE level was significantly ($p<0.05$) reduced in MPOA of uremic animals compared to that in both control groups, but the concentration of DOPEG, the major catecholamine metabolite, was increased in Group 1 compared to that in Group 2. The concentration of dopamine metabolite, DOPAC, was normal in Group 1, but it increased ($p<0.05$) in Group 3. Serotonin metabolite, 5-HIAA, level was decreased ($p<0.05$) in uremic rats compared to that in both control groups.
**Conclusion:** Our data provide *in vivo* evidence for a deficient stimulatory input of superior neuronal systems to the hypothalamic GnRH pulse generator during uremia.

Supported by Deutsche Forschungsgemeinschaft

## † 100

### ADDITIVE EFFECT OF INSULIN-LIKE GROWTH FACTOR 1 (IGF-1) AND GROWTH HORMONE (GH) ON GROWTH OF CONTROL AND UREMIC RATS

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**Background/aim:** Reduced production of IGF-1 and increased binding to IGF binding proteins may contribute to the development of secondary resistance to growth hormone in uremia. The aim of the present study was to reveal the effect of recombinant human IGF-1 and GH on the growth in control and uremic rats.
**Subjects:** Two groups of female Sprague-Dawley rats (150-170 g) were included: Group 1: uremic animals after subtotal (5/6) nephrectomy and Group 2: sham-operated pair-fed control rats.
**Interventions:** Four subgroups were set up in both groups depending on the hormonal treatment lasting for 12 days: A: vehicle-treated rats, B: animals treated with 1.5 mg/kg IGF-1/kg/bid, C: rats given 3.75 IU GH/kg/bid, and D: rats treated with both peptides. Weight and length gain was determined in each subgroup in the end of the experiments. Statistical analysis was performed using the analysis of variance followed by Duncan's test.
**Results:** Treatment with either peptide alone could increase the growth significantly ($p < 0.05$) compared to that in vehicle-treated subgroups both in control and uremic rats. IGF-1 treatment, however, could further enhance ($p < 0.05$) GH-induced weight and length gain with an increased ratio of weight gain over food intake in both groups.
**Conclusion:** Both GH and IGF-1 increased the weight and length gain in control and uremic rats. The additive effect of IGF-1 to the GH-induced growth in both groups indicates that these peptides may promote growth through different pathways.

Supported by Deutsche Forschungsgemeinschaft

## * 101

ZINC METABOLISM IN A CHILD WITH HYPERZINCAEMIA

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**Background:** We report on zinc kinetic studies in a 10 year old child with severe growth failure, marked hyperzincaemia (plasma Zn >200umol/L) and symptoms of zinc deficiency.

**Methods:** After an overnight fast $^{67}Zn$ was given orally with food and $^{70}Zn$ was injected intravenously. Serum samples were taken over a period of 3 hours and urine was collected over the following 5 days. Zn isotope ratios were measured by TIMS and systemic turnover ofZn was calculated using a two compartment model. Distribution of Zn in plasma proteins was examined by FPLC-ICPMS.

**Results:** There is a negligible rapid turn-over Zn pool (0%, normal 2-4%) and an increased slow pool (97%, normal 94-97%). Absorption of Zn from the oral dose was reduced. Separation of the serum proteins by FPLC-ICPMS shows that the endogenous and exogenous Zn bind to a previously uncharacterised protein of mass 120,000-180,000 kD. Zn metabolism in the child's mother is normal.

**Conclusions:** This child has an abnormality of Zn metabolism. This may be a previously unreported inborn error of Zn metabolism. The molecular defect is unknown, but we postulate that transport and storage of Zn in the liver is affected, leading to reduced metabolic availability of Zn.

## † 102

MODERATE HYPOTHERMIA REDUCES APOPTOSIS IN CULTURED NEURONAL CELLS DEPRIVED OF NERVE GROWTH FACTOR.

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**Background:** Moderate hypothermia after cerebral hypoxia-ischaemia protects against neuronal damage by reducing the degree of apoptosis. The aim of the present study was to determine whether a 3°C reduction in temperature could also protect neuronal (PC12) cells from apoptosis resulting from nerve growth factor (NGF) withdrawal in vitro.

**Methods:** Cultures of NGF dependent PC12 cells were incubated in medium containing NGF (0 to 50 ng/ml) for 24 hours at 37°C or 34°C. At the end of the experiment apoptotic nuclei were scored in triplicate culture wells following propidium iodide staining of fixed cells.

**Results:** At both temperatures NGF prevented apoptosis in a dose dependent manner, although at 34°C there was a significant reduction in neuronal apoptosis (t test, $p<0.05$). In the absence of NGF, 43% (37°C) and 32% (34°C) of PC12 cells underwent apoptosis and at lower concentrations of NGF (3 to 12 ng/ml) incubation at 34°C reduced cell death by up to 50%. At the highest concentration of NGF (50 ng/ml) there was no difference between the degree of apoptosis at 37°C (10%) and 34°C (8%).

**Conclusion:** Mild hypothermia can rescue neuronal cells from apoptosis resulting from NGF withdrawal in vitro.

## † 103

Langerhans Cell Histiocytosis of the Spine
--Early fourage for conserving the height of the vertebral body--
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Background: There is no general consens regarding the appropriate therapeutic procedure in the case of radiological suspicion of eosinophilic granuloma of the spine.There is however general agreement on confirming the diagnosis by performing a biopsy.

Traditional treatments include; biopsy, chemotherapy, low dose radiotherapy and immobilisation.It has been reported that the healing times of lesions did not differ significantly between any of the afore mentioned treatments, this also applies to untreated but resolved spinal eosinophilic granuloma.

As to whether any of the mentioned treatments actually stop the collapse of the vertebra has yet to be reported.

Subjects: Eight cases of Histiocytosis X involving the Spine were treated at the Orthopädische Universitätsklinik Frankfurt/Main between 1972-1995. There were 4 male and 4 female patients. The average age was 5.4J. Six patients had an isolated involvement only on the spine whereas 2 cases showed multiple bone lesions. In all cases the vertebral body had collapsed and 5 of these cases showed a significant kyphosis of the segment involved. Clinically all patients showed signs of back pain and one of them developed a paralysis of the legs.

Interventions:In cases of isolated lesions biopsy was done by transpediculare method. In case of 2 patients with multiple bone lesions we performed the biopsy from one of the affected bones, in these cases the femur. Five patients was treated with a plaster cast and 3 patients underwent surgery ( kyphotic instability- dorsal spondylodesis , paralysis- ventral dekompression).

Chemotherapy was given in case of multiskeletal lesions.

Results: In all cases ( surgical or conservative ) we saw no further collapse or instability of the segment involved. The height of the vertebral body rested reduced in all patients.

In the case of the ventral decompression the neurologic signs disappeard completely.

Conclusion: In our opinin, biopsy is mandatory for unclear osteolytic processes of the spine. If a malignant tumor can be excluded, surgical intervention is not necessary unless patients have neurologic deficits or the instability is increased.

## † 104

EXTERNAL RESPIRATION STUDIES IN PRETERM INFANTS.

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Aim:To investigate the changes in parameters of external respiration in preterm infants during two mounths of age

Subjects:Group I- 5I infant, age I4,6±I,0 days, weight 2,27I±0,036 kg;gr.II- 24, 43,3±2,8 days, 3,007±0,I30 kg.

Measurements:Intrathoracic gas volume per weight /IGV/kg bronchial resistance /$R_B$/, bronchial conductivity /$C_B$/, alveolar pressure /$P_A$/, spirographic results were examined by means of body plethysmography.

| Results: | IGV ml/kg | $R_B$ $H_2O$/l/s | $C_B$ l/s/$H_2O$ | $V_t$ ml |
|---|---|---|---|---|
| Gr.I | 38,24±I,4I | 26,22±I,26 | 0,040±0,002 | 20,66±0,97 |
| Gr.II | 3I,3I±3,I9 | 20,9I±I,62 | 0,053±0,004 | 29,88±I,63 |
| p | < 0,05 | <0,05 | <0,0I | <0,0I |

Conclusion:During growth IGV is stabilizing, $R_B$ is reducing, $C_B$ is improving. It is possible to use body plethysmography for investigation respiration in preterm.

## * 105

FETAL SEX, FETAL GROWTH AND BIRTH WEIGHT DISCORDANCE IN TWINS

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**Background:** Birth weight (BW) discordance in twins seems unrelated to zygosity, but is possibly influenced by fetal sex; the role of other factors is still poorly understood. The BW of twins appears to be unrelated to birth order. We studied the relation between BW discordance in twins and a set of mothers' and infants' variables.

**Study setting:** A nationwide prospective multicentre study on infant health.

**Subjects:** 778 non-malformed twin pairs. Like-sexed pairs=555 (MM=295, FF=260), unlike-sexed pairs=223 (larger twin: male,MF=121; female,FM=102).

**Measurements:** Intertwin BW difference expressed as percentage of the largest twin's BW. Cutoff for discordance was setted to 15% in like-sexed pairs; in unlike-sexed twins it was setted to 20% in MF pairs and to 10% in FM pairs, in order to account for a physiological average 5% higher BW in males than in females.

**Results:** The rate of discordance was 30.5% in like-sexed and 27.4% in unlike-sexed pairs. No relationship was found between BW discordance and area of residence, social class, maternal age and occupation, parity, smoking in pregnancy, use of ovulation induction and gestational age. Compared to pairs whose first born twin's BW was ≥2500 g the ORs for discordance were 1.45 (95%CI=1.03-2.06) and 2.40 (95%CI=1.29-4.47) when the first born twin's BW was 1500-2499 g and <1500 g, respectively.

**Conclusions:** The male-female BW difference must be taken into account when studying BW discordance in unlike-sexed twins. Factors that negatively affect birth weight seem to increase the likelihood of BW discordance in twins as well.

## ● 106

NEW MARKERS OF HEPATITIS B VIRUS IN MOTHER-INFANT TRASMISSION.

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**Background:** HBXAg (X) and Polymerase (Pol) are new antigens of Hepatitis B Virus (HBV) and their importance in diagnosis and follow-up of hepatitis from mutant and wild type virus has been recognized. X and Pol are specific markers of viral replication and suggest the presence of circulating HBV-DNA. Anti-X correlates with clearance of viral DNA. Pol is related to endogenous DNA polymerase activity in virus particles and its detection in serum without other markers may reflect a level of virus replication high enough for immunological recognition but not for detection of viral proteins in serum. We studied the presence of X and Pol in mother-infant pairs as markers of low replication level of wild or mutant type HBV.

**Subjects:** 7 mother with history of HBV infection, HBsAg and HBeAg negative, anti-HBs positive, with normal ALT level, and their 7 infants. 4 adults without history of HBV infection, as controls.

**Measurements:** serum samples were collected in the first week after birth from mothers and babies to test the presence of X and Pol with an ELISA assay using a rabbit antiserum.

**Results:** 2 mothers were X and Pol positive. One of their 2 newborns was X and Pol positive. One mother and her baby were only Pol positive. None of the controls were X or Pol positive.

**Conclusions:** these preliminary data confirm X and Pol as sensitive markers of HBV infection at low but persistent level of replication and suggest the possibility of infection from wild and mutant type of HBV. Mutant HBV in fact may not be recognized by the usual serological markers. Serial assays of X and Pol and particularly serial Polymerase Chain Reaction tests for detection of viral DNA, will be useful in studying the presence of mutant HBV and the risk of vertical trasmission.

## * 107

PLASMA HEXANAL:
A PEROXIDATION PRODUCT OF ω6-POLYUNSATURATED FATTY ACIDS

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**Background:** We investigated the occurrence of hexanal (HX), a specific LPO-product of ω6-polyunsaturated fatty acids (PUFA), in human plasma.
**Subjects:** 99 healthy children in various age groups, 17 adults on two different occasions, and one neonate with acute liver failure and iron overload.
**Methods:** Plasma HX was determined by HPLC using a modification of the method by Holley et al. *(Free Rad. Biol. Med. 1993;15:281).* Additionally, 5 plasma samples were analyzed by headspace GC/MS for the presence of volatile HX.
**Results:** HX could be detected in the plasma of all probands (range 56-409 nmol/l). No HX was found in headspace analyses. The intraindividual variability in 17 adults was remarkably low. There was a decrease of the average HX values from infancy to adolescens (median 0-1 years: 185 nmol/l vs. 13-18 years: 113 nmol/l; $p<0.01$). The extent to which HX may be increased in case of severe LPO was apparent in a neonate with iron overload (plasma ferritin 2075 µg/l; HX: 2075 nmol/l), who subsequently developed biochemical signs of ω6-PUFA deficiency.
**Conclusion:** The determination of plasma HX provides specific insight in the *in vivo* peroxidation of ω6-PUFA, e.g. linoleic acid, and may be used in clinical studies as an additional index for the presence of LPO. (BMFT; grant 07ERG07)

## ● 108

RECOMBINANT ERYTHROPOIETIN IN THE TREATMENT OF CHEMOTHERAPY-INDUCED ANEMIA IN PEDIATRIC PATIENTS

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BACKGROUND. Cancer is frequently associated with significant anemia and may be related to inadequated endogenous erithropoieitin (EPO). In recent years a number of data have been published concerning the therapy with recombinant human EPO (rh-EPO). OBJECTIVE. To assess the efficacy of rh-EPO in reducing the need of transfusion in children with solid malignant tumors. PATIENTS AND METHOD. An open, not randomized trial was performed, including 20 children (mean age±SD: 12.5±2.9y) who were treated with rh-EPO (150 U/kg) SC X 5/wk for 12 weeks. Patients were compared to 20 historical controls matched for age, sex and tumor type. RESULTS. Baseline hematocrit (Ht) and hemoglobin (Hb) were similar in both groups. Treated patients had significantly ($p< 0.001$) greater incease in Ht and Hb level than control group and the tansfusion requirements were significantly ($p< 0.001$) lower in the EPO-patients. No serious adverse effect of rh-EPO was observed. CONCLUSION. rh-EPO is safe and effective in reducing the blood transfusion requirements in pediatric patients with solid malignant tumors during chemotherapy.

## ● 109

ACUTE PHYSIOLOGICAL EFFECTS OF TWO DIFFERENT DOSES OF MAGNESIUM SULPHATE IN INFANTS WITH BIRTH ASPHYXIA

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**Background:** The endogenous NMDA channel blocker magnesium (Mg) may have cerebral protective effects after asphyxia by decreasing NMDA mediated calcium entry.
**Aim:** To assess the physiological effects and serum Mg concentration of 2 different Mg sulphate doses in severely asphyxiated (10 minute Apgar score < 6) term infants.
**Interventions:** 7 infants received 400 mg/kg magnesium sulphate and 8 infants 250 mg/kg. Blood pressure, respiration, heart rate, muscle tone and EEG were recorded for 24 hours and serum Mg was repeatedly measured.
**Results:** In the 400 mg/kg group, MAP fell by a mean of 6 mm Hg at one hour. Spontaneous respiration was abolished for 3-6 hours. EEG and heart rate were not significantly altered. Serum Mg increased from 0.79 to 3.6 mmol/l at one hour and was 1.6 mmol/l at 24 hours.In the 8 infants who received 250 mg/kg MgSO4, there was mild respiratory depression in one but no significant change in MAP, EEG, tone or heart rate. Serum Mg rose from 0.71 to 2.42 mmol/l at one hour and was 1.13 mmol/l at 24 hours.
**Discussion:** 400 mg/kg of MgSO4 has an unacceptable risk of hypotension. 250 mg/kg was not associated with hypotension. During Mg treatment, ventilation should be closely monitored and may need assistance. 250 mg/kg maintains serum Mg at two to three times normal mean value.

## † 110

HEMODYNAMIC IMPAIRMENT AND EEG SUPPRESSION FOLLOWING SURFACTANT REPLACEMENT THERAPY USING 2 VERSUS 6 ALIQUOTS.

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Background Previous studies have shown hemodynamic impairment and a decrease in EEG-activity following Curosurf treatment. Such an effect may be minimized by the use of smaller aliquots.
Study design/setting A randomized study of 20 preterm infants with RDS requiring mechanical ventilation in a tertiary neonatal service.
Interventions Infants were randomised to receive Curosurf 200 mg/kg in two or six aliquots with an interval of two minutes.
Measurements From ten minutes before surfactant administration to 20 minutes after the last aliquot mean arterial blood pressure (MABP), heart rate, oxygen saturation, transcutaneous $pO_2$ and $pCO_2$ and EEG burst rate was continuously monitored. Left ventricular output was measured every second minute in the period.
Results LVO increased in all infants (median(range):+29%(11-44%)). MABP decreased in 14 infants (median(range)-28%( -16--36%)) and increased in six infants (median(range)+12%(8-39%)). No difference was found in the maximal change in circulatory parameters between the groups. EEG burst rate was suppressed in all patients following Curosurf instillation and no difference was found between the six infants with increase in MABP(A) and the 14 infants with decrease in MABP(B), median(range) GrA -35(-45--12)% versus GrB -50(-76--10)%. No correlation was found between EEG and any circulatory change.
Conclusions No advantage was found by dividing the dosage of Curosurf into six aliquots. LVO increases substantially following treatment with Curosurf.The finding of EEG-suppression in infants with increase in MAP suggests a non-circulatory aetiology of the EEG-suppression.

## ● 111

THE EFFECT OF EITHER DOPAMINE OR VOLUME-EXPANSION ON CARDIAC FUNCTION AND CEREBRAL BLOOD FLOW IN MODERATELY HYPOTENSIVE, PRETERM INFANTS

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Background Hypotension is a wellknown risk factor for adverse outcome in preterm infants. The best choice of treatment remains unclear.
Study type/setting A clinical, randomised, controlled study in a tertiary neonatal service. Inclusion criteria: GA<33 weeks, invasively measured mean arterial blood pressure(MAP): 30-39mmHg.
Interventions The infants were randomly assigned to receive infusion of dopamine 5 µg/kg/min, plasma 15 mL/kg or no treatment.
Measurements Global cerebral blood flow(CBF) was measured using the Xe-clearance method. Left ventricular output(LVO) was calculated by measuring the internal aortic diameter by echocardiography and measuring the aortic blood flow velocity by Doppler ultrasound. Measurements were taken before treatment and two hours later.
Subjects (median(range)): GA 28(25-32) wks, BW 1183(680-2140) gm.
Results Mean(SD),CBF:mL/100g/min,LVO:mL/kg/min,MAP:mmHg,Stat:ANOVA.

| | Dopamine,n=13 | Volume,n=13 | Control,n=12 | p-value |
|---|---|---|---|---|
| ΔCBF | +2.6 (2.9) | +0.9 (7.9) | +0.3 (3.5) | 0.35 |
| ΔLVO | +21 (33) | +26 (51) | -12(25) | 0.03 |
| ΔMAP | +6.6 (4.4) | +2.0 (3.1) | -0.4 (2.6) | 0.0000 |

Conclusions Though dopamine is more effective than volume expansion at increasing blood pressure, no significant difference between the treatment regimens could be demonstrated regarding LVO and CBF.

## * 112

IMPACT OF SOLID FOODS ON PLASMA 20:4n-6 AND 22:6n-3 FATTY ACID STATUS OF TERM INFANTS AT 8 MONTHS OF AGE

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**Question:** Do weaning foods offer a sufficient supply of long-chain polyunsaturated fatty acids (LCP) to formula-fed infants.
**Subjects**: 70 healthy infants born at term after an uncomplicated pregnancy.
**Interventions**: 49 formula-fed (FF) and 21 breast-fed (BF) infants received meat containing solid food from 6 to 8 mo of age.
**Measurements**: Plasma phospholipid (PL) and cholesteryl ester (CE) fatty acid analysis with capillary GLC. Statistics: Difference between groups, Student's *t*-test
**Results**:

| | BF | | FF | |
|---|---|---|---|---|
| **% mean(SD)** | **6 mo** | **8 mo** | **6 mo** | **8 mo** |
| **PL 20:4n-6** | 10.45 (1.73) | 9.85 (0.97) | 8.08 (1.57)*** | 8.65 (1.10)*** |
| **PL 22:6n-3** | 5.21 (1.27) | 4.89 (1.17) | 2.93 (0.96)*** | 2.45 (0.40)*** |
| **CE 20:4n-6** | 6.88 (1.30) | 6.14 (1.01) | 4.74 (1.29)*** | 5.01(0.86)*** |
| **CE 22:6n-3** | 0.87(0.18) | 0.80(0.20) | 0.57(0.45)** | 0.38(0.09)*** |

In the FF group, plasma 20:4n-6 increased concomitantly with the amount of fat derived from solid foods, though not to the level obtained by the BF group.
**Conclusion**: The introduction of weaning foods containing meat improves the 20:4n-6 status of formula-fed infants, but has no effect on 22:6n-3.
Acknowledgment: Wyeth-Ayerst Research, Philadelphia, PA, USA.

## † 113

**CORRELATION OF SIMULTANEOUS $HbO_2$+$MbO_2$ AND $pO_2$ DURING ISCHAEMIA** Andrew J Macnab, Andrew I Minchinton, Roy E Gagnon
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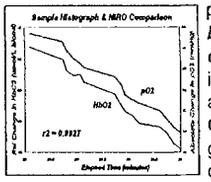
**Background:** Measurements of oxygenated haemoglobin and myoglobin ($HbO_2$+$MbO_2$) by near infrared spectroscopy (NIRS) are absolute changes relative to an unknown initial concentration. If the initial concentration can be determined, intra and inter subject variability can be assessed. **Interventions:** NIRS optodes were placed 30mm apart on the forearm of healthy adults with a histograph tissue probe (tissue $pO_2$ mmHg) inserted subcutaneously 50mm laterally. From simultaneous $HbO_2$+$MbO_2$ and $pO_2$ data, rates of change and correlation during four minute periods of ischaemia were compared. Initial concentrations of $HbO_2$+$MbO_2$ were calculated based upon the absolute change in $pO_2$. **Results:** Twenty-two paired data sets were obtained. Mean Rates of change during ischaemia: $HbO_2$+$MbO_2$ -6.82 ±0.73 umol/L/min, $pO_2$ -3.32 ± 0.99 mmHg/min. ***Mean correlation between $HbO_2$+$MbO_2$ and $pO_2$ during periods of occlusion: 0.974 $r^2$ ±2%.*** One third of the calculated inital concentrations had a mean of 146 umol/L ±8% and two thirds had a mean of 69 umol/L ±21%. **Conclusion:** The high correlation indicates histography can be used to determine initial $HbO_2$+$MbO_2$ concentration enabling NIRS values to be quantified.




## † 114

**NEAR INFRARED SPECTROSCOPY OXIDIZED CYTOCHROME $aa_3$ PATTERNS OF CHANGE DURING CARDIAC SURGERY IN CHILDREN** Andrew J Macnab, Jacques LeBlanc, Faith A Gagnon, Roy E Gagnon
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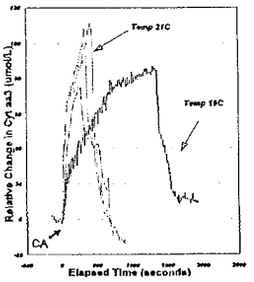
**Background:** Cardiac surgery during hypo-thermic cardiopulmonary bypass (CPB) ±circulatory arrest (CA) has significant neurological sequellae. Near infrared spectroscopy (NIRS) measures relative change in concentration of oxidized cytochrome $aa_3$ (Cyt $aa_3^{2+}$) offering insight into cerebral oxygenation. **Interventions:** In NIRS studies (10 sec data by cerebral reflectance) on 11 children (ages 6 days - 13 years) throughout CPB, we observed 6 episodes of CA. **Results:** Cyt $aa_3^{2+}$ increased steadily during all 6 episodes and fell rapidly on reinstituting perfusion. One episode (at nasopharyngeal temp 15°C) had a slower rate of change from the other 5 (at 21±1.8°C). **Conclusion:** Although these Cyt $aa_3^{2+}$ patterns of change appear unphysiological, the rate of oxidation may be affected by temperature and/or interrupted substrate delivery (during CA). Cyt $aa_3^{2+}$ accumulation could occur if lack of substrate terminates metabolism before oxygen stores are consumed.




## ● 115

**FACTORS RELATED TO TRANSFUSION IN VERY LOW BIRTH WEIGHT INFANTS DURING ERYTHROPOIETIN TREATMENT.** Rolf F Maier, Michael Obladen, Diethelm Messinger, Charles A J Wardrop, and the European Multicentre rhEPO Study Group. Coordinating Centre: Department of Neonatology, Virchow-Klinikum, Berlin, Germany.

**Background:** Transfusions are reduced but not eliminated by recombinant human erythropoietin (rhEPO) in very low birth weight (VLBW) infants.
**Objective:** To detect prognostic factors related to transfusion in VLBW infants during rhEPO treatment and to explain "non-responders".
**Patients:** 120 VLBW infants treated in the 2nd European multicentre trial.
**Intervention:** rhEPO 3 x 250 IU/kg/week subcutaneously.
**Methods:** The transfusion risk for various subgroups and covariables was tested with exact P value and Multivariate Cox's Regression Model.
**Results:** Sixty (50 %) infants received at least one transfusion during rhEPO treatment. Transfusion was 79 % in infants with extremely low birth weight (750 - 999 g), 70 % with gestational age ≤ 28 weeks, and 61 % in infants with initial hematocrit ≤ 48 % or initial reticulocyte count ≤ 9 %. Marked inter-center differences were found for sampling blood loss, iron supply, and transfusion rate which ranged from 13 % to 73 % between the 12 participating centers and was related to the volume of diagnostic blood loss (19 % vs. 80 % for blood loss < 1 vs. ≥ 1 ml/kg/day). The prognostic variables birth weight, initial hematocrit, and gestational age were found to be most predictive for transfusion.
**Conclusion:** To improve rhEPO response in VLBW infants, there is a need to minimize diagnostic blood loss, to raise initial hematocrit with placental transfusion, and to develop rational criteria for transfusion in VLBW infants.
Supported by Deutsche Forschungsgemeinschaft SFB 174/A9

## † 116

**DELAYED CEREBRAL VASODILATION AFTER CEREBRAL ISCHAEMIA IN FETAL SHEEP IS REDUCED BY INHIBITION OF NITRIC OXIDE SYNTHASE** K Marks, C Mallard*, I Roberts, C Williams*, PG Gluckman*, AD Edwards.
Department of Paediatrics and Neonatal Medicine, Royal Postgraduate Medical School, London, UK; *Research Centre for Developmental Medicine and Biology, University of Auckland, New Zealand.

**Background:** The study examined whether delayed cerebral vasodilation following cerebral ischaemia in fetal sheep is caused by excess nitric oxide production.
**Subjects:** Eleven chronically instrumented, late gestation (122-133 days) fetal sheep.
**Interventions:** After 30 minutes of transient cerebral ischaemia, 5 subjects received treatment with a nitric oxide synthase inhibitor, $N^G$-Nitro-L-arginine (50 $mg.hr^{-1}$ for 4 hours, then 20 $mg.hr^{-1}$ for 3 days), and 6 with phosphate buffered saline. Changes in cerebral vascular tone were then observed for 3 days by using near infrared spectroscopy to measure changes in the concentration of total cerebral haemoglobin ([tHb]). Severity of neuronal loss was quantified histologically 3 days after ischaemia.
**Results:** Treated and control subjects were of similar gestational age, weight and head circumference. Delayed cerebral vasodilation occurred in both groups commencing 18-24 hours after ischaemia. The mean±SEM peak height of [tHb] at 24-30 hours was significantly less in the treatment group (6±2 $\mu mol.L^{-1}$) compared to control group (14±3 $\mu mol.L^{-1}$) (ANOVA $p<0.05$).Treatment did not ameliorate histological injury.
**Conclusions:** Nitric oxide synthase inhibition attenuates the delayed cerebral vasodilation following cerebral ischaemia but does not reduce cerebral injury.

## † 117

EGF AND TGFb1 AFFECT EMBRYONIC LUNG DEVELOPMENT THROUGH CELL-SPECIFIC ALTERATIONS IN PROLIFERATION. Ana Martin, MaryAnn V. Volpe, Robert J. Vosatka, Heber C. Nielsen.
NEMC. Department of Pediatrics. Division of Newborn Medicine. Tufts University. Boston, MA. USA.

Background: Epidermal growth factor (EGF) and transforming growth factor b1 (TGFb1) have different effects on branching morphogenesis and cell proliferation and differentiation during lung development.Hypothesis: these contrasting effects are mediated through regional alterations in cell-specific proliferation.
Subjects: Embryonic mouse lungs (gestational day 10.5).
Interventions: Lungs were cultured in serum and hormone free medium as control or with added EGF (10ng/ml) or TGFb1 (2ng/ml).At 48 hrs cultures received 2μCi 3H-thymidine.After 72 hrs lungs were cryosectioned and prepared for autoradiography.
Results:Control lungs showed intermittent positive epithelium and mesenchyme.TGFb1 treated lungs showed more labelling of epithelium, especially in clusters around branching tips and less label of mesenchyme.EGF treated lungs showed increased uniform cell labelling both of mesenchyme and of epithelium.
Conclusions: EGF and TGFb1 affect branching morphogenesis through divergent effects on proliferation of embryonic lung mesenchyme and epithelium.

## † 118

**DIAGNOSTIC AND PROGNOSTIC VALUE OF QUANTITATIVE $^{31}P$ MAGNETIC RESONANCE SPECTROSCOPY (MRS) IN PERINATAL ASPHYXIA** E. Martin, R. Buchli, S. Ritter, R. Schmid, E. Boltshauser, R. Largo, S. Fanconi, G. Duc, H. Rumpel.
University Children's Hospital Zurich, Switzerland.

**Background:** To investigate the diagnostic value (Diag) of depressed high energy phosphates (HEP) estimated by $^{31}P$-MRS in the brains of asphyxiated neonates and to prognosticate (Prog) their neuro-developmental outcome at 3, 9 and 18 months, based on the HEP measured during the first week of life.
**Subjects:** 23 term neonates suffering from perinatal asphyxia.
**Interventions:** The neonates were classified into 3 categories according to the neurological achievement (NNS). Between day 1 and 14 (median day 3) pp. MRI and volume selective $^{31}P$-MRS to quantify the HEP in the parietal WM, including 20% of deep GM, were undertaken. 20 infants were available for follow-up examinations with a modified Griffiths developmental assessment (DQ).
**Results:** 1) Diag: Taken the NNS as "true" value, highly significant correlations between [PCr], [ATP] and NNS; PCr/Pi lower, but still significant, Apgar not.
2) Prog: Again, highly significant correlations between [PCr], [ATP] and DQ, PCr/Pi and NNS lower, but still significant, Apgar not significant.

| | Apgar | PCr/Pi | [PCr] | [ATP] | NNS |
|---|---|---|---|---|---|
| Diag (NNS) | 0.34 | 0.62 | 0.83** | 0.85** | 1 |
| Prog (DQ) | 0.17 | 0.69* | 0.77** | 0.77** | 0.65* |

*p<0.005; **p<0.001

**Conclusions:** [PCr] and [ATP] correlated well with the severity of hypoxic-ischemic encephalopathy, expressed as NNS, and are good predictors for outcome.

## † 119

### INFLUENCE OF DIETARY NUCLEOTIDES ON THE INTESTINAL PERMEABILITY AND THE DEVELOPMENT OF CIRCULATING ANTIBODIES IN PRETERM NEONATES

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Aim: To evaluate the influence of dietary nucleotides supplementation on the intestinal permeability to lactulose and mannitol and to ß-lactoglobulin and the development of circulating antibodies to $\alpha$-casein and ß-lactoglobulin in preterm infants during the first month of life. Subjects:27 preterm infants were studied, 11/27 fed a standard low birth weight formula and 16/27 fed the same formula supplemented with nucleotides at similar levels to those of human milk. Samples: blood and urine samples were obtained at 1, 7, 30 days of life. Methods: Serum ß-lactoglobulin, IgG to ß-lactoglobulin and IgG to $\alpha$-casein were measured by ELISA, and lactulose/mannitol excretion ratio was determined by gas-liquid chromatography. Results: intestinal permeability to saccharides or ß-lactoglobulin was not affected by the nucleotide supplementation. However, serum concentrations of IgG to ß-lactoglobulin and $\alpha$-casein were higher in preterm neonates fed the formula supplemented with nucleotides. Conclusions: dietary nucleotides seem to influence the maturation of humoral immune response in preterm newborn infants.

## † 120

### DIAGNOSTIC VALUE OF CSF $\beta_2$-MICROGLOBULIN ($\beta_2$m) TO ASSES CNS INVOLVEMENT IN INFANTS WITH SUSPECTED TORCH INFECTIONS.

Ana Martín-Ancel, Alfredo García-Alix, Teresa Ramos, Fernando Cabañas, José Jiménez, Fernando del Castillo, José Quero. *Autonoma University of Madrid. Spain.*

CNS involvement may be difficult to asses in infants with suspected TORCH infections because clinical manifestations may be delayed and CSF findings may overlap with reference values. $\beta_2$m is a nonspecific marker of CNS infection in neonates.[1] We hypothesized that CSF $\beta_2$m could be a useful diagnostic tool in these infants.

**Methods:** Neonates (GA>36wks) with suspected congenital TORCH infection were studied prospectively. The diagnosis of TORCH infection was based on serial serologic tests and/or viral isolation. CNS involvement was assessed by CSF, neuroimaging and neurophysiologic findings. $\beta_2$m was measured blindly by enzyme immunoassay.

**Results:** 14 neonates were studied: 5 had CNS infection (3 toxoplasmosis, 1 herpesvirus, 1 cytomegalovirus) and 9 did not (1 had systemic CMV infection and 8 had TORCH infections ruled out). Neonates with CNS involvement had significantly higher CSF $\beta_2$m levels compared to neonates without CNS involvement (8.01±5.21 vs 1.53±0.31 mg/L, p<0.001). All the infants with CNS infection had CSF $\beta_2$m levels higher than 2.25 mg/L (best operational diagnostic cut-off value obtained in a previous study[1]), while all the infants without CNS infection had lower levels. CSF $\beta_2$m was elevated (5.6 mg/L) in one infant with subclinical CNS infection by *Toxoplasma*; by contrast, $\beta_2$m was within the normal range in one infant with systemic CMV infection and no CNS involvement.

**Conclusion:** CSF $\beta_2$m is a useful ancillary tool in the diagnosis of congenital CNS infections by virus or protozoa, mainly in infants without overt neurological syndrome.

1. García-Alix A, Martín-Ancel A, et al. CSF $\beta_2$m in neonates with CNS infections. Eur J Pediatr. In press.

## † 121

### PEROXISOMAL METABOLISM OF 12- AND 15-HYDROXYEICOSA-TETRAENOIC ACID (HETE) IN MAN

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**Background:** HETEs are biological active monohydroxylated derivatives of arachidonic acid. *In vitro*, degradation by ß-oxidation of HETEs proceeds in rat liver peroxisomes. We studied the importance of peroxisomes in HETE oxidation in humans *in vivo*. **Subjects:** 8 patients with a peroxisome deficiency disorder (Zellweger syndrome) showing normal mitochondrial ß-oxidation capacity and 8 healthy subjects. **Interventions:** Urine samples were obtained from spontaneous micturition and excretion of 12- and 15-HETE was measured. **Measurements:** 12- and 15-HETE were analyzed by GC/NICI-MS and specific RIAs. **Results:** Both metabolites were found exclusively in the urine of peroxisome deficient subjects (12-HETE: median 26 pg/ml, range 17-36 pg/ml; 15-HETE: median 40 pg/ml, range 29-61 pg/ml) whereas both compounds were below the detection limit (<0.5 pg/ml) in the urine of normal subjects (p<0.002). **Conclusions:** Results implicate that peroxisomes are the main cellular organelle responsible for HETE oxidation *in vivo*. Analysis of HETE excretion in urine represents an additional new specific diagnostic tool in patients with Zellweger syndrome. (Supported by DFG grant Ma 1314/2-1)

## ● 122

### EARLY CORRELATES OF PATENT DUCTUS ARTERIOSUS (PDA) IN TRIGGER-VENTILATED VERY LOW BIRTH WEIGHT INFANTS

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**Aim:** Various factors including fluid overload, exogenous surfactant, and RDS, have been considered to increase the risk of PDA. In the present study we examined the relative impact of early, relevant variables on the incidence of PDA.

**Subjects:** 39 consecutive infants of 500-1500g birth weight, receiving triggered ventilation for at least 48h and surviving at least 5d. Of these 39 infants, 16 (41% ) developed PDA.

**Measurements:** Descriptive as well as physiological variables, and ventilatory parameters in the first 72h of life, were considered. PDA was diagnosed by color Doppler echocardiography. The significance of differences between the two groups of patients with or without PDA was assessed with the $X^2$ test and the Mann-Withney U test. The variables that differed significantly between the two groups were entered in a stepwise logistic regression .

**Results:** Demographic variables, fluid intake, and $SaO_2$ did not differ between the two groups.

| | SURF | $IsO_2$24h | $IsO_2$48h | $IsO_2$72h | PIP24h | PIP48h | PIP72h | pH24h | pH48h | pH72h | $PCO_2$24h | $PCO_2$48h | $PCO_2$72h |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| PDA | 81% | 0.45 | 0.42 | 0.38 | 20 | 21 | 21 | 7.33 | 7.31 | 7.31 | 42 | 46 | 49 |
| | ** | * | ** | | ** | *** | ** | | ** | | * | ** | ** |
| noPD A | 39% | 0.34 | 0.29 | 0.34 | 17 | 16 | 17 | 7.40 | 7.38 | 7.32 | 35 | 35 | 39 |

*p< 0.05, **p< 0.01, ***p<0.001 - SURF = % receiving surfactant - other values are means -

In the logistic regression, only PIP at 48h remained significantly associated to PDA. When variables were considered for birth weight, PIP at 48 h remained significantly associated in the 1000-1500g group but not in infants <1000g in whom only $PaCO_2$ at 72h was predictive of PDA.

**Conclusions:** The highly significant association of PDA with the PIP value at 48h confirmed the role of severe RDS in the development of PDA, whereas surfactant administration *per se* was apparently not relevant.In ELBW infants hypercarbia represented a strongly significant antecedent of PDA,raising the possibility of a cause-effect relationship. *Italian CNR Targ Proj PAIMA n 9300602.*

## † 123

### EFFECT OF INTRAUTERINE GROWTH RETARDATION ON POSTNATAL CEREBRAL HAEMODYNAMICS

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**Background:** There is evidence that fetuses subjected to intrauterine hypoxia divert blood flow from the systemic to the cerebral circulation.

**Hypothesis:** This 'brain sparing' effect may be reflected in abnormal cerebral haemodynamics in the first three days of life.

**Subjects:** 21 preterm babies (24-33 weeks gestational age); 11 weighed < 3rd centile and had evidence of intrauterine growth retardation (IUGR). None had significant abnormalities on cerebral ultrasound imaging.

**Interventions:** Cerebral blood flow (CBF) and volume (CBV) were measured on 1 to 3 occasions over the first 72 hours of life using near infrared spectroscopy.

**Results:** CBF increased in all the normally grown babies with no significant change in CBV, whereas for 5 IUGR babies there was a decrease in CBF. This group had significantly higher values of CBF on day 1, and of overall mean CBV.

| | IUGR (n=5) (decreasing CBF) | Normally grown (n=10) | p value |
|---|---|---|---|
| CBF ml.100g$^{-1}$.min$^{-1}$ | 22.00 ± 11.54 | 12.05 ± 3.89 | 0.002 |
| CBV ml.100g$^{-1}$ | 3.51 ± 0.83 | 2.41 ± 0.32 | 0.025 |

**Conclusion:** Some IUGR babies have raised CBF and CBV on day 1, probably resulting from fetal hypoxia.

## † 124

### VASCULAR CHANGES PLAYING A ROLE IN THE PATHOGENESIS OF POSTASPHYXIAL NECROTIZING ENTEROCOLITIS IN NEWBORN PIGS

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Departments of [1]Paediatrics, [2]Physiology and [3]Medicine, Albert Szent-Györgyi University Medical School, Szeged, Hungary and [4]Institut Henri Beaufour, Le Plessis Robinson, France.

**Background/aims:** Necrotizing enterocolitis (NEC) is the most common acquired gastrointestinal emergency in neonates. The aims of this study were to reveal the effect of neonatal asphyxia on (1) intestinal blood flow and cardiovascular data, and (2) cytoskeleton of endothelial cells in mesentery microvasculature in a porcine model of NEC (Ábrahám *et al.* 1994 *Pediatr Res* 35:210A).

**Subjects:** Two groups (asphyxiated, sham-operated) of newborn pigs (930-1680 g) were used.

**Interventions:** Asphyxia was induced by pneumothorax, after cardiovascular failure resuscitation (R) was performed followed by recovery period. Mean arterial blood pressure (MABP), heart rate (HR), flow in superior mesenteric artery (SMA) and abdominal aorta (AA) were measured in 6 animals in both groups. Endothelial changes in mesentery microvasculature of asphyxiated and control pigs were viewed after intravital F-actin labelling with bodipy phallacidin using confocal microscopy (Thurston & Baldwin 1994 *Am J Physiol* 266:H1896). Statistical analysis was done by Kruskal-Wallis test.

**Results:** Significant ($p<0.05$) cardiovascular changes developed during asphyxia and recovery:

| | 0 min | R | R+10 min | R+60 min |
|---|---|---|---|---|
| SMA flow (ml/min/100 g) | 22.2±2.6 | 9.8±2.3* | 26.8±1.6* | 23.8±2.3 |
| AA flow (ml/min/100 g) | 51.4±7.6 | 17.2±3.6* | 51.6±7.9 | 41.2±8.2 |
| MABP (mmHg) | 68.6±6.1 | 21.8±0.6* | 77.8±8.4 | 54.2±4.5 |
| HR (min$^{-1}$) | 169 ± 16 | 47 ± 2* | 178 ± 16 | 174 ± 7 |

Rearrangement of endothelial actin filaments was found in mesenterial vessels 24 h after asphyxia.

**Conclusion:** Vascular changes observed may take a part in the increased vascular permeability and development of NEC in asphyxiated newborn pigs.

Supported in part by grants from OTKA (F016682) and AMT (9/94/I).

## ● 125

A SERINE PROTEASE INHIBITOR BLOCKS PRIMING OF MONOCYTES FOR ENHANCED RELEASE OF SUPEROXIDE

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**Background:** Human monocytes isolated from blood and cultured for 18-24 h in endotoxin (LPS)-free, non-adherent conditions produced low amounts of superoxide ($O_2^-$). Addition of LPS, interferon-γ (IFN-γ), tumor necrosis factor α (TNFα), or platelet activating factor (PAF) at the beginning of culture "primed" the monocytes to maintain high $O_2^-$ response to phorbol ester for at least 96 h. Also, in response to LPS, monocytes secreted TNFα.
**Subjects:** *In vitro* human monocyte cultures.
**Interventions:** Protease inhibitors (aprotinin, soybean trypsin inhibitor, leupeptin, 4-(2-aminoethyl)benzenesulfonyl fluoride (AEBSF) were added to the monocyte cultures together with different "priming" agents such as LPS, PAF, IFN-γ or TNFα, to study the effect of protease inhibitors on "priming".
**Results:** The ability of LPS, TNFα, IFN-γ, or PAF to maintain high phorbol ester-triggered $O_2^-$ response was selectively blocked by addition of AEBSF, an inhibitor of serine proteases. AEBSF was most effective at 200 μM, and required 6 h for maximum effect. AEBSF did not effect phorbol ester-triggered superoxide release by unprimed monocytes, nor did it affect cell viability, nor did it interfere with TNFα secretion.
**Conclusion:** Enzymatic activity of a serine protease is required to maintain the high superoxide response of monocytes primed with LPS, IFN-γ, TNFα, or PAF.

## ● 126

**Maternal lymphocytes in breast milk engraft the infant gut.**

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**Hypothesis:** Maternal lymphocytes in breast milk are capable of binding to and crossing the infant gut epithelium.
**Subjects:** Human fetal gut explants grown in culture for 7-10 days.
**Measurements:** Breast milk cells were labelled with a fluorescent vital stain and incubated with fetal gut explants, with or without breast milk in the medium. After 6 hours explants were washed, snap frozen, sectioned and examined.
**Results:** Viable breast milk lymphocytes, both T and B cells, were observed binding to and crossing the epithelium of the gut explants. This phenomenon was observed more often if milk was included in the culture medium. Binding was observed at low cell concentrations, and peaked at 4-6 hours of incubation.

**Conclusion:** This human *in vitro* system suggests that as in other species, maternal lymphocytes may 'colonise' the infant gut. Their function there is uncertain at present.

## ● 127

**Asymptomatic congenital infection with CMV alters cytokine secretion by neonatal T-cells.**

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**Hypothesis:** Infection *in utero* alters cytokine secretion of cord-blood T-cells.
**Subjects:** Cord blood samples collected from 10 healthy term deliveries and 4 with known CMV infection (virus identified in the urine, infants otherwise healthy) following reactivation of maternal CMV in the third trimester.
**Measurements:** Using a plaque assay the frequency of cells secreting IL-2, IFN-γ, TNF-α, IL-4 and Rantes was estimated. Lymphocytes were activated using PHA or monoclonal antibodies against CD2.
**Results:** Activated lymphocytes from the CMV+ infants had significantly higher frequencies of cells secreting IFN-γ (6%±1%, controls 0%), TNF-α (4%±1%, controls 0%) IL-4 (3%±1%, controls 1%±0.5%) and Rantes (4%±1%, controls 2.5%). This effect was more striking if cells were activated using antibodies against CD2.

**Conclusion:** Clinically inapparent infection leads to significant functional changes in neonatal lymphocytes. This in turn may influence the development of the infant's immune system.

## ● 128

**Chemokine secretion by cord blood cells.**

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**Background:** Chemokine secretion by lymphocytes is an early component of their response to activation and costimulation; what is the frequency of this function in normal cord blood cells?
**Subjects:** 12 cord blood samples from healthy term births and 6 samples of healthy adults' lymphocytes, the latter purified using magnetic beads to remove all CD45RO+ T cells.
**Measurements:** Frequencies of peripheral blood lymphocytes secreting the chemokines RANTES and IL-8, as well as IL-2 were measured using a haemolytic plaque assay, before and 24 hours after activation with optimal concentrations of mitogen (PHA), antibody to CD3, paired antibodies to CD2, and antibody to CD28.
**Results:** Cord blood cells have a low frequency of chemokine secretion in response to all stimuli (2.5%±2% RANTES, 1.5%±1% IL-8), significantly lower than phenotypically matched CD45RA+ adult lymphocytes (5% ±2% RANTES, 3%±1% IL-8). In addition, we observed poor response to the use of the costimulus, CD28 (8%±2% cord blood cells secreted IL-2 following CD3+CD28, compared with 28%±1% adult cells).
**Conclusions:** Cord blood lymphocytes are limited in the frequencies of chemokine-secreting cells and responses to costimuli when compared with phenotypically matched adult cells. The mechanisms inducing this state of relative unresponsiveness are clearly of therapeutic interest.

## * 129

**TP/GFR THE RENAL PHOSPHATE THRESHOLD DECREASES WITH INCREASING POST MENSTRUAL (pm) AGE IN VERY LOW BIRTH WEIGHT (VLBW) INFANTS.**

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**Background:** Plasma phosphate ($P_P$) is mainly determined by the renal phosphate threshold (Tmp/GFR). In infants sufficiently substituted with P (Urine phosphate $U_P \geq 1$ mmol/l) $P_P$ decreased with increasing pm age whereas $U_P$ did not decrease. **Hypothesis**: $T_P$/GFR decreases with increasing pm age. **Study design**: Retrospective study; study period: 29-36 weeks of pm age. **Patients:** 71 VLBW infants. **Measurements:** In case of phosphaturia ($U_P \geq 1$ mmol/l) the maximum $T_P$/GFR ($P_P$-$U_P$ x $P_{Crea}/U_{Crea}$) together with $P_P$ and $U_P$ were recorded every two-week period. **Statistics**: Log-Rank test; data as median and range. **Results**: $T_P$/GFR and $P_P$ decreased ($p \leq 0.0002$) with increasing pm age whereas $U_P$ did not.

| | postmenstrual age (weeks) | | | |
|---|---|---|---|---|
| | 29 - 30 | 31 - 32 | 33 - 34 | 35 - 36 |
| phosphaturic infants | 29 | 35 | 27 | 19 |
| $P_P$ (mmol/l) | 2.5 (1.0-5.8) | 2.4 (1.1-3.4) | 2.2 (1.4-3.0) | 2.0 (1.4-2.7) |
| $U_P$ (mmol/l) | 4.4 (1.0-6.8) | 5.7 (1.1-1.4) | 6.4 (1.1-7.2) | 9.6 (1.2-1.8) |
| $T_P$/GFR (mmol/l) | 2.02(0.7-0.1) | 2.05(0.4-2.8) | 1.68(1.1-0.1) | 1.52(0.6-0.1) |

**Conclusion:** We speculate that $T_P$/GFR declines with increasing pm age because tubular reabsorption capacity increases more slowly then GFR.

## * 130

**HUMAN MILK INCREASES THE EARLY ENTERAL FEED TOLERANCE IN ELBW INFANTS (<1000 g) - RANDOMISED MULTICENTER TRIAL.**

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**Hypothesis:** Human milk increases the early enteral feed tolerance in ELBW infants. **Study design:** Randomised multicenter trial. **Setting:** Neonatal intensive care units of 7 tertiary care hospitals. **Patients:** 99 ELBW infants. **Interventions:** All ELBW infants born from 7/92 to 9/93 were randomly allocated to two different formulas and feeded following a standardised protocol. Formula was substituted by mothers breast milk if available. **Measurements:** Cumulative feeding volume from day 3 to 14 (CFV). **Statistics:** Kruskal-Wallis test, data as median and range. **Results:** CFV increased with an increasing human milk portion ($p<0.002$).

**Conclusion:** This is the first controlled data on early enteral feeding of ELBW infants. Explorative analysis shows that human milk should be the first diet in ELBW infants.

| | human milk portion | | |
|---|---|---|---|
| | 0% | <80% | ≥ 80% |
| n | 43 | 32 | 24 |
| CFV (ml/kg) | 501 0-962 | 624 80-936 | 867 72-1283 |

## * 131

HEMODYNAMICS AND REGIONAL BLOOD FLOW AFTER PORCINE SURFACTANT REPLACEMENT IN SURFACTANT DEPLETED NEWBORN PIGLETS.

Atle Moen* Terje Rootwelt*, Bengt Robertson, Tore Curstedt, Christian Hall, Ola D. Saugstad*. *Dept of Pediatric Research, Rikshospitalet, Oslo Norway.

**Background:** Several reports of changes in blood pressure after instillation of exogenous surfactant in preterm infants have been published.

**Methods:** We designed a study using newborn piglets to investigate the effect of porcine surfactant instillation on hemodynamics and regional blood flow in lung lavaged surfactant depleted piglets, comparing the effect of hypovolemia or hypoxemia prior to instillation. Blood flow measurements were done using radioactive microspheres. Three groups of piglets were studied, controls (n = 8), hypovolemia (n = 7) and hypoxemia (n = 7).

**Results:** Three to five minutes after instillation of surfactant mean arterial blood pressure (MABP) decreased significantly and similarily in all three groups with a mean decrease of 31(±12), 33(±9) and 29(±9) mmHg respectively ($p < 0.01$). Cardiac output only decreased in the hypoxemia group ($p = 0.025$), with no significant changes in the control and hypovolemia groups. Peripheral vascular resistance decreased significantly in all three groups immediately after surfactant instillation ($p < 0.01$) and returned to pre-surfactant level within 60 minutes. Blood flow did not change after surfactant instillation in any of the three groups in skin ($p = 0.16$), muscle ($p = 0.83$) and pancreas ($p = 0.31$). In liver ($p < 0.01$), kidney ($p = 0.022$) and intestine ($p = 0.018$) there was a decrease in blood flow with no differences between the three groups immediately after surfactant instillation with return to pre-surfactant levels within 60 minutes.

**Conclusions:** In newborn piglets MABP decreases significantly after porcine surfactant replacement. We were not able to demonstrate that hypoxemia or hypovolemia prior to surfactant instillation increase the hemodynamic instability after instillation. The decrease in MABP is caused by a decrease in peripheral vascular resistance and not a change in cardiac output.

## ● 132

BLOOD VELOCITY WAVE FORM OF THE INTERNAL CAROTID ARTERY (BVWF-ICA) AS A LEFT VENTRICLE (LV) FUNCTION INDICATOR.

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**Background:** Serial echographic estimation of LV-funtion in unstable (preterm) neonates is important but requires time and may induce apnoe. Experimental studies showed relation between BVWF-ICA and myocardial contractility. We studied this relation in the newborn.

**Patients:** 70 babies: GA>34wks: no asphyxia(A)/asphyxia(B), GA<34wks: no RDS(C)/RDS(D).

**Measurements:** On day 1,2,3,5-7,14 the time between Q(ECG) and peak velocity, acceleration time and time between Q(ECG) and ejection onset (preejection period; PEP-ICA) of BVWF-ICA and echocardiographically determined LV-output, fractional shortening, mean circumfer. fiber shorting, LVPEP, LVET, LVPEP/LVET-RATIO were measured simultaneusly.

**Results:** Although significant correlations were found between all BVWF-ICA features and LV-funtion indicators, the strongest was: PEP-ICA/LVPEP and PEP-ICA/RATIO (table)

| | | total n=70 | A n=26 | B n=15 | C n=13 | D n=16 |
|---|---|---|---|---|---|---|
| PEP-ICA/ LVPEP | r | 0.66 | 0.65 | 0.69 | 0.59 | 0.48 |
| | p | <0.001 | <0.001 | <0.001 | <0.001 | <0.001 |
| PEP-ICA/ RATIO | r | 0.55 | 0.55 | 0.53 | 0.51 | 0.48 |
| | p | <0.001 | <0.001 | <0.001 | <0.001 | <0.001 |

**Conclusion:** PEP-ICA could be used to investigate changes of LV-funtion even in the most unstable neonate.

## † 133

POSTPRANDIAL THERMOGENESIS IN OBESE ADOLESCENTS

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**Background:** Previous results concerning diet-induced (DIT) or glucose-induced (GIT) thermogenesis in obese children and adolescents are contradictory.

**Subjects:** 119 nonobese (C) (m/f=59/60; age [mean ±SD]: 13.0±1.7yr; weight: 44.3±10.4kg; LBM: 33.8±7.2kg; BF: 23.0%) and 92 obese (O) (m/f=53/39; age: 13.2±1.9yr; weight: 78.6±19.3kg; LBM: 48.6±10.7kg; BF: 37.8±4.4%) adolescents.

**Investigations:** Resting metabolic rate (RMR) was measured by indirect calorimetry (Deltatrac, Datex Inc., Finland) for 45 min before and for 3 hours after the consumption of either a mixed, liquid meal (energy content being 30% of the postabsorptive RMR), or a lemon-flavoured drink, conatining 1.75 g/kg ideal body weight (max. 100g) glucose.

**Results:** In the total sample DIT (% of the energy consumed) was significantly higher in the O as compared to the C children (4.7±2.2% vs 3.6±1.8%; $p<0.001$). The difference between O and C became non-significant when the cohort was divided into subgroups according to pubertal stage and sex. GIT (% increase in RMR) was similar in the C and O groups (6.8±3.9% vs 5.4±5.4%; $p>0.05$)

**Conclusion:** Defective thermic response to a mixed meal or to glucose in obese adolescents can be excluded.

Supported by Nat. Sci. Res. Fund (OTKA, T 5267) and Nestle Nutrition

## † 134

INCREASED FAT OXIDATION IN OBESE ADOLESCENTS.

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**Background:** Postabsorptive fat oxidation (FO) and its association with body composition (lean body mass [LBM], fat mass [FM]), age, and sex were studied

**Subjects:** 235 nonobese (C) (m/f=116/119; age [mean±SD]: 13.1±1,7yr; weight: 45.3±10.5kg; LBM: 34.3±7.1kg; FM: 11.0±4.5kg) and 159 obese (O) (m/f=93/66; age: 12.9±2.06yr; weight: 76.2±19.1kg; LBM: 47.4±10.9kg; FM: 28.8±9.2kg) adolescents.

**Measurements:** Postabsorptive fuel utilization was calculated from $O_2$ consumption, $CO_2$ production and urinary nitrogen as measured by indirect calorimetry (Deltatrac, Datex Inc., Finland) and Kjeldahl's method, respectively.

**Results:** Postabsorptive FO (absolute value and percentage of REE) was significantly higher in the O (76.7±39.7g/24h; 42.3±18.7%) than in C (40.1±26.3g/24h; 28.7±17.1%, $p<0.001$), even if it was adjusted for LBM, sex and age. The correlation between FM and FO (g/24h) was significant ($r=0.62$, $p<0.001$). The slope of the relationship indicated that for each 10 kg additional fat mass, FO increased by 20.7g.

**Conclusion:** Changes in fat mass significantly affect fat oxidation in adolescents and this process may contribute to long-term regulation of fat and energy balance.

Supported by Nat. Sci. Res. Fund (OTKA, T 5267) and Nestle Nutrition

## * 135

THE EFFECT OF NON-PHARMACOLOGICAL TREATMENTS ON CIRCULATING CORTISOL AND β-ENDORPHIN IN PRETERM BABIES.

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**Background:** Preterm babies in intensive care experience the stresses of severe illness, pain and a dysregulated environmental milieu. The alleviation of stress is central to care, but in addition, chronic stress, mediated through chronic hypercortisolaemia, may contribute to later impairments in cognitive function.

**Aim:** To study the effect of non-pharmacological treatments on circulating cortisol and β-endorphin levels.

**Subjects:** Three groups of preterm babies in an intensive care unit.

**Interventions:** The effects of massage, intrauterine-like sound and maternal-infant skin-to-skin contact were compared with control periods.

**Results:** Eleven babies, (median gestational age (GA) 29 weeks, birth weight (BW) 0.98 kg, postnatal age (PNA) 20 days) were studied before and after massage. Cortisol levels fell significantly (median difference - 35.8 nmol/l, 95% CI-0.5, -94.0). Plasma β-endorphin and cortisol were measured in 9 babies (median GA 27 wk, BW 0.960 kg, PNA 10 d) before and after exposure to intrauterine-like sound and in 15 babies before and after maternal skin-to-skin contact (median GA 31 wk, BW 1.42 kg, PNA 21 d). There was no change in either cortisol or β-endorphin after sound stimulation. After skin-to-skin contact, there was a highly significant fall in β-endorphin levels ($p=0.01$).

**Conclusions:** Certain non-pharmacological treatments may have positive benefit in reducing endogenous stress hormone secretion.

## † 136

LIPID PEROXIDATION IN CYSTIC FIBROSIS RELATED TO NUTRITIONAL STATUS AND LUNG INVOLVEMENT.

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**Background:** Oxygen reactive species are thought to be related to chronic pulmonary inflammation in cystic fibrosis (CF) patients. The role of tumor necrosis factor alfa (TNF) in this disease is more controversial. Also, poor nutritional status has been recognized as a poor prognosic factor.

**Subjects:** 89 CF patients free from an acute exacerbation.

**Measurements:** Malondialdehyde (MDA), measured by a fluorimetric method, was used as an index of lipid peroxidation. TNF was determined by ELISA. Body mass index (BMI) and IGF-1 (measured by RIA) were used as markers of nutritional status.

**Results:** MDA was increased compared with the control group (3.0 ± 0.6 versus 2.1 ± 0.4 nmol/mL; $p < 0.001$). In contrast, TNF values (2.1 ± 1.8 pg/mL) were within the normal range. 13.5% patients had a BMI below the 3rd percentile and 23.6% an IGF-1 value below the 3rd percentile. Decrease of both parameters correlated ($p < 0.001$) with disease severity as measured by Shwachman and Crispin-Norman Scores and pulmonary function tests.

**Conclusion:** Increased oxidative damage may be present in CF and may contribute to chronic pulmonary inflammation in a way independent of TNF. Severe pulmonary forms of the disease are associated with a poor nutritional status.

## † 137

HOW EFFECTIVELY ARE LONG CHAIN POLYUNSATURATED FATTY ACIDS (LCP) ABSORBED IN PRETERM INFANTS?

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**Background:** Optimal nervous system development requires LCP. Human milk contains both n-6 and n-3 LCP. Prematil-LCP is a recently developed preterm formula milk containing LCP in similar quantities to that found in human milk. Standard Prematil contains no preformed LCP.
**Subjects:** Preterm infants: birthweight 1000-1500g, gestation<32wks.
**Interventions:** Infants were randomized to receive Prematil-LCP (n=10) or Prematil (n=10). Fat balances (3 days) were performed from day 4 of full enteral feeds. A parallel breast fed group (n=11) was also studied. Milk and faecal lipids were analyzed using gas liquid chromatography.

**Results:** Fatty acid excretion/*absorption*

Median values are in bold with 95% confidence intervals for the median in parentheses.

| | Prematil | | Prematil-LCP | | Human milk | |
|---|---|---|---|---|---|---|
| Total fat (g/kg) | 2.36 | (1.24-3.29) | 2.64 | (1.50-3.87) | 1.65 | (0.48-2.72) |
| *Absorption (%)* | *82.0* | *(76.2-89.4)* | *82.9* | *(75.9-89.3)* | *87.8* | *(78.6-95.5)* |
| Total n-6 LCP (mg/kg) | 8.20 | (4.23-16.04) | 19.90 | (8.85-31.44) | 26.02 | (21.80-43.06) |
| *Absorption (%)* | *-55.2* | *(-84.0-34.6)* | *71.6* | *(57.5-86.9)* | *85.9* | *(81.9-91.2)* |
| Total n-3 LCP (mg/kg) | 8.27 | (3.91-24.99) | 13.55 | (0.00-24.74) | 9.69 | (0.00-19.92) |
| *Absorption (%)* | *72.1* | *(23.8-88.7)* | *77.5* | *(57.5-100.0)* | *94.8* | *(83.0-100.0)* |

**Conclusion:** Although LCP are well absorbed from Prematil-LCP, the absorption coefficients suggest less efficient LCP absorption than in breast fed infants. Poorer LCP absorption in formula fed preterm infants may mean LCP requirements are not met by feeding formulas that contain LCP in quantities found in breast milk.

## ● 140

NITRIC OXIDE MEDIATED VASCULAR HYPORESPONSIVENESS IN NEONATAL PIGLETS INDUCED BY GROUP B *STREPTOCOCCUS* AND *E. COLI*

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BACKGROUND: Enhanced production of nitric oxide (NO) following NO synthase (NOS) induction is responsible for the systemic hypotension in septic patients. We have studied the sepsis-related induction of the NOS in the pulmonary and mesenteric vessels in piglets.
SUBJECTS: Isolated pulmonary and mesenteric artery rings or lung parenchymal segments of neonatal piglets.
INTERVENTION: Rings were incubated in Krebs solution (control (C), n = 12) or containing *E. coli* lipopolysaccharide (LPS, 1 $\mu g\ ml^{-1}$, n = 14)) or GBS (3 x $10^7$ c.f.u. $ml^{-1}$, n = 14) for 1, 5 or 20 h and isometric tension was recorded thereafter. NOS activity was determined by the conversion of radiolabelled L-arginine to L-citrulline.
RESULTS: Long term incubation (20 h) with LPS or GBS significantly reduced the contractile responses to noradrenaline (NA) in either pulmonary (1027 ± 82, 475 ± 49 and 585 ± 56 mg in the C, LPS and GBS groups, respectively, $P < 0.01$ Student t test) or mesenteric arteries (5273 ± 718, 2380 ± 382 and 2330 ± 367 mg in the C, LPS and GBS groups, respectively, $P < 0.01$). The NO precursor L-arginine ($10^{-5}$M) increased the LPS- and GBS-induced vascular hyporesponsiveness to NA. In contrast, the NOS inhibitor $N^G$-nitro-L-arginine methyl ester (L-NAME, $10^{-4}$M), dexamethasone (3 x $10^{-6}$M), or the protein synthesis inhibitor cycloheximide ($10^{-5}$M) completely restored the reactivity to NA. LPS or GBS produced a significant increase in iNOS (but not cNOS) activity which was abolished by dexamethasone.
CONCLUSIONS: We conclude that long term incubation with and LPS of pulmonary and mesenteric artery rings induces iNOS activity resulting in vascular hyporesponsiveness to NA. NO could be a key mediator both in the systemic in the pulmonary vascular response to sepsis in newborns.

## † 138

**QUANTITATIVE CULTURES OF PROTECTED BRUSH SPECIMENS (PBS) AND ENDOTRACHEAL ASPIRATES (EA) IN VENTILATED NEONATES.**

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***Objective:*** to evaluate quantitative cultures of PBS and EA for differentiating pulmonary infection (PI) from tracheal bacterial colonization (C).
***Design:*** the results of PBS and EA were compared with the (reference) clinical diagnosis, which was made as follows : 1) PI = presence of ≥ 2 of the following criteria: -increased ventilator requirements, -elevated white blood cell count or C-reactive protein or fibrinogen, -infiltrate on chest X ray; 2) C = absence of PI criteria from the beginning until 5 days after the end of evaluation.
***Patients:*** neonates: 1) on mechanical ventilation for >7 days, 2) not receiving antibiotics (AB) for >3 days, were eligible. Ten infants (GA: 29.1 ±1.5 weeks; BW:1270 ±400 g; mean±SD) were studied, at 20 (±10) days of age. PI was diagnosed in 2/10 (AB started after sampling), and bacterial C in 8/10.
***Measurements:*** EA followed after 90 minutes by PBS, with a second study 48 hours later. Quantitative cultures considered positive, for PBS at ≥ $10^4$ CFU, for EA at ≥ $10^5$ CFU.

| ***Results:*** | n true + | n true - | n false + | n false - | Specificity | PPV* |
|---|---|---|---|---|---|---|
| **PBS** | 2 | 15 | 3 | 0 | 83 % | 40 % |
| **EA** | 2 | 10 | 8 | 0 | 55 % | 20 % |

(PPV* = positive predictive value, and sensitivity: are of little value, with only 2 PI).
**Conclusions:** As compared with EA, PBS is more specific, hence rules out pulmonary infection more accurately.

## † 141

**RELATIONSHIP AMONG VIROLOGICAL, IMMUNOLOGICAL AND CLINICAL PARAMETERS IN INFANTS WITH VERTICALLY ACQUIRED HUMAN IMMUNODEFICIENCY VIRUS (HIV-1) INFECTION.**

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**Objetive**: To investigate the relationship among virological, immunological and clinical parameters in infants with vertically acquired HIV-1 infection.
**Methods**: Sixty four infants born of HIV-1 seropositive mothers, younger than 12 months of age were studied. Viral phenotype was determined by cocultivation of the $HIV^+$ infant's PBMCs with PHA-stimulated donor lymphocytes. After 7-10 days virus were characterized for syncytium-inducing (SI) ability by culturing patient PBMCs with MT-2 cells. To determine the in vitro replication pattern of the HIV-1 infecting strain, p24 Ag was quantified sequentially in the coculture's supernatants. HIV RNA in the plasma of $HIV^+$ infants was quantified by using the PCR assay.
**Results**: Only 13 out of 64 (20%) infants were identified as infected on the basis of viral culture and PCR findings. Six out of 13 HIV-1 isolates from these patients were classified as rapid/high and seven as slow/low. We have found a significantly positive correlation between the replication rate of HIV isolates and their capacity to induce syncytia. In *in vitro* cocultures containing PBMCs from infants with AIDS, five out of six isolates had the rapid/high phenotype and induced syncytia. Whereas only one out of seven isolates from infants without AIDS showed these properties. HIV-1 isolates with rapid/high and SI phenotype, and isolates with slow/low and NSI phenotype were obtained from infants who had an HIV-1 RNA copy number/ml plasma ranging from 27654 to 83520, and 1342 to 34321, respectively.
**Conclusions:** Increase in viral burden and the presence of a more cytopathic viral phenotype correlated with $CD4^+$ T cell decline. This association was mainly found in infants with more severe clinical symptoms.

## * 139

CONCENTRATIONS OF ARACHIDONIC ACID AND DECOSAHEXANOIC ACID IN RED BLOOD CELL TOTAL LIPIDS DO NOT DIFFER SIGNIFICANTLY IN HUMAN MILK FED PRETERM INFANTS AND INFANTS FED NUCLEOTIDE SUPPLEMENTED FORMULA.

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**Background:** Large amounts of arachidonic acid (AA) and decosahexanoic acid (DHA) are deposited into the developing brain and retina during prenatal and early postnatal growth and thus these fatty acids are especially important for preterm infants (PI).
**Subjects and Methods:** We have compared the fatty acid profiles of red blood cell total lipids in 40 PI fed either human milk (HM) protein supplemented HM (N=14), nucleotide supplemented formula (N=13) or nucleotide unsupplemented formula (N=13) for 8 weeks from the start of oral feeding.
**Results:** At the end of the study period PI fed unsupplemented formula had significantly lower concentrations of AA and DHA than the HM fed PI, (13.5±2.2 vs. 14.9±3.0 g/100g lipids, and 3.8±2.3 vs 6.3±2.3 respectively). Total >C18ω3 LC-PUFA concentrations were also significantly lower in the PI fed unsupplemented formula. However, when PI fed nucleotide supplemented formula were compared with the HM fed PI no significant differences were found.
**Conclusion:** These results suggest a beneficial effect of nucleotide supplemented formula on the red blood cell LC-PUFA profile in PI. Supported by Wyeth-Ayerst.

## † 142

**INHALED NO (iNO): Dose-response curves in mild and severe RDS.**

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**Background:** We previously reported improved oxygenation in severe respiratory distress syndrome (RDS) with iNO. We further examined the efficacy of varying doses of iNO in improving oxygenation in infants with mild and severe RDS.
**Subjects:** 12 preterm infants mean G.A. 29.2 wks (range 25-33) ventilated for severe RDS, $FiO_2 \geq 0.6$ despite surfactant therapy, and 7 ventilated preterm infants with mild/resolving RDS, $FiO_2 \leq 0.45$, mean G.A. 29.1 wks (range 26-33).
**Interventions:** iNO at doses of 1, 5, 10, 20 and 40 ppm was administered at random with the inspired gas. Each dose was administered for 15 minutes with a 10 minute washout period while continuously monitoring oxygen saturation, transcutaneous $O_2/CO_2$ tensions ($tcpO_2/CO_2$), and systemic blood pressure (BP).
**Measurements:** Arterial blood gases were performed before and at the end of each dose. Methaemoglobin (MetHB) and $NO_2$ levels were also monitored.
**Results:** iNO improved oxygenation in mild and severe RDS at all doses. The percentage changes from baseline values (mean, range) in $paO_2$ at 1, 5, 10, 20 and 40 ppm were +39 (17-69), +36 (25-52), +30 (17-42), +26 (13-37) and +31 (9-61) respectively, in mild RDS and +52 (38-65), +69 (25-173), +62 (10-184), +50 (15-77) and +69 (23-160) in severe RDS. The corresponding percentage changes in $tcpO_2$ values were 60% and 45% of the actual blood gas values in mild RDS and severe RDS respectively. There were small reductions in the $paCO_2/tcpCO_2$ while systemic BP was unchanged. MetHB concentrations were 0.7% (0-1.9) [mean, range] in severe RDS and 0.6% (0-1.4) in mild RDS and $NO_2$ levels <1ppm.
**Conclusion:** iNO at doses as low as 1 ppm is effective in improving oxygenation in mild and severe RDS. All doses produced similar improvements in oxygenation with no adverse systemic effects. (Supported by the Royal Society).

## * 143

**Blood pressure and low birthweight - what *is* happening?**

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**Aims:** To investigate the relationship between birthweight and BP in childhood.
**Study design/subjects:** Population based cohort study of 300 VLBW children at 8-9 years in Scotland (96% follow-up rate) compared with 590 classroom controls matched for age and sex.
**Outcome measures:** Systolic and diastolic blood pressure, height and weight.
**Results:** The VLBW cohort were smaller and lighter than their controls whose growth closely followed the Child Growth Foundation's 1993 norms. Adjusting for current weight, the VLBW cohort had higher mean SBP and DBP than their controls. The relative increase in SBP was higher in VLBW girls (5mm) than in the VLBW boys (2.7mm). The DBP was significantly increased only in the VLBW girls (3.5mm). In the VLBW cohort, those children who were also SGA had significantly higher SBP than AGA VLBW children (2.9mm); this did not change after adjusting for maternal smoking. No association between SGA and BP was found in controls.
**Conclusion:** These findings support the hypothesis that BP and birthweight have an inverse relationship. The rise in BP with age has been shown to accelerate during periods of rapid growth; the observation of a greater increase in BP among the VLBW girls, at this age, may relate to their earlier prepubertal growth spurt. The contribution of VLBW to adult hypertension is, however, small. Nevertheless our findings should be further explored in a population stratified by birthweight.

## † 144

**Changes in Inflammatory Cells and Inflammatory Mediators in Bronchoalveolar Lavage Fluid after Surfactants.**

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**Background:** Tumour Necrosis Factor-α (TNF-α) and interleukin-8 (IL-8) are produced by alveolar macrophages in response to many insults and a high level of IL-8 at 24 hours may predict the development of chronic lung disease.[1] The aim of this study was to explore the inflammatory response to two different surfactants.
**Setting:** A tertiary neonatal intensive care unit, Edinburgh, Scotland.
**Subjects:** 23 ventilated newborn infants on the first day of life.
**Intervention:** Infants with respiratory distress syndrome and an a/A ratio < 0.22 were randomised to receive Curosurf (n=12, median gestational age 29 weeks, birth weight 1395g), or Exosurf (n=11, median gestational age 29 weeks, birth weight 1543g).
**Results:** Data are medians before and 24 hours after surfactant treatment.

| (pre vs post) | All Infants | Exosurf | Curosurf |
|---|---|---|---|
| IL-8 ng/ml | 4.4 vs 20.7 (p = 0.078) | 4.2 vs 23.7 (p = 0.04) | 6.2 vs 15.6 (p = 0.58) |
| TNF pg/ml | 0 vs 0 (p = 0.29) | 0 vs 0 (p = 1.0) | 0 vs 0 (p = 0.28) |
| % Neutrophils | 2 vs 77 (p = 0.001) | 22 vs 75 (p = 0.06) | 1 vs 77.5 (p = 0.01) |
| % Macrophages | 0 vs 5 (p = 0.13) | 6 vs 5 (p = 0.76) | 0 vs 8 (p = 0.10) |

Statistics performed with a Wilcoxon Signed Ranks Test
**Conclusions:** This preliminary data suggests there is a larger early inflammatory response of the inflammatory chemokine IL-8 with artificial surfactant.

1. McColm JR and McIntosh N. IL-8 as a predictor of chronic lung disease in premature infants. Pediatric Research 1994 34: 28A.

## † 145

**SHOULD PAEDIATRICIANS ATTEND FEWER DELIVERIES?**

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**Aims:** To establish risk factors associated with intubation, the time doctors spent at deliveries, and new safe guidelines for summoning doctors.
**Design & Subjects:** 3 month prospective study of 1012 consecutive births.
**Interventions:** None
**Measurements:** Doctors recorded reasons for attending a delivery, the resuscitation needed, and the time spent responding to a call.
**Results:** Doctors were called to 297 (29%) deliveries before birth. Median time to arrival was 1 minute. They spent 9.67 hrs/week attending 25 births. 7/45 (38%) babies delivered by emergency section under general anaesthetic (GA) were intubated, as were 5/23 (22%) born by GA elective section. 6/96 (6%) babies born vaginally through meconium stained liquor were intubated and added to the GA sections represented 28 (91%) of intubations but only 164 (55%) of attendances. 1/53 (2%) babies delivered by section under regional anaesthesia was intubated. The difference in intubation rates (30%, CI 19-42%) for section babies delivered with/without GA was highly significant. These non-GA sections, forceps, ventouse and others accounted for 133 babies, of whom only 3 (2%) were intubated.
**Conclusions:** Doctors could have attended 45% fewer deliveries and 'missed' only 3 (9%) intubations.

## * 146

**EFFECTS OF SERUM OR CRISTALLINE SOLUTION ON CIRCULATION IN PRETERM INFANTS**

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**Aim** of the intervention was to study whether serum is more effective than cristalline solution to prevent early hypotension in preterm neonates during the first hours of birth.
**Subjects:** Thirty neonates were given either 20 ml/kg of serum (Biseko®) or cristalloid solution over a period of 4 hours beginning within one hour of birth; 14 (birth weight 1185±194g; gestational age wk 28.2±1.4) with RDS (10 serum vs. 4 cristalline) and 16 (1450±389g; 31.5±2.5 wk) healthy neonates (8 serum vs. 8 cristalline) were studied. No catecholamines were given during this time.
**Interventions:** Blood pressure (BP), left ventricular output (LVO), mean cerebral blood flow velocity (mV) in the A. cerebri ant. (ACA) and A. carotis int. (ACI) were measured by pulsed-Doppler ultrasound before and after the infusion.

| Results: | RDS | serum | | controls | Healthy | serum | | controls |
|---|---|---|---|---|---|---|---|---|
| | before | after | before | after | before | after | before | after |
| ACI (m/sec) | 0.16±0.04 | 0.14±0.03 | 0.19±0.05 | *0.14±0.03 | 0.16±0.04 | 0.15±0.02 | 0.15±0.05 | 0.13±0.02 |
| ACA (m/sec) | 0.12±0.03 | 0.11±0.02 | 0.16±0.05 | *0.10±0.06 | 0.13±0.03 | 0.13±0.02 | 0.15±0.02 | *0.11±0.01 |
| LVO (ml/kg/min) | 279±65 | 288±79** | 256±55 | *196±56 | 323±53 | 282±49 | 270±60 | 262±51 |
| mean BP (mmHg) | 30±4* | 34±6** | 27±11 | 23±4 | 35±6 | *40±6 | 35±10 | 38±8 |

(*p<0.05 compared to the same group, *t*-test;**p<0.05 compared to the control group,Wilcoxon rank-test)
**Conclusion:** Our results suggest that serum is more efficacious than cristalloid infusion in improving the BP, systemic blood flow and cerebral blood flow velocity in preterm infants with RDS during the first hours of birth.

## † 147

**EFFECTS OF LATE CORD-CLAMPING ON LEFT and RIGHT SYSTOLIC TIME INTERVALS IN TERM NEONATES**

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**Aim:** Late cord-clamping may result in marked hypervolemia of the neonate. Purpose of the present investigation was to study effects of Leboyer childbirth on postnatal changes in right and left ventricular systolic time intervals by means of pulsed-Doppler echocardiography.
**Subjects:** Left and right ventricular pre-ejection periods (LPEP, RPEP), right time peak velocity (RTPV), left and right ventricular ejection times (LVET, RVET), and ratio of LPEP/LVET, RPEP/RVET and RTPV/RVET(c) corrected for heart rate were studied in 15 healthy fullterm neonates with early (<10 s) cord clamping and in 15 healthy fullterm neonates delivered according to Leboyer (cord clamping after 3 min) on day 1 (2-4 h after birth) and day 5.

| Results: (t-test) | Early cord clamping | | Leboyer childbirth | |
|---|---|---|---|---|
| Age | 2-4 hours | 5 days | 2-4 hours | 5 days |
| Hematocrit (l/l) | 0.53±0.07 | 0.50±0.07 | 0.61±0.06** | 0.57±0.02** |
| LPEP/LVET | 0.30±0.08 | 0.29±0.07 | 0.36±0.08** | 0.32±0.08 |
| RPEP/RVET | 0.33±0.08 | 0.29±0.10* | 0.41±0.11** | 0.30±0.04* |
| RTPV/RVET(c) | 0.41±0.09 | 0.54±0.09* | 0.31±0.08** | 0.52±0.09* |

*P<0.05 compared to values at 2 to 4 h of birth; **P<0.05 compared to early cord-clamped infants of same age.
**Conclusion:** Since elevated RPEP/RVET and decreased RPVT/RVET(c)-ratio indicate pulmonary hypertension, our findings suggest that transient pulmonary hypertension is prolonged in infants after Leboyer birth. Increased LPEP/ LVET ratio in the Leboyer group after birth suggest increase in afterload on the left ventricle due to increased hematocrit. Pulmonary vascular resistance and afterload on the left ventricle appear to become normal within a few days of birth.

## † 148

**Infant Feeding Practice and Hemoglobine Level in Children Under 2 Years Old**

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Investigation of infant feeding practice in Russia was one of the main objectives of the Nutritional Survey of Children under Two, which was organized by CARE-USA with the participation of Russian Inst.of Nutrition. The Survey was done in 3 large citis:Moscow, St.Petersburg, Ekaterinburg and surrounding regions. The information on infant feeding, mother's knowledge in nutrition was collected using questionnaires and data on infant morbidity and hemoglobine level were received from out-patient departments. Multistage random sampling method was used for sample selection. Statistical analysis was done with SPSS. The total number of sampled children under two was 4387. The main features of infant feeding practice are the following: the delay of the first breast feeding - 41-47% of infants were put to the breast for the first time more than 1 day after birth; 45-66% of mothers feed their infants according ti the strict schedule even during the first 3 months of life; early introduction of supplementary food and infant formulas (2,2-2,7 months); widespread usage of cow's milk, especially in Ural region, for the feeding of young infants.Thus about 50% of sampled infants there began to receive cow's milk before 4 months of age. The incidence of Hb level < 100g/l among this group of infants is 23%, among those who start cow's milk feeding after 6 months -11%. Such pattern of infant feeding decreases the prevalence of breast feeding and increases the risk of iron defficient anemia.

## † 149

SILASTIC CENTRAL VENOUS CATHETHERS (SCVC) FOR PARENTERAL INFUSION AND BLOOD SAMPLING IN NEWBORN INFANTS

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**Background:** Reducing neonatal pain and stress has become an important issue in recent years. In a one-year prospective study we have evaluated the feasibility of using silastic central venous catheters (SCVC) for both parenteral fluid, drug and nutrient supply as well as blood sampling in a NICU population.

**Subjects and intervention:** In 156 high risk neonates with mean bw 2260g (440 - 5800g), - 28 with bw < 1000g - ,SCVCs were inserted via a small cut-down without ligation and locating the catheter tip at the superior/inferior vena cava. Non-radiopaque SCVCs with outside-diameter 0.635 or 0.940 mm (Dow Corning Corp, Midland,MI) were used.

**Results:** In total 245 SCVCs were inserted at median postnatal age 4 (range 0-281) days. - Number of SCVCs per infant: - 1 in 105, 2 in 30, 3 or more in 21 infants. - Site of insertion: - forearm in 212 (87%), leg in 22 (9%), neck or scalp in 11 (4%) infants. The duration of SCVC placement was median 7 (range 0-84) days being in total 1877 patient days. - Blood sampling via the SCVC only, thereby avoiding painful punctures, was carried through for 1661 (88%) patient days. - Parenteral nutrition was administered via 140 (57%) SCVCs. - During the study period 159 of 245 (65%) SCVCs were electively removed according to treatment plans or still in situ at return discharge to referral units. -Despite using the SCVCs both for infusion and multiple blood sampling the infection rate was only 3/245 (1.2%): - 2 infants with clinical septicaemia and one with local site infection.

**Conclusion:** Our results show that stressful and painful procedures in sick and very preterm infants can be avoided by multiple use of SCVCs for blood sampling, drug and parenteral infusions still with low risk of catheter-related complications.

## † 150

FREE RADICALS IN BRONCHIAL ASTHMA, IN RESPIRATORY INFECTION AND IN CYSTIC FIBROSIS

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***Background:*** *Production of reactive oxygen species by stimulated neutrophils contribute to the* induction of airway hyperresponsiveness, inflammation and destruction both in allergic and nonallergic patients.

**Patients:** Four groups: CF patients (n=30), children with respiratory infections (n=30) and asthma bronchiale (n=30), age-matched healthy controls (n=30).

**Measurements:** The antioxidant enzyme activities, the reduced and oxidized glutathion concentrations, lipid peroxidation were measured as sensitive indicators of oxidative stress. The superoxide generation was also detected in the whole blood challenged with zymosan and phorbol myristate acetate. Glutathion instability, the proportion of hemoglobin oxidation products were measured after in vitro oxidative stress caused by acetylphenylhydrazine (APH).

**Results:** The superoxide production of granulocytes were moderately elevated in CF patients (10.6±0.065 vs 8.24±0.76 nanomol/$10^6$ granulocytes/min), significant increase could be detected in patients with respiratory infections (13.69±0.92; $p<0.05$) and in asthmatic patients (14.60±3.99: $p<0.05$). During the symptom-free period of childhood bronchial asthma a decreased catalase activity (3.91±0.93 vs 6.04±1.53 BU/g protein; $p<0.01$) and glutathione instability were demonstrated.

**Conclusion:** The antioxidant protection of the haemoglobin molecule in asthmatic children is considerably decreased and a more potent antioxidant therapy seems to be indicated especially in CF with progressiv symptoms.

## † 151

GLUTAMATE EXITOTOXICITY IN PERINATAL ASPHYXIA.

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**Background:** Asphyxia causes excessive glutamate release, a major cause of postasphyxial neuronal damage. **Objective:** to determine if there is any correlation between the levels of excitatory aminoacids (EA), the staging of Hypoxic-Ischemic Encephalopathy (HIE) and neurodevelopmental outcome. **Study design:** Prospective inception cohort study in a tertiary neonatal service. **Patiens:** 64 full-term neonates with perinatal asphyxia. Neonates were eligible for the study if they had signs of postasphyxial encephalopathy during the first 24 h of life, and\or fetal distress, a 5-minute Apgar score< 5, need for resuscitation after birth. Sarnat's modified classification was used for the staging of HIE.

**Measurements:** Amino acids were analyzed in serum, CSF and urine by chromatography (HPLC) the first day of life besides a full clinical-laboratory monitoring (EEG,US) and neonatal neurological examination. Neonates were followed up neurodevelopmentally for >24 mo.

**Results:** The neonates were entered in 4 groups (table). Glutamate was identified in CSF only in 50% of neonates without any correlation between HIE staging and neurodevelopmental outcome. However it was observed a significant increase in CSF-glutamine levels in neonates with seizures (group C+D) compared with neonates without seizures (group A+B) ($p<0.05$) and a significant correlation between levels of glutamine and neurological outcome ($p<0.05$).

| HIE | n= | Glutamine CSF(μmol/l) | Neurological outcome: Normal | Minocam | Malocubric | Death |
|---|---|---|---|---|---|---|
| A.Mild | 34 | 778±230 | 34 | 0 | 0 | 0 |
| B.Moderate without seizures | 8 | 820±144 | 8 | 0 | 0 | 0 |
| C.Moderate with seizures | 12 | 940±600 | 7 | 1 | 2 | 2 |
| D.Severe | 10 | 1070±980 | 0 | 0 | 5 | 5 |

**Conclusions:** The high levels of CSF-glutamine probably reflected excessive glutamate release followed asphyxia and were assosiated with poor neurodevelopmental outcome. Drugs antagonists of glutamate NMDA-receptors which produce impressive neuroprotection in experimental models may be the future in the management of infants suffered severe perinatal asphyxia.

## † 152

MODIFICATIONS IN VENTILATION AND OXYGENATION PARAMETERS IN R.D.S. WITH SURFATANT THERAPY.

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**Background:** We study the parameters: oxygenation index (OI), ventilation index (VI), alveolar-arterial oxygen gradient (A-aDO2), mean airway pressure (MAP), paO2/FiO2 ratio and arterial/alveolar oxygen tension ratio (a/A pO2) in very low birth weight infants (VLBW) to establish the modifications after the surfactant therapy (Survanta).

**Subjects:** 21 VLBW infants (≤1500 gr) and/or ≤32 gestational age affected by Respiratory Distress Syndrome (RDS) -clinical and X-ray criteria-needing mechanical ventilation during the first 36 hours of life with FiO2 >0.6 and 21 VLBW-control group-with the same caracteristics (weight, gestational age, initial pH-paO2-standard biarbonate, maximum peak inspiratory pressure and PEEP, mortality, prophilactic steroids and initial moment of mechanical ventilation). The congenital malformations and genetic syndromes were excluded.

**Interventions:** Randomized clinical trial from 1992 to 1994. The parameters was assesed before the administration and 1, 6, 12 and 18 hours after. Mann Whitney was applied as non parametric test. Statistical meaning was considered (* p <0.05 and ** p <0.01).

**Results:**

| | 0 hours | | 1 hours | | 6 hours | | 12 hours | | 18 hours | |
|---|---|---|---|---|---|---|---|---|---|---|
| | Surfact | Control | Surfact. | Control | Surfact. | Control | Surfact. | Control | Surfact. | Control |
| O.I. | 25±6 | 18±3 | 21±8 * | 23±3 | 13±3 * | 22±4 | 11±3 ** | 24±4 | 9±2 ** | 23±5 |
| V.I. | 526±70 | 493±43 | 601±97 | 504±59 | 518±77 | 533±63 | 483±85 | 533±72 | 415±75 | 613±103 |
| A-aDO2 | 507±29 | 439±34 | 362±36 * | 465±25 | 352±46 | 460±29 | 333±46 * | 465±29 | 307±42 ** | 450±35 |
| MAP | 11.4±1 | 12.6±0.8 | 12.7±1 | 13.1±1 | 11.5±1.3 | 13.7±1 | 10.1±1 * | 14±1.4 | 9.3±1 ** | 15.6±2 |
| pO2/FiO2 | 84±12 | 108±18 | 134±15** | 77±9 | 144±20 * | 86±8.6 | 131±17 * | 83±10 | 146±20 ** | 87±12 |
| a/A pO2 | 0.12±0.0 | 0.16±0.0 | 0.2±0.0** | 0.11±0.0 | 0.23±0.0* | 0.12±0.0 | 0.23±0.0** | 0.12±0.0 | 0.23±0.0* | 0.13±0.0 |

**Conclusions:** There were favourable modifications in all parameters after surfactant administration except in VI.

## † 153

NEUTROPHIL BRONCHOALVEOLAR RECRUITMENT IN PRETERM INFANTS WITH BLOOD NEUTROPENIA

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**Aim:** To investigate the recruitment of neutrophils into inflammed lung tissue in preterm infants with blood neutropenia.

**Subjects:** 5 preterm infants with proven pulmonary infection and normal or increased absolute neutrophil count (ANC, mean(range): 4,586/$mm^3$ (1,512-10,280)); 3 preterm infants with proven pulmonary infection and decreased ANC (mean (range) 473/$mm^3$ (373-655)).

**Measurements:** Interleukin-8 (IL-8), a potent neutrophil chemotactic factor, and neutrophils were determined in bronchoalveolar lavage (BAL) fluid, and their concentrations correlated (Spearman's coefficient).

**Results:** In all the neonates BAL fluid IL-8 levels were elevated (mean (SD): 5,233ng/ml (1,001)). However, neutrophil BAL fluid concentrations were high (mean(range): 1.5 $10^6$(0.9-1.8 $10^6$)) in infants with normal or increased ANC (mean(range):4,586/$mm^3$(1,512-10,280)) but not (mean(range): 0.01 $10^6$(0.0-0.03 $10^6$)) in those with decreased ANC values (mean(range): 473$mm^3$(373-655)). We found a strong positive correlation (rs=0.78,p<0.001) between IL-8 and neutrophils in BAL fluid of infants who presented with normal or increased ANC but not in those with low ANC. The neutropenic infants died. A postmortem examination of the lungs allowed to confirm the paucity of the inflammatory cellular component into the airways.

**Conclusions:** The lack of a significant positive correlation between IL-8 and neutrophil in BAL fluid of neutropenic infants suggests that adequate ANC is essential for the recruitment of neutrophils to the lung. Thus, treatments to restore the number of circulating neutrophils are required to defend lung tissue from infectious agents. *Italian CNR Targ Proj FATMA n.93.00602*

## † 154

EFFECT OF INDOMETHACIN AND IBUPROFEN ON CEREBRAL HAEMODYNAMICS AND OXYGENATION DURING TREATMENT FOR PATENT DUCTUS ARTERIOSUS (sPDA) IN PRETERM INFANTS.

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**Aim:** Indomethacin (IND) reduces cerebral perfusion and oxygenation in newborn infants, but other prostaglandin synthesis inhibitors may not have this effect. This study compared the effects of IND to ibuprofen (IBU).

***Subjects and Method:*** *IBU* (a) 5 $mg.kg^{-1}$ and (b) 10 $mg.kg^{-1}$, and (c) *IND* at 0.1 $mg.kg^{-1}$ were infused over 15 min in 10 infants (gestational age 23-29, median 26 wks) as treatment for sPDA, and changes in cerebral blood volume ($\Delta CBV$) and oxidised cytochrome $aa_3$ concentration ($\Delta[CytO_2]$) observed by near infrared spectroscopy. Data given as mean (SD) and compared by Student-Newman-Keuls test.

| Results: | (a) IBU 5 (n=7) | (b) IBU 10 (n=5) | (c) IND (n=6) |
|---|---|---|---|
| $\Delta CBV$ (ml.100$g^{-1}$) | 0.11 (0.18) | 0.03 (0.14) | -0.54 (0.19) |
| $\Delta CytO_2$ ($\mu mol.L^{-1}$) | 0.06 (0.14) | -0.02 (0.16) | -0.41 (0.15) |

For both variables IND differed from IBU 5 and IBU 10, which were not different ($p<0.05$). The response of CBV to changes in $PaCO_2$ was reduced after IND (n=4) but not after IBU (n=6) (paired t-test: $p<0.01$).

**Conclusion:** IBU should be investigated as an alternative therapy to IND.

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## * 155

MICROSATELLITE ANALYSIS IN THE CFTR GENE

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**Background:** Microsatellites IVS8CA, IVS17bTA and IVS17bCA of the CFTR gene (cystic fibrosis transmembrane conductance regulator) were analyzed to perform familial diagnosis and to evaluate the association between the presence of a certain mutation and the haplotype.
**Subjects:** 81 CF families and 182 CF single patients.
**Interventions:** Allele size determination by PCR amplification with an end-labelled primer and resolution of bands in denaturing polyacrylamide gels.
**Results and conclusions:** With the analysis of the three markers we got informativity in all the families under study. We found 9, 22 and 5 different alleles for markers IVS8CA, IVS17bTA and IVS17bCA respectively, and only 41 of the 990 possible different haplotypes were found in normal chromosomes. The most frequent haplotypes were 16-30-13, 16-31-13 and 16-32-13 (42,2 % of all normal chromosomes). With the analysis of both families and single patients we conclude the following: A. 15 different haplotypes have been found in ΔF508 chromosomes. Among these, haplotypes 23-31-13 and 17-32-13 are present in up to 70,7 % of the 150 ΔF508 chromosomes analyzed. B. Mutation G551D in unequivocally associated with haplotype 16-7-17 (46 G551D chromosomes). The mutation is identical by descent in these CF patients and its age has been estimated in, approximately, 155 generations. C. Mutation R117H was found in association with haplotype 16-30-13 (28 R117H chromosomes) except in a CBAVD patient (haplotype 16-29-13). The age of the mutation has been estimated in, at least, 216 generations.

## † 156

THE INFLUENCE OF ENERGY EXPENDITURE ON BODY FAT IN CHILDHOOD

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**Background.** Growth in childhood is a complex interplay between genetic and environmental influences, including nutrition and lifestyle. This research examined the relationship between energy expenditure (EE), energy intake (EI) and growth.
**Subjects.** 35 volunteer children age 6 - 9 years from a previous random population study of nutrition and growth at age 2 - 5 years.
**Measurements.** EE was estimated by the minute-by-minute heart-rate method over 3 - 4 days and EI by 7 day weighed record. Height, weight, limb circumference and triceps and subscapular skinfold measurements were taken. EE is expressed per kg body weight (EE/kg).
**Results.** A highly significant correlation was found between EE and EI ($r = 0.81^{***}$). Significantly inverse correlations were found for EE/kg with BMI ($r = -0.49^{**}$), arm circumference ($r = -0.43^{*}$) and with both triceps and subscapular skinfold values ($r = -0.52^{**}$ and $-0.57^{***}$). A significant inverse correlation was also found between EE/kg and change (mm) in triceps and subscapular skin fold values over the previous four years ($r = -0.54^{**}$and $-0.48^{**}$).
**Conclusion.** These results suggest that active children with a high energy expenditure and high energy intake tend to be slim. Conversely, children with a low energy expenditure, and correspondingly low energy intake, may have a tendency to accumulate body fat.
($^{*}P<0.05$ $^{**}P<0.01$ $^{***}P<0.001$)

## † 157

EFFECTS OF UNDERNUTRITION AND PROLONGED OXYGEN EXPOSURE ON LUNG GROWTH AND MATURATION

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Hyperoxia anf food deprivation, singly, retard growth during early period of life.We study the effect of hyperoxia and undernutrition singly and in combination on lung growth and maturation of newborn rats .
The study designe consisted of Wistar newborn rats from birth to 14 days.At birth half of litters (11 or 18 pups/dam) with their mothers were placed in >95%02 or room air. In some pups the lungs were weighted and homogenizated for antioxidant enzymes (AOE), DNA and proteins determinations. Separate group of rat lungs were used for determination of static espiratory Compliance (P-V loops). Anova test was done followed by Fisher test .P<0,05 was considerated
**Results:** Body grwoth, and lung growth were significantly reduced (p<0,01) by undernutrition. Hyperoxia inhibited those paramethers and lung DNA content in comparison with air groups. Nourished and undernourished groups showed values of superoxide dismutase, catalase and glutathion peroxidase significantly higher (p<0,05) in hyperoxia than in air groups. Normally nourished and undernourished rats in hyperoxia exposure showed lung compliance significatly lower (p<0,05) in comparison with air groups
**Conclusion:** This study suggest that hyperoxia has a serious detrimental effects on the lung growth and maturation and undernutrition may compromise repair of ongoing 02 induced lung damage

## † 158

POSTNATAL DEXAMETHASONE TREATMENT IN NEWBORN RATS DURING PROLONGED HIGH 02 EXPOSURE

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We questioned whether postnatal DEX treatment might have a salutary effect on the ability of the newborn rat to tolerate prolongate exposure to hyperoxia.
Four groups of newborn Wistar rats at 14 days of life were studied. At birth two litters were given intraperitoneal injections (i p) of DEX (0,4 mg/kg/d at 0, 1, 3, 5 and 9 day of life) and one of two litters were placed in >95% 02 or keep in room air. Two litters were given i.p of saline solution and one of two litters were placed in >95% 02 or keep in room air. In some pups the lungs were weighted and homogenizated for antioxidant enzymes (AOE), DNA and proteins determinations. Separate groups of rat lungs were the either used for determination of total phospholipid assay in bronchoalveolar lavage (BAL) and morphological study. Anova test was done followed by Fisher test .P<0,05 was considerated.
**Results:** Hiperoxia DEX treated pups demostrated a greater percentaje of survival than the hyperoxia non-DEX treated pups at 14 day of life .Groups of pups showed in Hyperoxia higher lung protein and DNA content significantly lower (p<0,05) in comparison with air control. Values of Superoxide dismutase, Catalase and Glutathion peroxidase in DEX-hyperoxia group were significantly higher (p<0,05) than DEX-Air. Total phospholipid was significantly changes with DEX treatment.correlative with increase of lamellar body in Neumocytes II
**Conclusion:** Hyperoxia for 14 days causes inflamatory changes and DEX treatment ameliorates this lung damage and increase of AEO response It may help to explain the protective effect of postnatal DEX on newborn 02 toxicity

## † 159

EFFECTS OF DEXAMETHASONE (DEX) THERAPY ON CEREBRAL HAEMODYNAMICS STUDIED BY COLOUR DOPPLER FLOW IMAGING (CDFI) AND NEAR-INFRARED SPECTROPHOTOMETRY (NIRS).

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**Background:** DEX is used widely in neonates to prevent chronic lung disease. **Aim:**To assess DEX effects on cerebral haemodynamics in preterm babies with lung disease and mechanical ventilation. **Subjects:** Group 1: 10 babies (BW 1237±381g, GA 28.7±2.8w, age 1st dose 12.4±6.2d). Group 2: 10 babies (BW 963.1±206g, GA 27.4±1.9w, age 1st dose 15.2±11.6d). **Interventions:** Administration of DEX (0.25mg/Kg/12h) 3 consecutive days. **Measurements:** Group 1: Blood flow velocity (BFV) [ peak systolic (PSFV), diastolic flow (EDFV), mean flow (TMFV)] and resistance index (RI) were determined in internal carotid (ICA), anterior cerebral (ACA) and ophthalmic (OA) arteries by CDFI before and 10,30,60,120 and 240 min after DEX. Group 2: Changes in cerebral blood volume (CBV) were estimated by NIRS before and 10,30,60,120,180, and 240 min after DEX. Both studies were done in the 1st, 3rd and 5th doses. **Results:** Group 1: Across the entire study period BFV increased significantly (p<.05 for ICA-PSFV, OA-PSFV and OA-TMFV; p<.01 for the other BFV measured). RI decreased significantly across the entire study period (p<.01 for ICA and ACA; p<.05 for OA). Group 2: CBV increased significantly across the 240 min-study period of doses 3rd and 5th ( p<.001).
**Conclusions:** DEX increments cerebral and ocular BFV as well as CBV. We speculate that these findings may be relevant to the development of brain injury, particularly when DEX is administered early in the neonatal period. (Supported by FIS 94/0198).

## † 160

REGIONAL VARIATIONS IN $^{1}$H-METABOLITE CONCENTRATIONS IN THE BRAINS OF NEWBORN INFANTS

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**Background:** We aimed to determine $^{1}$H-metabolite concentrations in the brains of normal infants, and to test the hypothesis that differences in concentrations would be found between the thalamus and the occipito-parietal (OP) region.
**Subjects:** Nineteen healthy newborn infants. Ten had thalamic studies at gestational plus postnatal ages of 32-42 (mean 37) weeks, and 9 had OP studies at 34-40 (36) weeks.
**Measurements:** $^{1}$H-NMR spectra (PRESS) were collected at 2.4 T from $(2cm)^3$ voxels at 135, 270 and 540 ms echo times. Water was used as an internal concentration reference.
**Results:** Metabolite concentrations are expressed as mean (SD) $mmol.kg^{-1}$ wet brain; the two regions were compared by unpaired *t*-test with the Bonferroni correction.

| | Thalamus (n=10) | OP (n=9) | p |
|---|---|---|---|
| Choline | 5.44 (1.89) | 1.96 (0.70) | <0.002 |
| Creatine | 12.02 (2.99) | 6.68 (2.13) | <0.002 |
| N-acetylaspartate | 10.07 (1.82) | 3.56 (1.27) | <0.002 |
| Lactate | 2.98 (0.97) | 3.94 (1.77) | NS |

**Conclusions:** Significantly higher concentrations of choline, total creatine and N-acetylaspartate were found in the thalamus, which may be due to its relative maturity, active myelination at the gestation studied, and its predominance of grey matter. The concentration of lactate in both regions was higher than in adult brain, implying a greater dependence on glycolysis to satisfy cerebral energy requirements in the neonatal period.

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**INTERCELLULAR ADHESION MOLECULE - 1 IN NEWBORN INFANTS**

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**Aim:** To evaluate the role of intercellular adhesion molecule-1(ICAM-1), a very early and sensitive marker of immune activation and response, in the development of the neonatal immune system.

**Subjects:** 39 (21F/18M) term, healthy newborn infants, mean birthweight (±SD) 3170 ± 452 g.

**Interventions:** Peripheral venous blood (1 ml) was collected in the 1st (1NS), 5th (5NS), and 30th (30NS) day of life.

**Measurements:** Serum ICAM-1concentrations were measured by EIA, (T Cell Diagnostics).

**Results:** Neonatal ICAM-1 values showed a very significant increase ($p<0.000$; paired t-test) from 1NS (125.0 ± 52.6 ng/ml) to 5NS (251.3 ± 126.0 ng/ml) and then to 30NS (384.5 ± 107.4 ng/ml), being significantly lower in 1NS ($p<0.002$; t-test), whereas significantly higher in 5NS ($p<0.02$; t-test), than those in healthy adults (305 ± 195 ng/ml). ICAM-1 values in 1NS were depended on the mode of delivery, (higher in neonates born vaginally), and sex, (significantly lower in male neonates). No significant correlation was found in ICAM-1 values between 1NS and 5NS.

**Conclusions:** Our findings on ICAM-1 release suggest a progressively increased activation of the neonatal immune system, which seems to be promoted by active labour and fully developed in the early neonatal life, probably, in response to environmental influences.

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FIBROPLAST GROWTH FACTOR RECEPTOR POINT MUTATION LEADS TO TANATOPHORIC DWARFISM PHENOTYPE.

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**HYPOTHESIS:** A sporadic occurrence of tanatophoric dysplasia (TD) strongly suggests a new mutation mechanism of the disease. **SUBJECT:** Term male newborn born to normal parents manifested a typical clinical and radiological appearance of TD. When one month old, the boy died due to severe respiratory distress. **METHODS:** A molecular screening of FGFR-3 gene was done by combination of a single strand conformation polymorphism (SSCP) and direct sequencing of amplified exonic fragments. **RESULTS:** No FGFR-3 mutation was found in the parents. In the proband, a transversion of the first nucleotide of the codon 807 (T→A) abolished this stop codon and led to transcription of the next 423 bases in the 3'untranslated gene region. The translation of these 141 additional aminoacids on the C-terminal end of the protein might have imposed a second hydrophobic domain to this receptor. Functionally, the proband, heterozygous for the mutation, was affected in a dominant manner because the protein kinase receptor which transduces the mitogenic signal of FGF to the nucleus was activated by oligomerisation of receptor molecules. **CONSLUSIONS:** Additional transmembrane domain impairs zipping of receptors, which normally occurs after the presentation of heparan sulfate linked agonist molecules, leading to abnormal proliferation of chondrocytes in the growth plate.

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**TUMOUR NECROSIS FACTOR (TNF) AND sTNF RECEPTORS IN NEONATAL INFECTION**

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**Background:** TNF production occurs in the early phases of the inflammatory response and endotoxic shock, followed by the appearance of TNF receptors in the circulation. We thus studied TNF and sTNFR utility as early markers of neonatal infection.

**Objectives:** 1) Determination of plasma TNF and sTNFR in cord blood of normal newborns in order to establish reference values; 2) Analysis of plasma TNF and sTNFR in peripheral blood from neonates with risk factors of infection during the first 24 h of life; and 3) Compare plasma TNF and sTNFR values in neonates that developed infection with those who do not.

**Results:** Mean TNF value in cord blood from 111 consecutive neonates was 12 ±7.8 pg/mL. From 84 neonates with risk factors 42 remained normal with a mean TNF value in peripheral blood of 11.3 ± 9.7 pg/mL ; 28 developed clinical and/or laboratory signs of infection with negative blood culture and TNF values of 58.7 ± 70 pg/mL , 14 had positive blood culture with TNF values of 583 ± 981 pg/mL , and 5 had positive blood culture and septic shock with TNF values of 1,392 ± 1,330 pg/mL. sTNFR (p55 and p75) were both elevated during neonatal infection (31.9 ± 0.88 and 98.75 ± 90 ng/mL *versus* 3.2 ± 1.4 and 6.3 ± 2.8 ng/mL) and overall were positively correlated with TNF values (r=0.57 and 0.88, repectively; $p<0.001$).

**Conclusions:** TNF and sTNFR constitute useful markers of early neonatal sepsis. There is a positive correlation between the severity of the infection and TNF values. In septic shock of very early onset TNF was extremely high while CRP was < 10 mg/L.

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AN ACUTE CHANGE FROM A FETAL TO A POSTNATAL PO2 INCREASES AMILORIDE SENSITIVE ION TRANSPORT BY FETAL DISTAL LUNG EPITHELIUM (FDLE).

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The perinatal period is characterized by the conversion of the lung from a fluid secreting ($Cl^-$) to fluid absorbing ($Na^+$) organ. Data suggest that the low fluid content of postnatal alveoli is maintained through $Na^+$ transport. We investigated if a sudden change in ambient oxygen concentration, as occurs at birth, influenced $Na^+$ transport by FDLE. FDLE from rats of 20 d gestation were initially cultured at a fetal $PO_2$ of 20 mmHg. Some FDLE monolayers were then transferred to 150 or 300 mmHg $PO_2$ to emulate normal room air and hyperoxic levels, respectively. The $Na^+$ transport was measured 4-48 h later by mounting the FDLE monolayers in Ussing chambers. After a 4-h exposure to a $PO_2$ of 150 and 300 mmHg the monolayer resistance decreased markedly; it recovered by 8 h at 150 mmHg $O_2$ but remained low beyond 8 h at 300 mmHg $O_2$.The resistance had fully recovered within 18 h in both non-fetal $O_2$ concentrations. Treatment for 18 h with 150 mmHg $PO_2$ increased the amiloride sensitivity of the FDLE from 30.6±8.8 % to 63.8±2.9 % (mean±sem) of the maximum equivalent short circuit current. After 48 h of 20, 150, and 300 mmHg $PO_2$ the amount of amiloride sensitive $Na^+$ transport was respectively 0.46±0.1, 3.5±0.3, and 3.5±0.4 $\mu A/cm^2$. These studies demonstrated that an increase in $PO_2$ initially perturbs tight junctions followed by activation of $Na^+$ transport. An acute rise in ambient $O_2$ at birth may be an important trigger for the early clearance of lung fluid and also for the advent of $Na^+$ absorptive pathways in the newborn lung.

## † 165

BLOOD VOLUME EXPANSION TEST IN HYPOVOLEMIC NEONATES

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Background : Clinical evaluation is not precise enough to estimate the necessity of volume expansion in neonates. We designed a study to evaluate our echographic indications of volume expansion and the effects of colloid expansion on hemodynamic parameters.

Subjects : 12 neonates < 7 days presenting without cardiac dysfunction and with a low left ventricular output (LVO) (< 260 $ml.kg^{-1}.mn^{-1}$ in 5 NN with PDA, < 200 $ml.kg^{-1}.mn^{-1}$ in 7 without PDA).

Interventions : Newborns received 10% albumin (20 $ml.kg^{-1}$) for a 3 hour period. Measurements were made before infusion, 1 hour after, and at volumes of 5, 12.5 and 20 $ml.kg^{-1}$. The evolution of the diameter of inferior vena cava (IVC) during the course of respiratory cycle was used as an indication of right ventricle preload.

Results : LVO increased after 20 $ml.kg^{-1}$ (from 180 ± 44 to 275 ± 94 $ml.kg^{-1}.mn^{-1}$, $p < 0.001$). Mean blood flow velocity in ascending aorta rose from 15 ± 4.5 to 22.4 ± 6.8 $cm.sec^{-1}$, ($p < 0,01$) and mean arterial pressure increased from 41 ± 8 to 46 ± 5 mmHg, ($p < 0,05$). No significant difference was found for these values between infusions of 12.5 and 20 $ml.kg^{-1}$ .Cutaneous refilling time decreased from 7"2 ± 1"9 before infusion to 3"8± 0"8 after infusion ($p < 0,001$). IVC compressibility and systemic arterial resistance decreased after filling ($p < 0,05$). Cardiac dysfunction appeared in 2 cases during filling.

Conclusions : In hypovolemic neonates, we recommend an initial filling test of 10 to 15 $ml.kg^{-1}$. Half of this volume can be given rapidly (10 to 15 mn). The infusion of volume greater than 15 $ml.kg^{-1}$ necessitates an evaluation by Doppler-echocardiography.

## † 166

**SURFACTANT ANALYSES IN PHARYNGEAL ASPIRATES FROM HEALTHY TERM NEONATES: I. BIOPHYSICAL PROPERTIES**

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**Background:** In neonates with respiratory distress, it is not always clear whether symptoms are due to a deficiency or inhibition of surfactant or whether they have other causes. To better address this issue, knowledge of normal surfactant function at birth is required. This should ideally be determined in pharyngeal aspirates obtained at birth, since this material can be easily and safely obtained during all deliveries.

**Subjects and Methods:** Surfactant function was determined in pharyngeal aspirates obtained in 33 term healthy newborns during routine suctioning immediately after birth (mean GA 39.8 (SD 1.0) wk; birthweight 3510 (SD 215) g. Surfactant was purified and its static and dynamic properties studied in the pulsating bubble surfactometer at 20 cycles/min. Minimal surface tension values were calculated 10 s after formation of the bubble ($\gamma_{eq}$) and after 1, 3, 9, 30 and 100 cycles ($\gamma_{min}$).

**Results:**

| | $\gamma_{eq}$ (mN/m) | $\gamma_{min}$ (mN/m) | | | | |
|---|---|---|---|---|---|---|
| N cycles | 0 | 1 | 3 | 9 | 30 | 100 |
| Median | 24.3 | 17.2 | 16.6 | 2.3 | 1.5 | 1.1 |
| IQR | 23.9-24.5 | 10.1-19.6 | 2.7-13.2 | 1.6-3.1 | 1.1-2.2 | 0.8-1.7 |
| Range | 23.7-24.9 | 5.6-22.7 | 1.8-21.6 | 0.8-19.7 | 0.4-11.1 | 0.4-4.7 |

**Conclusions:** $\gamma_{min}$ always fell to <5 mN/m within 5 min. of cycling. However, there were considerable differences in the speed with which these low surface tension was reached, which may reflect differences in surfactant spreading and/or refinement. Whether these differences are related to variations in the biochemical properties of the surfactant between different infants will be subject of a separate communication.

## ● 167

**EFFECTS OF ENDOTOXIN AND EXOTOXIN ON NEONATAL AND ADULT RED BLOOD CELL DEFORMATION AND HEMOLYSIS.**

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**Background:** Increased risk of neonates for bacterial infections suggests that bacterial toxins may also have different effects on neonatal and adult red blood cells.
**Patients:** 10 adults, 10 full-term and 10 preterm neonates
**Interventions:** 60 min incubation of red blood cells with 100μg/ml lipid A or 1HU/ml group A streptolysin O(SLO).
**Results:** Red blood cell (RBC) deformation (rheoscope) of adults, full-term and preterm infants were decreased after 15 (10%,8%,9%), 30 (10%,3%,5%) and 60 min (8%,2%,5%) lipid A incubation and after 60 min SLO incubation (21%, 15%, 17%). After 60 min lipid A incubation hemolysis was below 3.5% in neonates and adults. 60 min SLO incubation caused linearly increasing hemolysis for adult RBC reaching 100 %, whereas maximum hemolysis of neonatal RBC was below 60%.
**Conclusions:** Neonatal RBC are less affected by lipid A and SLO than adult RBC. Less lipid A induced impairment of neonatal RBC deformation may be a result of low content of PUFA in neonatal RBC. Since SLO primarily binds to cholesterol in RBC membrane, reduced hemolysis and less pronounced impairment of RBC deformation may be due to higher cholesterol content of neonatal RBC.

## † 168

EFFECT OF L-NITRO-ARGININE METHYL ESTER (L-NAME) ON CEREBRAL BLOOD FLOW AND VASCULAR REACTIVITY IN NEWBORN PIGLETS

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Introduction: This study examined the effect of nitric oxide synthase (NOS) inhibition on cerebral blood flow (CBF) and the response of CBF to changes in $PaCO_2$ ($CO_2R$) and mean arterial blood pressure (MAPR).
Subjects and Methods: CBF was measured by $^{133}$Xenon clearance 6 times at varying $PaCO_2$ levels (2.7-8.9) in 8 anaesthetised mechanically ventilated newborn piglets. After the third measurement, L-NAME was administered as a bolus (20 $mg.kg^{-1}$), then infused at 10 $mg.kg^{-1}.hr^{-1}$. L-arginine (1g) was given at the end of the study. Mean arterial blood pressure (MAP) was recorded through an umbilical artery catheter. CBF data were analysed by ANOVA and MAP data by paired t-test.
Results: MAP (mmHg) increased after L-NAME from 61.3 (SD±8.1) to 74.8 SD±9.3) ($p < 0.05$), and after L-arginine decreased to 55.2 (SD±6.1) ($p < 0.05$). CBF decreased by 14% (95% CI 1.9-27.4) following L-NAME. $CO_2R$ (%.$kPa^{-1}$) was 18.4 (95% CI 14.1-22.2) before and did not change after L-NAME. CBF and MAP were not related before or after L-NAME.
Conclusion: NOS inhibition induces small changes in CBF, but does not impede CBFR or MAPR.

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**NTRAORAL SUCROSE ADMINISTRATION REDUCES THE PAIN RESPONSE N PREMATURE INFANTS.**

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**Background**: a small volume of intraoral sucrose has been shown to reduce the crying time in healthy full-term babies. This effect is suggested to be due to endorphin release of endogenous opiates. **Aim**: to evaluate the role of sucrose in reducing the pain response in a group of healthy preterm newborns. **Subjects**:15 infants with median gestational age (range) of 33 wks (29-34) and postmenstrual age of 34 wks (32-34). **Interventions**: subjects were tested in a blind cross over manner on two separate occasions no more than two days apart. Either 1 ml of 25% sucrose solution or sterile water was syringed into the baby's mouth 2 minutes before routine heel lancing (BM stick or bilirubin) performed by the same experienced operator. Response to the painful stimulus was measured by duration of cry and by facial expression (pain score). The Wilcoxon Matched Pairs Signed Rank Test was used for statistical analysis. **Results**: there was a significant reduction in both the duration of the first cry (12 vs 23 sec; p=0.004) and the percentage of time spent crying in the five minutes after heel prick (6 vs 16.6%; p=0.018) in the sucrose treated group. There was also a significant reduction in the pain score at one and three minutes after heel prick in the sucrose group. **Conclusions**: intraoral sucrose has analgesic effects in healthy premature infants.

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**COSLEEPING AND SLEEP PROBLEMS IN YOUNG ITALIAN CHILDREN**

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**Background:** in our western, developed society cosleeping (CS) is not routine and it has been associated with sleep problems (SP). Many child health professionals commonly advice parents not to bring children into their bed. We studied the prevalence and the demographic correlates of CS in an Italian urban population, as well as the association of CS with SP.
**Subjects and measurements:** a questionnaire consisting of closed-ended, forced choice questions about sleeping behavior was completed by parents of 1414 children, aged 4 to 72 months, before a routine health visit. Children were subdivided into age groups (0 to 5 yrs). Based on the routine sleeping behavior, they were divided into 4 groups: a) 'no cosleepers' (NoCS); b) 'partial cosleepers' (sleeping in parental bed for less than half of the night) (PCS); c) 'cosleepers' (sleeping in parental bed for more than half of the night) (CS); d) 'supercosleepers' (sleeping in parental bed for the whole night) (SCS).
**Results:** the prevalence of NoCS was 79% in the first year of life, 49% from 2 to 4 yrs and 58% at 5yrs. The global prevalence of CS from 0 to 5 yrs was 41%, and it was strongly associated with the presence of a SP (frequent night wakings=fNW and/or bedtime struggles=BS) ($p < .0001$). Compared with the group of NoCS, children PCS and CS were more likely to have fNW ($p < .0001$), BS ($p < .007$), resistence going to bed ($p < .001$) and longer time to fall asleep ($p < .003$). On the contrary the SCS children (6% of the total sample, with a peak of 9% from 2 to 4yrs) did not differ from NoCS, except in the need of longer time to fall asleep ($p < .02$), and were more likely than the rest of the population to have parents with lower education, no sibling and less NW ($p < .05$).
**Conclusions:** cosleeping is a common practice in our population. It is usually a response to a SP of the child. A small group of parents seems to accept it for the whole night and this is associated with a reduction of NW.

## † 171

**PROGNOSTIC SIGNIFICANCE OF OPTO-KINETIC NYSTAGMUS (OKN) AND CEREBRAL ULTRASOUND (US) FOR THE DEVELOPMENT OF STRABISMUS AT ONE YEAR IN HIGH RISK INFANTS.**

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**Background:** the development of the naso-temporal component of the OKN takes place around 4 months (m) of age. Its disruption is related to the development of impaired binocular vision and to strabismus in infancy. Infants affected by neonatal CNS damage are also prone to the development of strabismus. We study the role of a complete OKN response at 6m of age, combined with neonatal neurological damage assessed by US, for the prognosis of strabismus at one year (yr) of age in high risk newborn.
**Subjects:** infants admitted to our NICU, from 1987 to 1992, with g.a. ≤ 34 wks and all the newborns who had neurological or ophthalmological diseases at discharge.
**Measurements**: 341 infants had 2 ophthalmogical assessment at a mean c.a. of 5.7±1.1m (4 to 8m) and 11.3±1.7m (9 to 18m). The OKN was classified as: normal, pathological, dubious.
**Results**: at the 1st visit 34 infants had strabismus. In 8 of them ocular motility was normal at the 2nd control. Their neonatal US and the OKN at the 1st visit differed from those of the 26 strabic infants whose ocular motility did not normalize by the 2nd control ($p < 0.01$). A normal OKN (n=5) was always associated with a subsequent normalization of ocular motility and a pathological OKN (n=13) was always associated with the subsequent persistence of strabismus. In the 16 dubious cases the US data increased the sensibility and the specificity of ocular assessment: the 3 infants whose ocular motility normalized at 12m had a normal US, while 10 of the 13 who did not normalized had an abnormal US.
**Conclusions**: OKN assessment combined with neonatal US is highly prognostic for the evolution of ocular motility at 1 yr in high risk infants. This can assist in the therapeutic management of a strabismus at 6m.

## † 172

**NEONATAL CNS DAMAGE AND VISUAL FUNCTION AT 4-7 YEARS IN PRETERM INFANTS.**

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**Background:** we studied the correlation between site, severity and kind of hypoxic-hyschemic/haemorrhagic CNS insult and later visual function development in preterm infants.
**Subjects and measurements:** 73 infants with GA ≤ 31 wks or BW ≤ 1500g discharged by the NICU of A.Meyer Children's Hospital of Florence, Italy, in the years 1987-90, were reassessed by experienced ophthalmologists at 4-7yrs of age (mean 5.2±1 yrs), who evaluated the presence of abnormalities in ocular motility (PMot), refraction (PRef), fundus (PFun), visual acuity (PVis), stereopsis (PSter) and of anisometropia (Anis) and ambliopia (Ambl). Based on the severity of CNS parenchimal damage, neonatal cerebral ultrasound (US) was classified as: normal (N), with mild to moderate (M) or severe (S) damage. Site, side and kind (hypoxic-ischemic or haemorrhagic) of the lesion were also considered.
**Results**:

| US | N | P Mot | PRef | PFon | PVis | PSter | Anis | Ambl |
|---|---|---|---|---|---|---|---|---|
| N (43) | 23 | 6 | 11 | 2 | 11 | 7 | 3 | 4 |
| M (20) | 7 | 3 | 9 | 1 | 7 | 6 | 2 | 5 |
| S (10) | 1 | 8 | 7 | 7 | 7 | 7 | 4 | 7 |
| Tot (73) | 31 | 17 | 27 | 10 | 25 | 20 | 9 | 16 |

58% of the children showed one or more ophthalmological abnormalities. Their presence was correlated with severity of CNS parenchimal damage ($p<.05$), but not with g.a., bw, % AGA, presence of occipital lesion, or kind of lesion. Only in 5/25 cases PViswere not associated with PMot, PFon or PRef. PMot and PFon were correlated with the severity of the CNS insult ($p <.05$). The left hemisphere was more often affected than the right; the left eye was affected twice more than the right by PMot and PFon, while the PRef was mainly bilateral (77%).
**Conclusions:** assessment of neonatal CNS damage by US has a prognostic value for later visual development, particularly for abnormalities of the ocular motility and the fundus.

## ● 173

DERANGED CEREBRAL OXIDATIVE PHOSPHORYLATION FOLLOWING BIRTH ASPHYXIA AND NEURODEVELOPMENTAL OUTCOME AT FOUR YEARS.

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**Hypothesis:** Cerebral phosphocreatine/inorganic phosphate ratio (PCr/Pi) measured by phosphorus magnetic resonance spectroscopy in term infants following birth asphyxia (1) is related to neurodevelopmental outcome at 4 years.

**Study design:** Prospective case study in a tertiary referral centre.

**Subjects:** 41 term infants who survived birth asphyxia.

**Measurements:** Minimum PCr/Pi in the first week. A structured neurological examination and McCarthy General Cognitive Index (GCI) were done at 4 years.

**Results:** 7 infants had values for PCr/Pi sds above 0, including only one >+1.99. The main results are tabulated:

| | | Impairment at 4 yrs. N (%) | | IQ at 4 yrs |
|---|---|---|---|---|
| N | PCr/Pi mean(sds) | with disability | Total | GCI mean±sd |
| 28 | ≥ -1.99 | 5 (18) | 14 (50) | 89 ± 20 |
| 7 | - 2.00 to - 3.99 | 5 (71) | 5 (71) | 71 ± 27 |
| 6 | ≤-4.00 | 5 (83) | 6 (100) | 57 ± 12 |

**Conclusion:** Minimum PCr/Pi in the first week following birth asphyxia was significantly related to neurodevelopment ($p<0.05$, df 2) and GCI ($p<0.005$, one way analysis of variance) at 4 years.

1. Roth et al. Dev Med & Child Neurol 1992;34:285-295.

## † 174

QUANTITATIVE $^1$H MAGNETIC RESONANCE SPECTROSCOPY (MRS) OF THE BRAIN IN NONKETOTIC HYPERGLYCINEMIA (NKHG)

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**Background:** NKHG is an inborn error of amino acic metabolism in which large amounts of glycine (glyc) accumulate in the brain due to a molecular defect in the glycine cleavage system. High concentrations (conc) of glyc are found in the CSF.

**Aim:** Can $^1$H-MRS detect differences in Glyc conc in various areas of the brain of neonates with NKHG *in vivo*?

**Subject and Intervention:** 7-day old boy born at term after uneventful pregnancy and birth. Progressive hypotonia and seizures during first week of life, arificial ventilation. At age 3d pp. elevated glyc levels in plasma 4176 µmol/L and urine 4966 mmol/mol creatinine lead to the diagnosis of NKHG. At day 7 pp. MRI was carried out and multivoxel quantitative $^1$H-MRS were obtained from volumes of 3.5ml in Frontal White Matter (FWM), Parieto-Occipital WM (POWM), Basal Ganglia (BG), Cerebellar WM (CBWM), and from 1ml of CSF (lateral ventricle).

**Results:** Glyc conc as measured by $^1$H-MRS were: FWM 4mmol/L, POWM 5mmol/L, BG 5.5mmol/L, CBWM 8mmol/L and CSF < 1mmol/L.

**Conclusions:** *In vivo* $^1$H-MRS demonstrated that: 1) there are variations of glyc conc of up to 100% in different areas of the brain; 2) the CBWM had the highest glyc conc and showed also an elevated lactate conc of 1mmol/L; and 3) there was barely glyc detectable in the CSF in which the simultaneous biochemically measured conc was 646µmol/L.

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TEMPORAL EVOLUTION OF HYPOXIC-ISCHEMIC BRAIN EDEMA IN THE NEONATAL RAT BY MAGNETIC RESONANCE (MR)

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**Background:** In experimental studies on the development of postasphyxic brain lesions in rat pups (unilateral common carotid artery (CCA) ligation plus hypoxia) we have demonstrated a threshold duration of hypoxia-ischemia (HI) which determines whether a vasogenic edema and subsequent infarction follow the initial cytotoxic edema [1].

**Aim:** Is it possible to demonstrate the time-dependent formation of cytotoxic and vasogentic brain edema following longterm HI with functional MR examinations.

**Subject and Intervention:** 16 7-day old rats were subjected to unilateral CCA occlusion and 8% $O_2$ for 30 min. Diffusion weighted (DWI) and T2 weighted (T2WI) imaging, and single shot localized T2 relaxation (T2) measurements were performed for the first 12h.

**Results:** In control animals T2 of subcortical WM was bi-exponential: 85ms and 270ms, reflecting intracellularly bound water and free water of unmyelinated WM. Changes in DWI (cytotoxic edema) following onset of hypoxia were accompanied by an initial decline of T2 (<85ms). Thereupon, hyperintensities in DWI and T2WI and an increase of T2 to >150ms could be demonstrated simultaneously at 4h following HI, indicating the beginning of vasogenic edema.

**Conclusions:** Changes of T2 correlated well with the formation of cytotoxic and vasogenic brain edema as shown in DWI and T2WI. The mono-exponantial decline of T2 at 4h following HI indicates free water exchange beween differently affected tissue compartments.

[1] H. Rumpel, E. Martin et al., Magnetic Resonance Imaging of Brain Edema in the Neonatal Rat: A Comparison of Short and Long Term Hypoxia-Ischemia, *Pediatr. Res.*, 1995 in press.

## * 176

DIET AND MINERAL STATUS AND LINEAR GROWTH IN PRETERM NEONATES ASSESSED BY KNEMOMETRY

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**Background:** Knemometry allows accurate and precise measurement of linear growth. We used this technique to test the hypothesis that linear growth is influenced by dietary mineral supply and body mineral status.

**Subjects:** 46 preterm neonates <32 weeks gestation underwent knemometry weekly until discharge, daily leg length velocity (LLV) being calculated weekly.

**Interventions:** During each week predominant diet (preterm formula {high phosphate}, breast milk or parenteral nutrition (PN) {low phosphate}), blood alkaline phosphatase (AP), calcium (Ca) and phosphorus (P) concentrations were recorded. The relationship between LLV and biochemical values was assessed by linear regression, that between LLV and diet by t-test, as the data were normally distributed.

**Results:** 159 LLV values were measured (median gestation 27 weeks, birthweight 970g). Mean (SD) LLV was 0.29(0.22) mm/day. LLV was significantly related to P ($r=0.23$, $p=0.02$) and negatively to Ca ($r=0.24$, $p=0.016$) but not to AP. Mean LLV (SD) on different diets was as follows:

| | | | |
|---|---|---|---|
| Formula | n47 | 0.32(0.19) mm/day* | (*sig.diff. p=0.02) |
| Breast | n16 | 0.24(0.24) mm/day | |
| PN | n45 | 0.21(0.25) mm/day* | |

**Conclusion:** We have shown an association between reduced linear growth and low dietary phosphorus intake and low P. The negative relationship between LLV and Ca was surprising, but explainable because of the tendency to hypercalcaemia when P is reduced in preterm neonates. We now aim to use knemometry to assess the effectiveness of mineral supplementation of breast milk and PN.

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ALFENTANIL FOR SHORT-TERM PAIN RELIEF IN PRETERM INFANTS

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**Background:** Certain procedures in neonatal intensive care may require pain relief. Our aim was to assess this, and the suitability of alfentanil (ALF) for this purpose.

**Subjects:** 10 ventilated preterm infants (bw 2177±526 g, gest.age 32.7±2 weeks).

**Interventions:** Each infant received placebo, 10 and 20 µg/kg ALF in random order 2 min before 3 separate endotracheal suctions at least 6 h apart. Heart rate (HR) and mean arterial blood pressure (MABP) were monitored. Plasma noradrenaline (NA) and ß-endorphin (ßE) concentrations were measured before and 30 min after suction. Pain was measured with a pain scale for neonates (score 0-8, NIPS).

**Results:** Changes (mean±SEM) caused by the painful stimulus.

| | NIPS | HR | MABP | NA % change |
|---|---|---|---|---|
| Placebo | 3.9 ± 0.7 | 13 ± 2 | 8.5 ± 3.3 | 118 ± 53 |
| 10 µg/kg | 2.2 ± 0.6 | 10 ± 7 * | 2.2 ± 2.8 | 83 ± 55 |
| 20 µg/kg | 0.4 ± 0.8 * | -8 ± 3 # | 0.9 ± 3.6 | -9 ± 22 |

* $p<0.05$, # $p<0.01$ In placebo group, ßE decreased 20 ± 23 %. Rigidity was noted in 2, 2, and 5 cases in the placebo, 10, and 20 µg/kg ALF groups, respectively.

**Conclusions:** Pain relief is indicated for tracheal suction. ßE does not reflect pain. 20 µg/kg ALF relieved pain but caused rigidity, and thus should be used only with muscle relaxant.

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ERYTHROPOIETIN (EPO), GM-CSF AND INTERLEUKIN 3 (IL3) IN THE PATHOGENESIS OF ANEMIA OF PREMATURITY.

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**Background:** Impaired erythropoietin production seems to be the main cause of the anemia of prematurity. The results of clinical trials show a good response to rhEPO administration in about 60-70% of patients, while a subset of preterm infants fail to respond to rhEPO, suggesting that other factors (cytokines) could play a role in the pathogenesis or maintenance of the anemia.

The objective of the present study was to determine the role of EPO, and other cytokines like GM-CSF and IL3 in the pathogenesis of the anemia of prematurity.

**Subjects:** The control group consisted in 30 term newborns. The study group was formed by 47 preterm infants less than 34 weeks of gestational age.

**Interventions:** Measurements of hematological parameters (by automatized hematological counter) and cytokines: EPO, GM-CSF, IL3 (by ELISA), were performed on day 1 in the control group (cord blood) and on days +1, +14 and +28 in the study group (peripheral blood).

**Results:** Low levels of seric EPO were found in preterm newborns (13.04 ± 9.82 mU/mL vs. 78.34 ± 115.43 mU/mL in control group. $p<0.004$). No increment of EPO levels were observed with diminishing Hb values in preterm infants. GM-CSF levels were higher in preterm infants than in term newborns (4.51 ± 6.92 vs. 0.19 ± 0.73 pg/mL. $p<0.001$) at birth. No changes in GM-CSF levels were observed in the succesive determinations. No differences in IL3 levels were found between both groups.

**Conclusion:** Inadecuate production of EPO was confirmed in the preterm population from birth to the end of the study period. Our data suggest a role for GM-CSF as a compensatory mechanism to increase impaired erythropoiesis. Further studies are needed to elucidate this hypothesis

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HEMODYNAMIC EFFECTS OF MORPHINE INFUSION IN VENTILATED PRETERM BABIES

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Background: morphine is used as an analgesic and to obtain optimal adaptation for the ventilator in sick premature infants. Aim: to evaluate the hemodynamic effects of morphine. Subjects: 20 ventilated preterm babies (GA 30±3 wks, range 27-33, BW 1,740±840 g, range 1,020-2,580). Interventions: MABP, HR and Doppler evaluations before (M0) and at 15 (M15), 30 (M30), 60 (M60) and 120 min. (M120), during 2hrs infusion (100 µg/Kg/h) were studied. The Doppler parameters used were Peak systolic (Vs), end-diastolic (Vd), mean flow velocity (Vm) and Pourcelot' Resistance Index (RI) of anterior cerebral artery and Cardiac Output (CO). Statistical evaluation has been performed by analysis of variance, then the significativity was calculated by Student-Newman-Kenfeld test. Results: there were no statistically significant changes in the cerebral and cardiac measured Doppler parameters. A relevant, although not significant, fall in MABP and HR was noted.

| TIME | MABP | CO | HR | Vs | Vd | Vm | RI |
|---|---|---|---|---|---|---|---|
| M0 | 48±7 | 256±35 | 148±12 | 0.60±0.10 | 0.10±0.09 | 0.18±0.05 | 0.72±0.08 |
| M15 | 46±8 | 260±40 | 148±12 | 0.58±0.08 | 0.12±0.08 | 0.17±0.05 | 0.72±0.10 |
| M30 | 45±7 | 262±38 | 144±20 | 0.56±0.06 | 0.14±0.06 | 0.20±0.04 | 0.68±0.12 |
| M60 | 43±8 | 258±34 | 142±20 | 0.60±0.06 | 0.12±0.07 | 0.18±0.03 | 0.68±0.10 |
| M120 | 42±4 | 250±32 | 140±16 | 0.58±0.04 | 0.12±0.08 | 0.18±0.03 | 0.70±0.08 |

Conclusions: i.v. morphine over 2hrs did not have any significant effect on MABP, HR or cerebral and cardiac hemodynamics. No adverse effects were noted.

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VERTICAL TRANSMISSION OF HEPATITIS C VIRUS

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Background: The risk of mother-to-infant transmission of hepatitis C virus (HCV) varies according to the population studied and the tests used. Objective: to detect the vertical transmission rate of HCV from mothers infected to their babies. Design: prospective clinical, serologic and molecular biologic follow-up (24 months) of infants of anti-HCV positive mothers. Setting: Dept. of Pediatrics, tertiary Care Center. Patients: 30 anti-HCV positive mothers and their 30 infants. Methods: We investigated the potential vertical transmission of HCV by identifying HCV antibody seropositive pregnant women, by analyzing HCV-RNA in the peripheral blood using PCR and by prospectively following their offspring until 24 months of age. During the third trimester, 2.980 consecutive pregnant women were examined for anti-HCV antibodies by a second generation Enzyme-Linked Immunosorbent Assay (EIA2) and re-assayed by a second generation Recombinant Immunoblot Assay (RIBA2). A total of 32 mothers were positive for EIA2 test and 30 of them were positive for RIBA2 test. These 30 mothers and their 30 babies formed the study cohort. Results: Of the 30 anti-HCV positive mothers, 10 were also positive for serum HCV-RNA by PCR. All babies were initially negative for HCV-RNA (cord blood specimens), but three babies became positive at three months of age and remained positive thereafter. These babies had been born from 3 of the 10 mothers with viremia during the third trimester of pregnancy. Conclusion: These results suggest that HCV vertical transmission is possible in 10% of anti-HCV positives and in about 33% of the HCV-RNA seropositive mothers.

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COGNITIVE ABILITIES OF ADOLESCENT EXTREMELY LOW BIRTHWEIGHT AND CONTROLS: A REGIONAL COHORT STUDY. Saroj Saigal, Barbara L Stoskopf, Peter L Rosenbaum, Lorraine A Hoult. Spn. by Barbara Schmidt. Dept. of Peds, McMaster University, Hamilton, ON., Canada, **Objectives:** To compare the intellectual status, academic achievement and school performance of teenaged extremely low birthweight ELBW) and control children (C). **Design:** Longitudinal follow-up. Children were administered the WISC-R (abridged version), and WRAT-R by trained psychometricians; parents completed a validated self-administered questionnaire regarding school performance. **Setting:** Geographically defined region in central-west Ontario. **Subjects:** 150/169 (89%) ELBW survivors born between 1977 and 1982, and between 12 and 16 years of age (including 41 children with neurosensory impairments), and 124/145 (86%) demographically matched term controls (C). **Results:** The mean WISC-R DQ was: ELBW 89 ± 19; C 102 ± 13 ($p < 0.0001$); proportion of children with DQ ≥ 85 (1 SD of mean) was: ELBW 70%, C 92%; proportion with DQ < 70 (2 SD < mean): ELBW 15%, C 0%. Exclusion of 41 children with neurosensory impairments improved the mean DQ (95 ± 12) in ELBW. There was no difference in DQ by sex. ELBW children did less well on WRAT-R reading, spelling and math ($p < 0.0001$), and the proportions who scored < 70 on these test items were: ELBW 23%, 24% and 37%; C 2%, 3% and 4%, respectively. Children < 750g BW performed at the same level as 750 to 1000g BW, except in WRAT math ($p < .05$). A significantly higher proportion of ELBW children were receiving special education (48% vs 10%, $p < 0.0001$), and had repeated a grade ELBW 25%; C 6%, $p < 0.0001$). **Conclusions:** Although 70% of ELBW survivors assessed had mean DQs within the normal range, a 13-point lower DQ is both statistically and clinically relevant. ELBW teens were disadvantaged on every test measure compared to C, and did particularly poorly in math (only 30% scored ≥ 85). The high utilization of special educational resources has economic implications.

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HOW PREMATURE TEENS PERCEIVE THEIR OWN HEALTH-RELATED QUALITY OF LIFE: COMPARISON WITH CONTROLS. Saroj Saigal, David H Feeny, William J Furlong, Peter L Rosenbaum. Spn. by Barbara Schmidt. Depts. of Peds. & Clinical Epidem. & Biostatistics, McMaster Univ., Children's Hospital at Chedoke-McMaster, Hamilton, ON, Canada. **Objective:** To estimate and compare the health-related quality of life (HRQOL) from the perspective of teenage extremely low birthweight (ELBW) and control (C) children. **Design:** The study utilized the Standard Gamble (Chance Board) method which measures preferences under conditions of *uncertainty*, (and yields a single cardinal utility score between 0.0 and 1.0, where 0 = death and 1.0 = perfect health) to quantify the teen's own self-reported subjectively-defined health state. **Setting:** Geographically defined region in central-west Ontario. **Participants:** 140 ELBW children aged between 12 and 16 years, and 124 C. **Results:** Chance Board ratings of HRQOL utility scores were ELBW = 0.89 ± 0.22; C = 0.93 ± 0.11, $p = 0.10$; there was greater variability in the scores of ELBW children compared to the controls ($p = 0.01$). Proportion of children who scored 1.0 (perfect health) for HRQOL was ELBW 61%, C 49%, $p$ 0.08; proportion with scores < 0.80 was ELBW = 19%; C = 11%, $p = 0.11$. **Conclusions:** These data are derived from direct measures of HRQOL obtained from teenage children, rather than proxy measures of HRQOL usually reported in pediatric populations in the past. Although data on direct measures of self-reported health status (not presented here), indicate that ELBW children suffer from a greater burden of morbidity, preference measurement techniques suggest that ELBW children do not perceive themselves to be very different from C. Thus, ELBW children appear to place a higher valuation on their own health status, despite recognition of their disabilities. This positive self-perception is important and may differ from the values placed by other assessors for the same health states.

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MEASURING PREFERENCES FOR HEALTH STATES WORSE THAN DEATH: PERSPECTIVE OF TEENAGE PREMATURE AND CONTROL CHILDREN. Saroj Saigal, David H Feeny, William J Furlong, Peter L Rosenbaum. Spn. by Barbara Schmidt. Departments of Pediatrics & Clinical Epidemiology & Biostatistics, McMaster University, Children's Hospital at Chedoke-McMaster, Hamilton, Ontario, Canada. **Background:** Preference measurements are employed to quantify health-related quality of life (HRQOL). The conventional utility scale is between 0.0 and 1.0, where 0.0 = dead and 1.0 = perfect health. **Objective:** To quantify preferences obtained from teenagers for health states considered to be worse than death. **Design:** We utilized the Standard Gamble (chance board) method which offers a lottery approach with varying probabilities and measures preferences under conditions of *uncertainty*. Professional interviewers presented respondents with 4 hypothetical health scenarios and the teen's own self-reported subjectively defined health state. Some of the hypothetical scenarios (eg "Sandy" and "Pat") included combinations of severe disabilities such as blindness, mechanical aids for mobility and self-care, special educational assistance, and/or emotional problems. **Setting:** Geographically defined region. **Participants:** 142/169 (84%) extremely low birthweight (ELBW) survivors and 124/145 (86%) term controls (C) were interviewed between 12 and 16 years of age. **Results:** A high proportion (50%) of both cohorts rated some of the above hypothetical health scenarios as worse than death ("Pat": ELBW 40%, C 43%; "Sandy": ELBW 29%, C 39%. Less than 1% of ELBW and none of C rated their own health state as worse than death. **Conclusion:** Teenage children are able to quantify preferences for health conditions, and a minority report certain disabling hypothetical health states to be worse than death. No significant differences in frequencies were observed between the ratings of ELBW and C. States worse than death should be incorporated in health services research and in medical decision-making.

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PARENTS' PERCEPTIONS OF THE HEALTH-RELATED QUALITY OF LIFE OF TEENAGE EXTREMELY LOW BIRTHWEIGHT AND CONTROL CHILDREN. Saroj Saigal, William J Furlong, David H Feeny, Peter L Rosenbaum, Elizabeth A Burrows. Spn. by Barbara Schmidt. Departments of Peds. & Clin. Epid. & Biostat., McMaster University, Hamilton, ON, Canada, **Objective:** To compare measurements of health-related quality of life (HRQOL) of teenage extremely low birthweight (ELBW) and control (C) children from the perspective of their parents. **Design:** Measurements of health status of teens were obtained by direct parent interviews. A utility approach using a Standard Gamble technique (Chance Board) which offers a lottery approach with varying probabilities, was employed to measure preferences of respondents for their own child's health state. This approach yields scores which can be used to estimate a single cardinal utility between 0.0 and 1.0, where 0 = death and 1.0 = perfect health. **Setting:** Geographically defined region. **Subjects:** Parents of 149/169 (88%) ELBW children between 12 and 16 years of age (including 41 children with neurosensory impairment) and 126/145 (87%) controls. **Results:** Mean HRQOL scores were lower for ELBW (0.91 ± 0.20) than for C (0.97 ± 0.08), $p$ 0.002; only 53% of ELBW children had scores of 1.0 compared with 72% of C; the variability in scores was also greater for ELBW ($p < .01$). **Conclusions:** The advantage of using parents as respondents is that we were also able to include untestable children. Based on the health state descriptions, parents of ELBW children reported a greater burden of disability than parents of C. However, these differences were not fully reflected in the HRQOL scores assigned by parents of ELBW children, which were rated fairly high. Thus, differences in reported functional status are not necessarily predictive of valuation of perceived HRQOL. These data have implications when involving parents in making decisions in the neonatal intensive care unit.

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### DEVELOPMENT OF MUSCLE POWER IN HIGH RISK PREMATURE INFANTS AT THE CORRECTED AGE OF 24 WEEKS

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**Background:** Low risk preterms show large, mostly temporary, fluctuations in the development of active and passive muscle power. A warning sign for deviant development is an increased passive muscle tone after the corrected age of 12 weeks.[1] We looked for abnormal development of muscle power in high risk premature infants at the corrected age of 24 weeks.

**Patients:** 87 preterms with GA < 32 wk (mean 30) and/or BW < 1500 g (mean 1380).

**Methods:** Only infants with a "Neonatal Medical Index (NMI)"[2] ≥3 (=high risk) were included. The development of active and passive muscle tone in the whole body, shoulders, trunk and legs at the corrected age of 24 weeks was measured with a method described by de Groot et al.[3]

**Results:** Discrepancy between active and passive muscle tone in the whole body was highest in the infants with NMI ≥ 4. In more than 10% the passive muscle tone in trunk and legs was increased in the preterms with NMI = 5.

**Conclusion:** The infants with the most complicated neonatal period showed the highest incidence of abnormal active and passive muscle tone, especially high passive muscle tone in the trunk and legs was found in this group. This abnormal finding may adversely affect development in general and may be an early sign of pathology.

1.Groot L de.et al.Neuropediatr.1992;23:298-305. 2.Korner AF.et al.Infant Behavior and Developm.1994;17:37-43. 3 Groot L de.et al.Neuropediatr.1992;23:172-179.

## † 186

### HEMODYNAMIC EFFECTS OF PROPORTIONAL ASSIST VENTILATION (PAV) IN PIGLETS BEFORE AND AFTER MECONIUM INSTILLATION.

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PAV increases the airway pressure in proportion to the inspiratory airflow of spontaneous breathing ($\dot{V}$PAV, compensation for airway resistance) or volume (VPAV, compensation for lung elastance) or both $\dot{V}$ and V ($\dot{V}$+VPAV).

**AIM:** To investigate whether PAV causes deleterious effects on cardiac output (CO), and pulmonary artery, pulmonary wedge (PWP), right atrial (RAP) and arterial blood (BP) pressure.

**Subjects:** 11 anesthetized, tracheotomized piglets (< 11 days old) with normal lungs (n=11), and after instillation of 4 - 7 mL/kg of 20% meconium solution (n=10).

**Interventions:** Randomized 10-minute periods of $\dot{V}$PAV, VPAV, and $\dot{V}$+VPAV were applied with different gains (ratio of increase in pressure per unit of $\dot{V}$ or V) and compared to CPAP-baseline measurements obtained before each setting change.

**Results:** When compared to CPAP baselines, a small but significant increase in RAP occurred during $\dot{V}$+VPAV in normal ($\bar{x}$ ± SD; 1.4 ± 1.6 vs 2.4 ± 1.7 mm Hg; p<.05) and injured (0.6 ± 1.7 vs 1.6 ± 1.3; p<.05) lungs. PWP showed a small significant increase (mean difference < 2mm Hg) during $\dot{V}$+VPAV, both before and after meconium. Similarly, CO decreased by 5% in normal lungs during resistance overcompensation and BP was lower (mean difference < 5mm Hg, post meconium) during $\dot{V}$PAV. No significant changes were observed in any of the other hemodynamic measurements nor in arterial blood gases.

**Conclusion:** PAV has no clinically significant hemodynamic consequences. It is a safe mode even when a high gain (overcompensation of lung resistance/elastance) is used provided that appropriate pressure limits are in place to prevent overdistension.

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### *SUBMAXIMUM EXERCISE PARAMETERS IN NORMAL CHILDREN*

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Background: Cardiovascular and respiratory diseases are best known to reduce not only ***maximum*** exercise performance in children, but also to impair the time course (=kinetics) of adaptation to a given work load (***submaximum*** parameters). Regressions of ventilation against $CO_2$-production ($V_E/V_{CO2}$), oxygen uptake against work rate ($VO_2$/Watt), heart rate against work rate (HR/Watt) and determination of the anaerobic threshold (AT) allow assessment of the kinetics of adaptation to different work loads. We performend these measurements in normal children to establish normal maximum together with submaximum parameters in the same subject group.

Subjects and Interventions: 105 children (ca. 5 per age and sex from 8-18 years) were bicycle exercised using a steady-state (StSt) protocol (1, 16, 64 and 160 watts per 5min step) and a non-steady-state (NSS) protocol (adapted from Jones-16 Watts/min increment). Measurements included ventilatory and pulmonary gas exchange parameters, heart rate, blood pressure and pulse oxymetry by Jaeger equipment. Maximum values of the NSS as well as submaximal slopes of $V_E/V_{CO2}$, $VO_2$/Watt, HR/Watt and AT were determined from the NSS, the StSt, compaired, and referred to age.

Results: Maximum values during the NSS protocol were similar to published values. Submaximum slopes from the NSS protocol were statistically not different from those of the StSt-protocol (p allways >.15) :

| *(x=age in years)* | *steady-state* | *Pct* | *non-steady-* | *Pct* |
|---|---|---|---|---|
| *(Pct=percentile)* | *protocol* | *(25/50/75%)* | *state-protocol* | *(25/50/75%)* |
| *y=HR/100Watt* | y=129.4-5.7x | 46.4/58.3/72.5 | y=121.3-4.9x | 43.5/53.5/75.3 |
| *y=VO2/Watt* (ml/Watt) | y=12.7-0.3x | 10.3/11.1/12.0 | y=11.5-0.03x | 8.2/9.2/10.6 |
| *y=VE/VCO2* (L/L) | y=32.9-0.5x | 24/26/28 | y=30.7-0.3x | 24/26/28 |

Conclusions: In healthy children, submaximum slopes during a StSt-Test and an incremental Jones protocol are not statistically different, but might become different in disease. The calculation of these slopes does not require a maximum performance, thus making it possible that also tests from disabled or incoordinate children can be evaluated.

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### EFFECTS OF DEXAMETHASONE ON GROWTH AND BONE MINERALISATION IN PRETERM INFANTS WITH BRONCHOPULMONARY DYSPLASIA (BPD).

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**Aim:** To measure effects of Dexamethasone on growth and bone mineralisation in preterm babies.
**Subjects & Design :** Prospective longitudinal study of infants of birthweight <1500g.
**Measurements :** Weekly measurements from birth of weight (Wt), head circumference (OFC), lower leg length (LLL) by kneemometry, length (RL) of radius and mineral content (BMC) by dual energy X ray densitometry. Repeated mineral balances were performed in the first 6 weeks of life.
**Results :** 15/26 babies with BPD were treated with dexamethasone and in all growth velocity decreased during first week of treatment - means(SEM) - OFC 0.13±.02 to 0.08±0.01 cm/day: p=0.02; Wt 19.4±2.6 to 4.1±2.3 g/d:p<<0.001; LLL 0.42±0.05 to 0.08±0.03 mm/d:p<<0.001; RL 0.15±0.03 to 0.08±0.01 mm/d:p=0.03. By 3rd week of treatment these rates were similar to those pre steroid and to the non treated group (OFC 0.14cm/d; Wt 28.3g/d; LLL 0.5mm/d; RL 0.16mm/d). At 40 weeks gestation there were no differences in OFC or Wt but the steroid group had significantly shorter LLL (114.7±2.9 vs 126.2±2.7 mm) and RL (46.7±1 vs 50.4±0.8 mm). In the first week of steroid treatment, calcium absorption and retention fell significantly (61±2.7% to 42±3.2% and 61±7.3% to 41±5.3%:p<0.05 respectively); phosphate retention fell (62±3.3% to 50±5%:p,0.05) but phosphate absorption was not affected (89±1.1% to 92±1%). By 3rd week all values were similar to untreated group. There was no significant difference, at any time, between the groups for BMC.
**Conclusions :** Dexamethasone was associated with a rapid and significant fall in growth which recovered as the dose was reduced, but with evidence that LLL and RL had not caught up by 40 weeks. Steroids caused an acute disturbance in mineral balance. These effects of steroids may be dose related.

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### THE ATTENUATION OF GROWTH IN PREMATURE INFANTS TREATED WITH DEXAMETHASONE FOR BRONCHOPULMONARY DYSPLASIA.

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**Background**: Dexamethasone, a synthetic glucocorticosteroid, is widely used to treat bronchopulmonary dysplasia (BPD). Given the known adverse effects of steroids on growth, we examined the effect of dexamethasone on growth in premature infants with BPD. **Subjects**: 10 ventilated infants (8M,2F; mean birth weight 882g, range 640-1210 g; mean gestational age 25 weeks, range 24-29 weeks) in whom a diagnosis of BPD was made on clinical and radiological grounds. The mean age of entry into the study was 20 days. Dexamethasone was initially given in a dose of 0.5 mg/kg/day, the dose thereafter being gradually reduced over the treatment period (median length 29 days, range 10-70). **Measurements:** daily weight (g), weekly occipital-frontal circumference (OFC)(cm) , total body length (TBL)(cm), crown-rump length (CRL)(cm) and knee-ankle length (KAL)(cm) and weekly serum levels of IGF1 and IGFBP3. Each subject was studied during treatment and for 3 weeks afterwards and acted as his/her own control. **Results**: Results were expressed as mean rate of change during and after treatment, i.e. g/day for weight and cm/week for OFC, TBL, CRL and KAL. There were significant differences (p<0.01) in the mean values of all physical parameters measured except CRL, during and after treatment: weight gain - 13.2 vs 30.0 g/day; OFC - 0.75 vs 0.99 cm /week; TBL - 0.69 vs 1.07 cm/week; CRL - 0.53 vs 0.68 cm/week and KAL - 0.13 vs 0.35 cm/week. There was a similar significant trend in mean serum IGF1 (1.57 vs 3.56 mMol/l) and IGFBP3 (0.94 vs 1.12 mg/l) levels on and off treatment. The weekly dose of dexamethasone (mg/kg/week) had a significant negative correlation (p<0.01) with changes in all parameters of physical growth (r=-0.50 - 0.60) but no correlation with serum IGF1 and IGFBP3 levels. There was a significant correlation (p<0.01)between changes in weight gain and protein intake (r=0.28) and also between changes in TBL and protein intake (r=0.32). There were also significant correlations between protein intake and serum iGF1 levels (r=0.57) and IGFBP3 (r=0.30)(p<0.01). **Conclusion**: Despite adequate protein and caloric intake, dexamethasone treatment is associated with significant attenuation of growth in premature infants with BPD but the mechanism of its action on the growth process as well as the effect of BPD itself require further study.

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### SERUM OSTEOCALCIN CONCENTRATION IN INFANTS WITH CONGENITAL HYPOTHYREIDISM.

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Serum osteocalcin ,an index of osteoblastic activity, is increased in hyperthyreoidism indicating an increased bone turnover essentially due to a higher bone resorption.Generally low osteocalcin concentration is observed in adults with hypothyreoidism.
The aim of this study was to evaluate the osteocalcin concentration in 10 infants ( aged 20 days to 8 months with congenital hypothyreoidism (C.H.) during L-throxin therapy and 20 healthy infants.
In all subjects serum concentrations of osteocalcin, $T_3$,$T_4$ and TSH ,$FT_3$,$FT_4$ using radioimmunoassay were performed.
No signifant differences in osteocalcin level between C.H. group (6,12 ±2,3 nmol/l) and controls (5,6 ± 1,8 nmol/l ) were found. In C.H. the significant correlation between osteocalcin and $FT_3$ was stated ( r = 0,58 p<0,05 ).
We conclude that early and properly treated children with C.H. have normal bone metabolism.

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### ON THE VALUE OF SCREENING TEST IN LEAD TOXICITY

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**Background:** Zinc protoporphyrin (ZPP) has been used to screen population for lead toxicity. At the level of blood lead (BPb) currently considered as toxic (5-10 µg/dL), this test seems to have less value. The aim of our study is to evaluate lead exposure in children and the cut-off value of ZPP useful for screening.
**Study design/setting:** Cross-sectional study in a pediatric population in Barcelona.
**Subjects:** 1134 children from routine controls in the Hospital.
**Measurements:** Blood obtained by venipuncture was used to determine blood lead concentration by atomic absorption spectrometry and ZPP with a hematofluorometer. These data were processed to obtain measures of sensitivity (sen), specificity (spe), positive predictive value (PPV), positive likelihood ratios (LR) and receiver operating characteristic curves for the different cut-off values.
**Results:** 65 children (5.7%) had a BPb over 10 µg/dL.

| ZPP | 30 | 40 | 50 | 60 | 70 | 80 | 90 | 100 | 110 | 120 |
|---|---|---|---|---|---|---|---|---|---|---|
| Sen | 98,1 | 80,8 | 57,7 | 40,4 | 26,9 | 23,1 | 15,4 | 13,5 | 7,7 | 5,8 |
| Spe | 1,9 | 19,2 | 42,3 | 59,6 | 73,1 | 76,9 | 84,6 | 86,5 | 92,3 | 94,2 |
| PPV | 5,5 | 5,7 | 6,7 | 7,9 | 8,9 | 11,5 | 13,1 | 17,5 | 11,8 | 11,5 |
| LR | 1 | 1,03 | 1,23 | 1,47 | 1,67 | 2,24 | 2,57 | 2,93 | 2,26 | 2,23 |

**Conclusions:** The prevalence of lead intoxication in our children is low. No cut-off value of ZPP has proved useful to screen lead intoxication in our setting.

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### ARE VERY LOW BIRTHWEIGHT INFANTS AT A HIGHER RISK FOR SUDDEN INFANT DEATH ?

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**Background:** Very low birthweight (VLBW) infants are considered to be at a higher risk for sudden infant death (SID) than normal birth weight infants. No specific causes are identified up to now.
**Study design/patients:** Descriptive study / included were all VLBW infants, born at the city of Heidelberg between January 1986 and Dezember 1993 (four different hospitals, one perinatal centre).
**Sources for collection of data:** Official statistics from the registry office (name, date of birth and death) and hospital records including autopsy findings.
**Results:** 701 infants with birth weights below 1500 g were born in Heidelberg in the study period, 97 died until the end of the first year. 80 infants died between 1st and 28th day of life, the other 17 infants died between 29th day and 12th month after birth. In 13 infants of the latter group severe cardiopulmonary problems (n=3), infections (n=4), heart defects (n=2), other malformations (n=3) or metabolic disease (n=1) were diagnosed as the main cause of death. In four infants, who died at home, SID was diagnosed - all had bronchopulmonary dysplasia (BPD) and additional respiratory infection. Pulmonary hypertension and right heart failure might be the main cause of death in these cases.
**Conclusion:** In all VLBW infants, who died between four weeks and one year of age a possible cause of death could be found and no unexplained death was observed. We speculate that VLBW infants without additional risk factors, especially BPD are not necessarely at a higher risk for SID.

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### FINE MOTOR ABILITIES IN PRETERM INFANTS AT 4 YEARS

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**Background:** Learning difficulties in preterm infants often emerge as a hidden handicap in early schoolage, neurological development has been considered normal so far. Since fine motor abilities are known to influence a child's learning at school, we looked for differences between preterm and term infants at four years.
**Patients:** 83 term infants (normal) and 40 preterm infants, born before 32 weeks of gestation at the Perinatal Centre in Heidelberg (no neurological deficits).
**Measurements:** Tests of drawing (modified from Visual motor integration-Test) and cutting out of geometrical figures (task modified from Lincoln-Osseretzki-Test).
**Results:** means for the preterm infants were significantly lower in comparison to term infants in all subtests, girls performed better than boys in both groups.

| | term infants | | preterm infants | |
|---|---|---|---|---|
| | male | female | male | female |
| number | 41 | 42 | 18 | 22 |
| age at test (months) | 45.6 ± 1.8 | 46.4 ± 1.7 | 44.7 ± 2.1 | 45.9 ± 1.6 |
| drawing (N figures) | 4.9 ± 1.6 | 5.3 ± 2.1 | 2.4 ± 1.4 | 3.9 ± 1.2 |
| drawing (quality) | 5.6 ± 1.6 | 6.0 ± 1.7 | 3.2 ± 2.0 | 5.2 ± 1.6 |
| cutting out (accuracy) | -9.1 ± 6.6 | -5.8 ± 6.0 | -16.3 ± 8.2 | -12.8 ± 7.1 |
| cutting out (quality) | 4.7 ± 2.0 | 5.5 ± 2.0 | 2.0 ± 1,7 | 4.1 ± 1.9 |

**Conclusion:** At the age of four years fine motor deficits are detected in preterm infants, even if no other neurological impairments are present. Developmental screening tests in this age group could identify children at risk and allow early intervention before school age to possibly prevent later learning difficulties.

## † 194

### MAGNESIUM MONOTHERAPY OR IN COMBINATION WITH KETAMINE IN PERINATAL HYPOXIC-ISCHEMIC BRAIN DAMAGE ( PRELIMINARY STUDY).

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**Background:** Evaluation of possible protective effect of $MgSO_4$ and of its combination with ketamine on neonatal hypoxic-ischemic damage in rats.
**Subjects:** Two groups of newborn Wistar rats.
**Interventions:** A modified Levine preparation consisted of left carotid ligation followed by exposure to a hypoxic (8%$O_2$) environment for 2 h was used. The animals were treated (in multiple doses (6) after the hypoxic-ischemic insult): group A (8 animals) $MgSO_4$ (500mg/Kg), group B (4 animals) mixture of $MgSO_4$(500mg/Kg)+ketamine(5mg/Kg). In controls (8 animals) an equal volume of saline was administered. The pups were perfusion-fixed at 12 days of age. Their brains were grouped in 4 categories: normal, mild, moderate, severe, based on the gross morphologic appearence of the left cerebral hemisphere. Only those that appeared less damage were examined histologically. The hypoxic-ischemic changes in the dorsal hippocampus were assessed according to a semiquantitative 4-point scale based on the percentage of necrotic neurons:0=0%, 1=< 10%, 2=10-50%, 3=>50%.
**Results:** Significantly less damage was noticed in the $MgSO_4$-treated animals compared to controls. None of them had more than a moderate damage and the 50% fell into the mild category. Semiquantitative ischemic neuronal scores of the hippocampal substructures confirmed the neuropathologic grading. Administration of the mixture showed no significant amelioration.
**Conclusions:** Our results indicate that there may be a neuroprotective effect of $MgSO_4$ on the hypoxic-ischemic brain damage. Further studies are required to define the effectiveness of combined administration of ketamine and $MgSO_4$.

## † 195

### Randomised Controlled Trial of Pulmonary Function Monitoring in Neonatal Intensive Care.

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Centre for Research into Human Development, Ninewells Hospital, Dundee †.

*Background:* We aimed to determine whether the clinical outcomes of ventilated newborn infants could be improved by routine pulmonary function testing.
*Subjects:* 245 newborn infants that required mechanical ventilation from admission.
*Intervention:* Respiratory system compliance (Crs) was measured regularly (single breath technique). Infants were randomised to have their Crs data revealed as an aid to management (group 1, n=123), or not revealed (group 2, n=122). The groups were similar at study entry. Outcome measures were days ventilated, days in >40% $O_2$, days in $O_2$ and number of infants with adverse events (death, pneumothorax, pulmonary interstitial emphysema, pulmonary haemorrhage, intubated on day 15, $O_2$ dependent at 36 weeks, abnormal cranial ultrasound at 6 weeks).
*Results:* Data are median (quartiles) or number (%).

| All infants | Days vent. | Days $O_2$>40% | Days $O_2$ | Adverse events |
|---|---|---|---|---|
| Group 1 | 4 (2-9) | 3 (1-5) | 6 (2-34) | 63 (51%) |
| Group 2 | 5 (2-12) | 2 (1-8) | 6 (3-36) | 67 (55%) |
| | p=0.20 | p=0.87 | p=0.71 | p=0.56 |
| Survivors | (post hoc analysis) | | | |
| Group 1 | 3 (2-8) | 2 (1-4) | 6 (2-35) | 44 (42%) |
| Group 2 | 5 (2-13) | 2 (1-8) | 6 (3-43) | 51 (48%) |
| | p=0.03 | p=0.54 | p=0.33 | p=0.40 |

*Conclusion:* Routine measurement of Crs did not reduce adverse outcome but was associated with a reduction in the duration of ventilation in survivors. If this hypothesis were confirmed it would have important resource implications.

## * 196

### CLATHRIN COATS ARE NEEDED FOR SP-A MEDIATED SURFACTANT RECYCLING IN TYPE II PNEUMOCYTES.

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**Background:** Surfactant protein A (SP-A) is involved in surfactant lipid uptake and recycling by type II pneumocytes.
**Aim:** To elucidate the molecular mechanisms of SP-A-mediated surfactant uptake and recycling
**Methods:** Freshly isolated rat type II pneumocytes were incubated under different conditions with labeled surfactant-like liposomes, labeled SP-A and or antibodies against the SP-A-binding type II cell membrane protein bp55. Biochemical and immune electronmicroscopic assays for endocytosis and intracellular trafficking.
**Results:**
- Antibody against bp55 inhibits the SP-A mediated surfactant endocytosis.
- Internalization at 16°of SP-A after lipid endocytosis and removal of material adhering unspecifically to the cell membrane leads to lipid recycling.
- SP-A is internalized and recycled within 15-20 min.,i.e. kinetics different from those of endocytosed surfactant lipids.
- Under conditions that inhibit clathrin coat formation (intracellular $K^+$-depletion) surfactant quantitative lipid uptake is comparable , SP-A internalization is reduced to 30% of control (normal intracellular $K^+$). Inhibition of clathrin coat formation leads in the presence of SP-A to loss of surfactant lipid recycling.

**Conclusions:** SP-A reacts with its receptor bp55 at the cell membrane. This complex interacts with clathrin coats to enable surfactant lipid recycling.

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**The effect of magnesium infusion (Mg) on retinal (RBF) and choroidal (ChBF) blood flow during normoxia and hyperoxia.** Tom A. Stiris, Dorothea Blanco, Panayotis Fantidis, Jose Quero. Autonoma Univ. of Madrid, Hospital La Paz, Dep of Pediatrics and Surgical Res. Madrid, Spain.
**Introduction:** Magnesium may have protective properties on the brain in the asphyxiated newborn baby and may cause vasodialtion. Previously we proposed that changes in ocular blood flow may alter retinal metabolism that may be important in the pathogenesis of ROP. Thus, we studied the effect of magnesium infusion on RBF and ChBF during normoxia. Secondly, the mechanisms involved in hyperoxic vasoconstriction are not known. We have speculated that hyperoxia may cause its effect on retinal and choroidal vessel wall through alteration in calcium metabolism. Since Mg is a calsium blocker, we also examined the effect of hyperoxia after magnesium infusion.
**Material and method:** 14 newborn piglets < 7 days old were used, divided into a Mg group (n=7), receiving 200 mg MgSO4 I.V or a control group (n=7), receiving saline. Blood flow was measured using the radiolabelled microsphere technique at BL (RA1), 30 min after either MgSO4 or saline infusion in room air (RA2) and finally after 90 min of exposure to hyperoxia ($FiO_2$=1) ($O_2$).
**Results:** Results are expressed as ml/min/100gr tissue.

| | Mg - Group | | | Control group | | |
|---|---|---|---|---|---|---|
| | RA1 | RA2 | O2 | RA1 | RA2 | O2 |
| RBF | 43±5 | 59±7** | 28±3* | 49±5 | 51±7 | 30±2* |
| ChBF | 3417±507 | 3535±563 | 2416±697 | 3520±677 | 3394±599 | 1783±209* |

mean±SE; **p<0.01 fromRA1, *p<0.03 from RA1 and RA2. RBF increased significantly after Mg infusion. In both groups RBF decreased significantly during hyperoxia, the decrease being more pronounced in the Mg group. ChBF decreased significantly only in the control group, whereas the apparent decrease in the Mg group was not significant.
**Conclusion:** Mg cause vasodilation of the retinal vessels, but not the choroidal. Furthermore, Mg infusion modulates both the retinal and choroidal hyperoxic response.

## ● 200

Experimental Neuronal Injury in the Newborn Lamb: A Comparison of NMDA Receptor Blockade and Nitric Oxide Synthesis Inhibition on Lesion Size and Cerebral Hyperemia.
GA Taylor, WH. Trescher, MV. Johnston, , RJ. Traystman

BACKGROUND- Little information is available regarding the hemodynamic effects of NMDA and NO synthase antagonists in the neonatal animal, and whether the protective effects of these agents are in part due to alterations in regional hemodynamics. This study was performed to compare the effects of MK-801, L-Nitro-Arginine-Methyl-Ester, (L-NAME) on focal excitotoxic brain injury and associated hemodynamic response in the newborn lamb.
SUBJECTS: Neonatal lambs (1-7 days)
INTERVENTIONS- A 27 gauge needle was placed into the right striatum in 28 anesthetized animals. Seven lambs were placed in each group: A negative control group receiving 0.2 ml of buffered saline, a positive control group receiving 5 μ mole NMDA alone, and 2 groups receiving NMDA and pretreatment with MK801, or L-NAME. Ultrasound images, and cerebral blood flow (CBF) determinations (microspheres) were obtained before, and at 20, 40, and 60 minutes after intrastrial injection. Three animals in each group underwent histopathological evaluation.
RESULTS- Sonographic lesions were visible immediately after intracerebral injection. Saline injection resulted in small lesions ( mean volume; 13.6±5 $mm^3$) without hyperemia. NMDA alone resulted in larger lesions (92.9±24 $mm^3$) and hyperemia to both hemispheres, while pretreatment with MK-801 reduced lesion size (11.7±6 $mm^3$), and completely ablated cerebral hyperemia. Pretreatment with L-NAME showed no effect on lesion size (69.9±20 $mm^3$), and hyperemia only in the ipsilateral hemisphere. Sonographic lesions correlated well with gross and histopathological appearance.
CONCLUSIONS- NMDA-induced focal brain injury and associated hyperemia in the newborn lamb appear to be specific NMDA receptor mediated events. NO production probably does not play a major part in NMDA-induced neonatal neuronal injury, and may be only partly responsible for regional hyperemia during NMDA injection.

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**The effect of magnesium infusion (Mg) on total ($CBF_t$) and regional ($CBF_r$) cerebral blood flow during normoxia.** Tom A. Stiris, Panayotis Fantidis, Dorothea Blanco, ,Jose Quero. Autonoma Univ. of Madrid, Hospital La Paz, Dep of Pediatrics and Surgical Res. Madrid, Spain.
**Introduction:** Magnesium may have protective properties on the brain in the asphyxiated newborn baby. Mg is also known to cause vasodilation and thus may have an effect on organ blood flow. Little is known whether Mg affect total or regional cerebral blood flow in the newborn period. We have therefore studied the effect of Mg infusion.
**Material and method:** 17 newborn piglets < 7 days old were used, divided into a Mg group (n=10), receiving 200 mg MgSO4 I.V or a control group (n=7), receiving saline. Blood flow was measured using the radiolabelled microsphere technique at BL, 30, 60 and 120 min after either MgSO4 or saline infusion .
**Results:** Results are expressed as ml/min/100gr tissue (mean±SE).

| | BL | 30min | 60 min | 120min |
|---|---|---|---|---|
| $CBF_r$-Mg | 75±6 | 98±8* | 104±8* | 105±10* |
| $CBF_r$-Cntr | 72±6 | 69±7 | 76±7 | 79±8 |

*p<0.03 from BL (only total CBF are shown). Mg increased total CBF significantly. Furthermore, apart from hipocampus, all anatomical regions examined had increased blood flow 60 and 120 min after Mg infusion. Although most regions showed an increased blood flow 30 min after Mg infusion, in the cerebellum and caudate nucleus there was no significant change after 30 min, only after 60 and 120 min.
**Conclusion:** Mg increases total and regional cerebral blood flow, however there are some regional differences.

## † 201

**ELEVATED VASOPRESSIN mRNA LEVEL IN THE SUPRAOPTIC BUT NOT IN THE PARAVENTRICULAR NUCLEUS IN A NEW MODEL OF BACTERIAL MENINGITIS IN 14-DAY-OLD RATS.**
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**Background/aim:** Despite the newly introduced programme of vaccination, bacterial meningitis remains one of the main clinical problems during the early period of human life. The disease is very often accompanied by disturbed water and salt balance leading to brain oedema. The aim of the study was to develop an animal model of bacterial meningitis in suckling rats with measurements of the arginine vasopressin (VA) mRNA levels in hypothalamic brain nuclei.
**Subjects:** Three groups (number of animals = 12 in each) of 14-day-old male Wistar rats anesthetized by intraperitoneal pentobarbitone (30 mg/bwkg).
**Interventions:** Group 1: Cerebrospinal fluid (CSF) was obtained from the cisterna magna, and 200 ng/bwkg *Escherichia coli* O111 B4 endotoxin, dissolved in artificial CSF, was given intracisternally. Group 2: Pure artificial CSF was given intracisternally. Group 3: sham-operated animals. Four hours later cisternal CSF was sampled, white blood cells (WBC) and protein concentration were determined. Expression of the VA mRNA in the nucleus supraopticus (NSO) and paraventricularis (NPV) was investigated on brain cryostat sections by in situ hybridization techniques.
**Results:** A highly significant ($p < 0.001$) pleocytosis and elevation in CSF protein concentration developed in group 1 (520 ± 113 WBC/ul, 2.12 ± 0.43 g protein/l) compared both to values measured in group 2 (4.4 ± 1.6 WBC/ul, 0.22 ± 0.08 g protein/l) and in group 3 (6.5 ± 2.2 WBC/ul, 0.18 ± 0.1 g protein/l). Significantly ($p < 0.01$) increased VA mRNA levels were observed in the NSO (percent change 120.3 ± 2.4 %) in group 1, compared to values obtained in group 2 (100%). There were no significant differences regarding to VA mRNA levels in the NPV. (data are X ± SD, Student t-test)
**Conclusion:** Our results showed that during the very early stage of bacterial meningitis, an enhanced VA gene expression occurred in NSO, which phenomenon might have a pathogenetic role in the development of the accompanying brain oedema.

## † 199

PERTUSSIS - EFFECTS ON APNOEAS IN VERY YOUNG INFANTS
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**Background:** Pertussis may cause severe apnoea, bradycardia and cyanosis in very young infants. The cough is frequently absent and ventilatory support or intensive care monitoring is reported in about 5% and 10%, respectively. **Methods:** Between 1992-1994 42 infants (25 boys, 17 girls; birth weight 3315±640 g, gestational age 39±2 weeks, age at admission 3.2±2 month) were admitted with pertussis. The diagnosis was based on clinical findings (cough, whoop), lymphocytosis and serological findings. Only 4 infants had received the first DPT immunisation shot. Apnoeas >10s were documented on an event recorder (Edentec Assurance III, Minneapolis, USA) over 72 hours. The event recorder allowed the recording of pneumocardiograms and revaluation of each event. **Results:** The frequencies of apnoeas >10s averaged 218 per day at one, 395 at two and 160 at three months of age. At 4 to 6 months, the frequencies were less than 90 per day. Compared to healthy infants the mean duration of apnoeas was 7s and the maximum duration 8s longer. **Conclusions:** Very young infants with pertussis show significantly more and longer apnoeas than healthy infants. The maximum at two months suggests, that pertussis may be contibuted to SIDS. Earlier immunisation should be considered.

## † 202

INTRATRACHEAL PRESSURES OF NEWBORN PIGS IN HIGH FREQUENCY OSCILLATORY VENTILATION
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Background: In high frequency oscillatory ventilation, mean airway pressure can only be measured at the y-piece with commercially available ventilators. Air trapping can therefore not be detected. We have investigated if it occurs.
Subjects: Four female domestic pigs, age 1 day, weight 1.6 - 1.9 (mean 1.76) kg
Interventions: Pigs were anaesthetized, the trachea exposed, an endotracheal tube (ETT, Ø 3.5mm) and a pressure gauge inserted. Another pressure gauge and a pneumotachograph was inserted between the y-piece and the ETT. HFV-Infantstar (IS), Babylog 8000 (BL) and SensorMedics 3100A with 30% (SM-30) or 50% (SM-50) inspiratory time were interchanged. Mean airway pressure was 5.5 - 12 $cmH_2O$, amplitude was adjusted to achieve physiologic $paCO_2$-values at 10 Hz. Pressures and flow waveforms under various oscillation frequencies and the pressure change when cross-clamping the ETT at 10 Hz were recorded.
Results: Mean intratracheal pressure was, dependent on oscillation frequency, 1 - 4.7 $cmH_2O$ (mean 2.2, IS), 0.3 - 3 (1.1, BL), 0 - 1.4 (0.7, SM-30) lower than at the y-piece, but 0.1 - 0.3 (0.2) higher with SM-50. When cross-clamping the ETT at 10 Hz, pressure dropped by 0.8 $cmH_2O$ (IS, median), 0.8 (BL), 1.2 (SM-30), but rose by 0.4 with SM-50.
Conclusion: 1. With asymmetric oscillation (IS, BL, SM-30) mean pressure is lower intratracheally than at the y-piece, but with symmetric oscillation (SM-50), pressures are equal. 2. Air trapping was not observed.

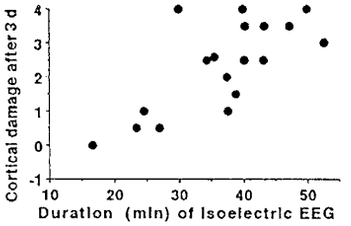
## ● 203

A PIGLET MODEL FOR POSTHYPOXIC ENCEPHALOPATHI. M.Thoresen* K. Haaland*, E.M. Loberg†, F.Apricena†, E.Hanko* A.Whitelaw‡ P.A.Steen¶ Dept. of Surgical and Pediatric Research, The National Hospital*., Dept. of Pathology.† and Experimental Research ¶, Ullevål Hospital., Dept. of Pediatrics Aker Hosp.‡ University of Oslo, Norway.

**Aim:** To develop an animal model which mimics the encephalopathy of the asphyxiated infant. Vessel ligation was avoided as it does not occur in asphyxia.

**Method:** 22 1-2 d old piglets were halothane anaesthetised, intubated and kept at tympanic T. 39°C. The insult was commenced by reducing the inspired oxygen fraction ($FiO_2$) to the maximum concentration of $O_2$ at which the EEG amplitude was $\leq 3.4\mu V$ (nearly isoelectric EEG) (n=18, 4 controls) lasting up to 64 minutes with transient increases in $FiO_2$ if hypotension or bradycardia occurred. pH was 7.1±0.12 after the insult. Anaesthesia was stopped 4-5h after the insult and the pig was extubated if the breathing became adequate.

**Results:** 14 pigs showed varying degree of neurological abnormality of which 4 had seizures The minimum duration of near iso-EEG which produced neuropathological damage (graded 0.0 -4.0) after 3 days survival was 17 min (fig) The severity of damage correlated with duration of iso-EEG (r=0.75). Low pH but not MABP added to the variability. The vulnerability to hypoxia was similar in cortex/white matter (2.3±1.6) hippocampus (2.3±1.6) and cerebellum (2.2±1.3) but less in basal ganglia (1.3±1.4) and thalamus (0.5±0.7), resembling the pattern in severly damaged infants. An EEG amplitude of <7$\mu$V at 1 hour predicted damage score ≥3.0 (corresponding values for control piglets 27-32 $\mu$V).




Conclusion: EEG guided hypoxemia produces a cerebral insult with subsequent encephalopathy and neuropathology similar to the asphyxiated infant.

## † 206

AGE DEPENDENCE OF CRANIAL DIFFERENTIAL PATHLENGTH FACTOR FOR NEAR INFRARED SPECTROSCOPY (NIRS) OF PRETERM INFANTS.

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**Background:** In order to quantify data measured with current NIRS instrumentation a laboratory measured optical pathlength (OP) and calculated differential pathlength factor (DPF) are used. (DPF=OP/interoptode spacing.) We have measured optical pathlength directly at the bedside using phase resolved spectroscopy and aimed to determine the dependence of DPF on gestational plus postnatal age (GPA).

**Subjects:** 15 preterm infants (gestational age 24-34 weeks) were studied at GPA of 28 to 42 weeks. There were no major abnormalities on cerebral ultrasound scans.

**Measurements:** An intensity modulated optical spectrometer which measures the OP at four wavelengths was used. OP was measured at a fixed interoptode spacing of 4cm at weekly intervals, on the parietal area of the cranium. 63 measurements were taken in total. The DPF for each wavelength was calculated.

**Results:** The results of DPF (SD) and the gradient of the regression of DPF against GPA are expressed for each wavelength. No significant gradient was detected.

| wavelength | 744 nm | 807nm | 832nm | 859nm |
|---|---|---|---|---|
| DPF | 5.68 | 5.74 | 5.40 | 4.99 |
| SD | 0.46 | 0.42 | 0.42 | 0.55 |
| gradient | 0.01 | 0.01 | 0.01 | 0.00 |

**Conclusion:** There was no detectable change of DPF with GPA in preterm infants.

## * 204

A CORRELATION BETWEEN RED CELL DEFORMABILITY AND THE DOCOSAHEXAENOIC CONTENT OF THE RED CELL MEMBRANE PHOSPHOLIPID IN MATERNAL AND UMBILICAL CORD BLOOD

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**Background Hypothesis:** that red cell deformability is poorer in blood of mothers and fetuses deficient in the long chain polyunsaturated fatty acid docosahexaenoic acid (DHA).

**Subjects:** venous blood was obtained from 16 mothers at term delivery and from the cord blood of 10 of their infants.

**Interventions:** 3 women were supplemented with 2.7 g fish oil/day from the 16th week of pregnancy, 1 with 2.7 g olive oil and 12 had no supplements.

**Results:** the DHA content of red cell membrane phospholipids was inversely correlated with the transit time of the red cells across a 5 µm Millipore filter (correlation coefficient 0.58, $y = 5.75 - 0.501 \cdot x$ ; $p = 0.001$). Red cell deformability is therefore increased when the DHA content of the membrane is greater.

**Conclusion:** Fish oil supplements given to women during pregnancy reduce the incidence of pre-eclampsia and increase birthweight. The findings of this study may in part explain the mechanisms underlying pre-eclampsia and the role of fish oil in its prevention.

## † 207

ADEQUACY IN NCPAP AND MECHANICAL VENTILATORY SUPPORT IN RELATION TO ADMISSION PHYSIOLOGICAL STABILITY INDEX (APSI) IN NICU BABIES.

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**Objective:** To study an effect of ventilatory support mode (nasal prongs continuous positive airway pressure - nCPAP and mechanical ventilation - MV) in reference to APSI values.

**Design:** A prospective, cohort study. **Setting:** Pediatric ICU in University Hospital. **Patients:** 151 consecutive outborn newborns with respiratory distress admitted to PICU over a 12 months' period of time. Mean birth weight 1875g (range 500-5000g), mean gestational age 34 weeks (range 22-43) **Method:** At the admission all babies had perinatal and demographic data taken. APSI values and paO2/FiO2 were depicted during the first day of intensive care. APSI score was modified to neonatal physiology. Decision of application respiratory supports and type of this support was based on previously established criteria (Crit. Care Med. V 21, No 9, S-364, 1993). Initial ventilatory mode, type of support within first 48h of treatment, and final outcome was correlated with APSI. **Results:**

| APSI (points) | 0-8 | 9-15 | 16-25 | >25 | |
|---|---|---|---|---|---|
| Number | 72 | 46 | 23 | 10 | |
| Mean paO2/FiO2 | 333 | 133 | 125 | 42 | |
| Only supplemental O2 | 24 | 2 | 0 | 0 | |
| nCPAP | 43 | 17 | 9 | 2 | p /chi2 test/ |
| IMV | 5 | 27 | 14 | 8 | p<0,0001 |
| Change nCPAP-IMV | 8 | 6 | 3 | 2 | p>0,05 |
| Change IMV-nCPAP | 5 | 20 | 4 | 2 | p<0,0001 |
| Final outcome-death | 3 | 12 | 10 | 6 | p<0,0001 |

**Conclusion:** We did not find significantly misapply nCPAP according to APSI values. APSI values had strong impact on brisk change from more invasive IMV mode to preferred nCPAP mode. We suggest that APSI evaluation should be considered in respiratory support decision making for critically ill newborns.

## † 205

SURVEILLANCE OF CONGENITAL RUBELLA IN ENGLAND SCOTLAND AND WALES

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**Background:** The National Congenital Rubella Surveillance Programme was established in 1971 to monitor the impact of rubella immunisation on congenital rubella (CR). The original selective programme of vaccination for adolescent girls and adult women was supplemented by a mass programme in 1988: measles/mumps/rubella vaccine (MMR) for all children in the second year of life. In November 1994 all 5-16 year-olds were offered measles/rubella vaccine (MR).

**Subjects:** Infants and children with suspected/confirmed CR. Active surveillance through British Paediatric Association Surveillance Unit supplemented by notifications from other sources.

**Interventions (Methods):** Diagnosis confirmed for notified cases, follow-up into early adult life. Vaccine uptake, rubella infection in the community and terminations for rubella monitored.

**Results:** 1108 individuals are registered; 78% have confirmed or compatible CR syndrome/infection; 22% are unclassified. Annual notifications declined from 70 in 1971-75 to 25 in 1986-90; since 1991 only 20 infants have been notified, including triplets.

**Conclusions:** Few infants are now born with CR in Great Britain. Since 1991, 14 of 18 mothers were themselves born abroad and came to Britain after the age of schoolgirl immunisation (including 3 women who acquired rubella abroad). Even with low rates of circulating infection, susceptible women are at risk. Ways of offering immunisation to recent immigrants should be considered.

## † 208

SOUTHERN BLOT AND PCR ANALYSIS OF δ T-CELL RECEPTOR LOCUS IN PEDIATRIC LYMPHOBLASTIC LEUKEMIA (ALL)

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**Background:** we analyzed the TCR-δ gene locus in 40 pediatric ALL. Southern Blot analysis of TCR genes rearrangements is useful for diagnostic studies on clonality of leukemias; for a better assigment of the lineage of leukemic cells and gives a molecular marker for detection of minimal residual disease.

**Patients:** 40 pediatric patients studied at the onset of the disease were classified on immunophenotypical criteria as B-lineage ALL (33/40) and T-lineage ALL (7/40).

**Methods:** DNA was isolated from bone marrow digested with three different restriction enzymes and, after Southern blot, TCR δ gene locus was studied using TCRDJ1 probe. PCR amplification, using specific primers, allowed to define exactly the gene segments involved in the rearrangements.

**Results:** B-lineage ALL: 32% germline (no rearrangement detected), 54% with at least one allele rearranged, 14% with a deletion. Identified rearrangements : Vδ2-Dδ 3 (65.5%); Dδ2-Dδ3 (19%). T-lineage ALL: 43% germline; 57% rearranged. Predominant rearrangement: Vδ1-Jδ1

**Conclusions:** TCR δ gene rearrangements can be also detected in B-lineage ALL, that shows predominant and specific types of rearrangements. These are specific of leukemic clone and can be used as molecular markers for the follow-up of the disease.

## † 209

POLYCHLORINATED BIPHENYLS AND CHILDRENS' DEVELOPMENT

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Polychlorinated Biphenyls (PCBs) are widespread industrial pollutants. They are lipophilic, stored in human tissue and toxic for human organism. PCBs are excreted in fat of breast milk. There are no established "normal" or "abnormal" values for clinical interpretation (Reigart J.R. et all. // Pediatrics. - 1994. - Vol. 94. - P. 122-3).

The goal of this study was to evaluate physical and neurodevelopmental status of children by three years of age, depending on PCBs level in breast milk, duration of breast feeding, integral clinical criteria and anthropometric data of the neonates.

We have analysed samples of breast milk of 75 women. The amount of extracted PCBs was determined by ECD-GS (analysis made with *Shimadzu GC-14A*), using integrator *Chromatopac C-R 6A* and method of internal standardization. Children's development was evaluated using *Denver-II* scale and neurological examination included evaluation of cranial nerves, muscle tone, tendon reflexes, pathological reflexes. All data were analysed using linear and stepwise regression analysis.

PCBs level in breast milk of Vilnius women was between 0.006 mg/kg and 0.032 mg/kg. Evaluating the physical development we found the highest linear correlation between PCBs level in breast milk and childs' weight at 2 years of age (r=0.64) and high at 3 years of age (r=0.71). In the newborn period PCBs level mostly correlated (in decreasing sequence) with height, Apgar score at 1 minute and signs of dysmorphology (r sq.=0.79). The sequence of predictors of psychomotor development of the child till 3 years of age was following: birth weight, gestational age, PCBs level in breast milk, signs of dysmorphology, duration of breast feeding, Apgar score at 5 min. (r sq.=0.91).

Our investigations support the idea that PCBs, received by children with breast milk, have long-term effect on physical growth and neurobehavioral maturation.

## * 210

THE EFFECT OF 0.5 VERSUS 1.0 UNIT INSULIN/KG/DAY ON PROTEIN BREAKDOWN IN BPD-INFANTS DURING CORTICOSTEROIDS

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1. Background. Corticosteroids are frequently used for the management of bronchopulmonary dysplasia (BPD) in very-low-birth-weight (VLBW) infants. Studies in infants show increased protein breakdown and turnover rates during high doses corticosteroids. Insulin is known to decrease protein breakdown.

2. Subjects. 12 VLBW-infants were studied receiving corticosteroids for BPD.

3. Interventions. Dexa treatment was according to Avery (1985). During the first 4 days 0.5 IU/kg/day short acting insulin was administred continuously intravenously in 7 patients and 1.0 IU/kg/day insulin in 5 patients. Protein breakdown and turnover rates were studied before dexa, on day 2, 4 and 7 by parenteral administration of [1-$^{13}$C]leucine. Leucine breakdown was calculated according to the usual equations. Plasma C-peptide, an indication of endogenous insulin production, was determined every study day.

4. Results.

| | 0.5 unit insulin/kg/day | | | | 1.0 unit insulin/kg/day | | | |
|---|---|---|---|---|---|---|---|---|
| $B_l$ | 0 | 2 | 4 | 7 | 0 | 2 | 4 | 7 |
| MEAN | 289.70 | 274.01 | 210.53 | 242.87 | 249.23 | 175.61 | 266.97 | 240.07 |
| SD | 61.78 | 72.12 | 62.64 | 64.87 | 109.90 | 44.28 | 79.01 | 66.50 |
| C-pept. | 0.74 | 1.20 | 1.54 | 1.79 | 0.58 | 0.95 | 0.91 | 1.34 |

$B_l$ = leucine breakdown in micromol/kg/hr

There were no side effects or hypoglyceamia observed.

5. Conclusion: Insulin administration during high dose corticosteroids avoids the increase of protein breakdown in BPD-infants. There is no difference in leucine breakdown between 0.5 and 1.0 unit insulin/kg/day. Insulin administration does not seem to suppres endogenous synthesis and might be advantageous for VLBW infants.

## ● 211

BLOODPRESSURE AND HEARTRATE FLUCTUATIONS IN PRETERM INFANTS.

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**Background:** In contrast to the amount of literature available on neonatal heartrate (HR) variability, there are few papers concerning fluctuations in arterial bloodpressure (ABP).

**Subjects:** The study population consisted of 10 healthy, spontaneously breathing, appropriate for gestational age preterm infants with a median postmenstrual age of 30.2 (range 27.1-33.4) wks (postnatal age 3-15 d).

**Measurements:** The ABP signal was extracted from an arterial catheter used for routine monitoring. The R-R intervals and the duration of each respiratory cycle were calculated from the ECG and thoracic impedance signal. Each measurement series consisted of a period of 3 min, marked by regular respiration. Short term variability (STV) indices were obtained for both HR and systolic BP (SBP). Spectral analysis was performed by FFT. The high frequency (HF) band covered the individual breathing range; the low frequency (LF) band consisted of the area between 33 mHz and the HF band. Total power in each frequency band was defined by the sum of moduli of each component.

**Results:** The SBP spectrum usually showed a peak around the respiratory frequency, whereas the HF band in the HR power spectrum displayed a dispersed pattern. In each infant the LF/HF ratio in HR was higher compared to the same ratio in SBP (p=0.008). The LF/HF ratio in SBP was positively correlated with postmenstrual age (p=0.003).

In SBP both HF power and STV index showed a significant decline with advancing age (p=0.004 resp. p=0.014). We could not find a significant correlation between postmenstrual age and the LF/HF ratio in HR variability. The ratio of the LF/HF ratio's in HR and SBP was negatively correlated with postmenstrual age (p=0.002).

**Conclusion:** SBP and HR variability show significant differences. With increasing postmenstrual age SBP shows a decline in fast fluctuations in the respiratory range. Our data are consistent with the hypothesis that the neural control mechanisms in the cardiovascular system mature with advancing postmenstrual age. This might be associated with a change in the sympathovagal balance.

## * 212

CHORIOALLANTOIC ARTERY BLOOD FLOW OF THE CHICK EMBRYO FROM STAGE 34 TO 43.

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**Background:** Little is known about the allantoic blood flow adaptations during advancing gestational age of the chick embryo. It is reported that the chorioallantoic artery blood flow represents about 50% of the combined cardiac output in the 17-19 days old chick embryo, this is comparable to the placenta in mamalians.

**Subjects:** chick embryo.

**Methods and interventions:** The baseline blood flow profiles of the chorioallantoic artery and the heart rate and changes with 5 minutes anoxia (100% $N_2$) were measured in 100 chick embryos from stage 34 (day 9) until stage 43 (day 17) with a transonic flow-probe (VB-series 0.5 mm). The eggs were opened and placed in a small plexiglass box with continuous flow of a $N_2/O_2$ mixture (5 l/min). The chorioallantoic artery was localized near the fetal abdomen and placed in the lumen of a transonic flow-probe. Heart rate was derived from the blood flow signal.

**Results:**

| | | | normoxia (21% $O_2$) | | anoxia (100% $N_2$) | |
|---|---|---|---|---|---|---|
| Stage | n | weight (g) | flow (ml/min) | heart rate (bpm) | flow (ml/min) | heart rate (bpm) |
| 34-36 | 30 | 2.2 | 0.41 | 202 | 0.16 | 144 |
| 37-40 | 40 | 6.4 | 1.22 | 246 | 0.55 | 150 |
| 41-43 | 30 | 13.3 | 3.04 | 280 | 1.08 | 136 |

After anoxia there was an overshoot only in blood flow during the reperfusion, which lasted for about 6 minutes.

**Conclusions:** Chorioallantoic artery blood flow and the heart rate increases with advancing gestational age of the chick embryo. The chemoreflex seems to be elicitable since early in fetal life. The chicken embryo could be an useful and attractive model for perinatal research.

## * 213

**CLINICAL EFFECTS OF RECTALLY ADMINISTERED ACETAMINOPHEN (APAP) ON INFANTS DELIVERED BY VACUUM EXTRACTION (VE)**

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**Hypothesis:** Rectally administered APAP reduces pain and associated symptoms in infants following VE.

**Study type/setting:** Double-blind, randomized, placebo controlled study in a perinatal center.

**Patients:** 124 term infants born after VE, birthweight > 2500 gms, APGAR 5' $\geq$ 7.

**Interventions:** 61 infants received 4 subsequent doses of APAP 20 mg/kg, 63 infants received 4 doses of placebo rectally q6h, the first dose within one hour of birth.

**Measurements:** Clinical condition and "facies pain" were scored 1 hr after APAP dose. Clinical symptoms: vomiting, poor feeding, pain on handling, abdominal distension, irritability, and grunting, were recorded on day 1. Statistics: Student's-t test and Mann-Whitney U test.

**Results:** Clinical condition was significantly better in APAP infants one hour after the first dose ($P < 0.05$). No significant difference was found between the groups after subsequent doses and for "facies pain" score or any of the clinical symptoms.

**Conclusion:** Rectally administered APAP improves clinical condition after the first but not after subsequent doses in VE infants.

## † 214

AUTOMATED AUDITORY BRAINSTEM RESPONSE (ABR) HEARING SCREENING IN AT RISK NEWBORNS.

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**Background:** Automated ABR hearing screening (ALGO-1) has been introduced for healthy newborns. The aim of this study is to test the validity of this ALGO-1 screener in at risk newborns in a neonatal intensive care unit (NICU).

**Subjects:** 250 at risk newborns (median gestational age: 30.0 wks, median birthweight 1350 g) selected according to criteria of the American Joint Committee on Infant Hearing.

**Interventions:** ALGO-1 automated ABR-hearing screening at a level of 35 dB was performed in the neonatal intensive care unit. When bilaterally referred, further audiologic screening and/or therapeutic intervention took place. When passed uni- or bilaterally, children enrolled in a) a nation wide screening programme (EWING) at the age of 9 months and b) in a half yearly follow-up programme in which hearing and speech-and language development were observed according to Egan an Illingworth.

**Results:** 245 (98%) Newborns passed ALGO-1 screening. 5 (2%) did not pass bilaterally. 1 of 5 with a congenital rubella died shortly after screening.In 4 of 5 bilateral congenital hearing loss of ≥35 dB was confirmed. 235 of the newborns passed were still alive at the age of 1 year. Ewing screening was performed in 183 of 235 (77,9%). 161/183 passed, 15 of 183 had passagere conductive hearing loss, in 7/183 no further investigation was performed. All 235 children enrolled in the 1/2 yearly follow-up programme had normal speech-and language development. In this study all 4 at risk newborns with bilateral congenital hearing loss were detected with ALGO-1 screening. Screening results showed no fals negatives at follow-up.

**Conclusion:**The ALGO-1 infant hearing screener can be used as a valid automated ABR-screener to detect hearing loss in at risk newborns in a NICU.

## † 215

THE SCOPE OF PEDIATRICS IN THE NETHERLANDS; A POPULATION BASED ANALYSIS OF SPECIALISTIC PEDIATRIC CARE

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Background/aim: Pediatrics has changed remarkably the last decades. Therefore epidemiological data are needed on the pattern of services and how this is changing. The aim of this study was to gain an insight in the scope of secondary and tertiary care delivered by pediatricians to a well-defined population.
Study design: Detailed registration of all consultations at the pediatric outpatient department, identification of all admissions with the hospital information system and an investigation of the patient-files in general practice on pediatric care in the neonatal period during a year regarding 7,854 children and adolescents aged 0-19.
Results: The proportion of the population referred to the pediatrician and the part of the population receiving pediatric care declines with age. Of all 0-year-olds 29% received pediatric care. Of the new referrals 76% concern children under the age of five. Admissions regarded 78% emergencies. There is a distinct difference in morbidity presented by the new referred children and those who remain under surveillance. Most children were referred for acute interventions and minor problems. Only a small proportion of the children referred to the pediatrician need longterm follow-up; these are especially children with respiratory illnesses and problems regarding growth, puberty and physical and mental development.
Conclusion: A view is given on the scope of specialistic pediatric care. It can be a guide for pediatric education, research as well as manpower planning.

## ● 216

HALF OF THE CHILDREN WITH TSH-DEFICIENCY (INCLUDING MULTIPLE PITUITARY HORMONE DEFICIENCIES) AS FOUND BY NEONATAL THYROID SCREENING SHOW POSTERIOR PITUITARY ECTOPIA BY MAGNETIC RESONANCE IMAGING AT THE AGE OF THREE MONTHS.

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Background: The Dutch type of neonatal thyroid screening (initial T4 and subsequent TSH and TBG determination in heel puncture samples) enables detection of congenital TSH-deficiency syndromes (CTDS).
Interventions: In a nationwide prospective study, protocolized endocrine examinations and Magnetic Resonance Imaging (MRI) are being performed within the first three months of life to determine hypothalamic/pituitary insufficiency and cerebral malformations.
Subjects: Newborns with screening results indicative of CTDS (i.e. low T4 *and* TSH; normal TBG).
Results: So far, 8 patients were found to be TSH-deficient; 3 of whom have multiple pituitary hormone deficiencies (MPHD). All MPHD-patients and one with isolated TSH-deficiency showed posterior pituitary ectopia (PPE) by MRI. Three of the patients with PPE and 2 of the others showed additional cerebral developmental disorders, such as corpus callosum dysgenesis and gray matter heterotopia.
Conclusions: 1) PPE is a frequent and early feature of congenital hypothalamic/pituitary disorders as found by neonatal screening.
2) MRI is a valuable tool in the diagnosis of hypothalamic/pituitary disorders and enables early detection of cerebral malformations.

## * 217

RELATIVE RATE OF PHENYLALANINE AND LEUCINE METABOLISM IN LOW BIRTH WEIGHT INFANTS; EFFECT OF ROUTE OF NUTRITION.

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**Background:** The effect of the route of nutrient feeding on the relative rate of leucine and phenylalanine kinetics and energy metabolism was examined.
**Subjects:** 10 LBW infants (group 1) received special premature formula, 10 LBW infants (group 2) were fed fortified human milk and 10 LBW infants (group 3) received parenteral nutrition.
**Interventions:** After 3 days full enteral feeding (group 1 and 2) and at postnatal day 6 in group 3, a tracer kinetic study was performed using L-[1-$^{13}$C]leucine, L-[$^{2}H_5$]phenylalanine and L-[$^{2}H_2$]tyrosine tracers in combination with respiratory calorimetry.

| Results: | Leu Ra | Phe Ra | Protein intake | Leucine intake | Phe intake | Ratio Ra Phe/Leu |
|---|---|---|---|---|---|---|
| Group 1 | 434±51 | 115±16 | 3.2±0.2 | 103± 6 | 30.2±1.9 | 0.335 |
| Group 2 | 377±33 | 94±18 | 3.0±0.2 | 104±15 | 37.8±7.9 | 0.341 |
| Group 3 | 359±50 | 108±24 | 1.8±0.3 | 63±12 | 19.2±3.1 | 0.361 |

(Leu and Phe parameters expressed in $\mu mol.kg^{-1}.hr^{-1}$, protein in $g.kg^{-1}.d^{-1}$)
**Conclusion:** The relative rate of phenylalanine and leucine Ra expressed as Phe Ra/Leu Ra ratio was in all three groups lower than that expected from reported whole body protein composition - 0.47 and lower than that reported in adults. These data in preterm infants suggest that whole body protein kinetics calculated from a single amino acid tracer may not adequately represent whole body protein metabolism.

## ● 218

THYROXINE ADMINISTRATION TO INFANTS OF LESS THAN 30 WEEKS GESTATIONAL AGE DECREASES PLASMA TRIIODOTHYRONINE CONCENTRATIONS; RESULTS OF A RANDOMIZED TRIAL.

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Background: Transient hypothyroxinemia of preterm infants is related with severity of neonatal disease and with a risk of impaired developmental outcome. A trial was set up to investigate whether thyroxine (T4) administration to very preterm infants improves clinical and/or 2-years' developmental outcome. In an earlier trial report we did not find an effect of T4 administration on clinical outcome. The effects of T4 administration on thyroid hormone metabolism are presented here.
Study type: Randomized, double-blind, placebo-controlled trial.
Patients: 200 infants of less than 30 weeks gestational age.
Intervention: 100 infants received 14. 8 µg/kg birtweight/day during the first 6 weeks after birth, starting 12-24 hours after birth (T-group); 100 infants received placebo (P-group).
Measurements: T4, FT4, T3, rT3, TSH and TBG were measured weekly during the treatment period, and 2 weeks thereafter.
Results: Plasma T4 and FT4 were significantly increased in the T-group during the treatment period; after termination of trial medication, T4 and FT4 levels became similar in both study groups. TSH secretion was depressed in the T-group. T3 levels were decreased in the T-group from day 14 on, until the end of the treatment period. rT3 levels were significantly higher in the T-group.
Conclusions: T4 administration according to our protocol increases plasma T4 and FT4 levels sufficiently. In contrast, it decreases plasma T3 concentrations, probably by depressing the TSH release. However, neither the increase in plasma T4 levels, nor the decrease in plasma T3 levels has an effect on mortality or morbidity.

## † 219

DEPENDABILITY OF OESOPHAGEAL pH MONITORING DATA ON THE SOFTWARE

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**Background:** 24-Hr oesophageal pH monitoring is considered as the "golden standard" of all reflux investigations. However, the data recorded depend on a number of patient dependent factors (feeding, activity, gastric acidity, ...) and on the used hardware (type of electrode). The aim of this study was to demonstrate the influence of the software used.
**Study design:** The results of 37 consecutive pH monitoring investigations (GastrograpH Mark II, MIC, Switzerland) were read out with 3 different computer programs, using identical definitions except for the number of reflux episodes. Program 1 (Pr1) and 2 (Pr2) were developed by the company (MIC), and differ in the calculation of medians (43200 per 24 hr in Pr1, and 360 in Pr2). Program 3 (Pr3) was developed by another company, but was designed to be a copy of Pr2.
**Results:** The mean reflux index (RI; % time pH<4.0) was 4.85 ± 3.84 (mean ± 1SD) with Pr1, 4.86 ± 3.90 with Pr2 and 5.02 ± 4.15 with Pr3 (p=NS; r= 0.71-1.0). The number of reflux episodes per 24 hour was 87.38 ± 149.1 with Pr1, 16.05 ± 10.38 with Pr2 and 19.05 ± 9.85 with Pr3 (p(Pr1-Pr2) and p(Pr1-Pr3)<.001; p(Pr2-Pr3)<.05; r= 0.14, 0.59 and 0.61, respectively). The number of reflux episodes lasting > 5 min was 2.32 ± 2.42 with Pr1, 2.27 ± 2.25 with Pr2, and 2.92 ± 2.78 with Pr3 (p(Pr1-Pr2)=NS; p(Pr2-Pr3) and p(Pr1-Pr3)<.05; r= 0.98, 0.77, 0.80; respectively). The duration of the longest reflux episode (in min) was 18.54 ± 18.07 with Pr1, 17.45 ± 16.84 with Pr2 and 15.33 ± 11.17 with Pr3 (p=NS; r= 0.98, 0.65 and 0.65, respectively). "Regression analysis" was also performed for the RI: if the data are identical, the "constant" factor should be zero, but ranged from 0.92 to 1.51 (p<0.05).
**Conclusion:** Data depend on the software, since differences are significant for some parameters. As a consequence, "borderline" pH monitoring data should be regarded with criticism, since data depend on many factors. One of these, appears to be the software.

## ● 220

DAY-NIGHT DIFFERENCES OF AMBULATORY PRESSURE MONITORING IN NORMAL SUBJECTS

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**Background:** Long-term oesophageal manometry is frequently used to diagnose motility disorders of the upper gastro-intestinal tract. For the interpretation of the results it is of primary importance to establish normal values.
**Study design:** An oesophageal pressure monitoring with a Gaeltec catheter with 3 pressure sensors (at the tip (P1), and 5 (P2) and 10 cm (P3) above the tip), connected to a Gastroscan (MIC, Switzerland), was performed in 60 asymptomatic adolescents.
**Results when awake:** The *number of contractions/hr* was 86.3 ± 29.1 (mean ± 1SD) in P1, 83.3 ± 25.2 in P2 and 82.0 ± 32.6) in p3 (p=NS). The mean *amplitude* was 51.2 ± 15.3 in P1, 48.1 ± 17.5 in P2 and 41.2 ± 11.5 in P3 (p(P1-P2),p(P2-P3), p(P1-P3) <.001). The *duration* (in seconds) was 3.9 ± 0.5 in P1, 3.6 ± 0.4 in P2 and 3.5 ± 0.4 in P3 (p (P1-P2), p(P2-P3), p(P1-P3) <.001).
**Results during sleep:** The *number of contractions* per hr was 26.0 ± 10.3 in P1, 25.1 ± 11.1 in P2 and 19.4 ± 8.9 in p3 (p(P1-P2)=NS; p(P1-P3)<.001; p(P2-P3) <.05). The *amplitude* was 52.1 ± 15.8 in P1, 51.8 ± 18.1 in P2 and 46.9 ± 15.7 in P3 (p(P1-P2)=NS; p(P1-P3), p(P2-P3)<.05). The *duration* (in seconds) was 4.7 ± 1.1 in P1, 4.1 ± 0.6 in P2 and 3.8 ± 0.6 in P3 (p(P1-P2), p(P1-P3)<.001; p(P2-P3)<.05). **Day/night:** The number of contractions is smaller during sleep (p<.0001). However, the contractions during sleep tend to have a greater amplitude and to last longer than when awake (all differences day/night p<.001 except NS for the amplitude in P1).
**Conclusion:** The nearer too the lower oesophageal sphincter, the more contractions and the greater their amplitude and the longer their duration, both during sleep and wake periods. The number of contractions is significantly increased when awake if compared to sleep, but the contractions are weaker and of shorter duration.

## † 221

**OXIDATIVE STRESS CAUSED BY FOETAL-NEONATAL TRANSITION IN HUMANS.**

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**Background:** The effect of foetal-neonatal transition on blood glutathione status (indicative of oxidative stress) and antioxidant defences in humans has been studied.
**Subjects:** Full-term healthy newborn infants (38-42 weeks gestation).
**Interventions**: Cord venous blood samples were collected at time of delivery previous placental detachment (foetal sample) and perypheral venous blood samples were obtained on posnatal day 3 (neonatal sample). We have measured glutathione status, antioxidant enzyme activities (superoxide dismutase, catalase and glutathione peroxidase) and total antioxidant activity (TAA) in all samples. Student t test (paired samples) was applied between foetal and neonatal status (*p < 0.05; ** p < 0.01).
**Results:**

| | Foetuses | Neonates (n) |
|---|---|---|
| GSH (μM) | 1070 ± 273 | 864 ± 241 (12)* |
| GSSG (μM) | 21 ± 5 | 31 ± 9 (12)** |
| SOD (U/mg Hb) | 1.6 ± 0.3 | 1.8 ± 0.3 (14)** |
| Catalase (K/g Hb) | 161 ± 71 | 206 ± 49 (15)* |
| GSH Px (U/g Hb) | 48 ± 12 | 49 ± 14 (14) |
| TAA (TROLOX Equ.) | 1.06 ± 0.13 | 1.38 ± 0.44 (12)* |

**Conclusions:**
1.- Foetal-neonatal transition causes oxidative stress evidenced by an oxidation of blood glutathione.
2.- This oxidation occurs in spite of the fact that the activity of antioxidant enzymes and the total antioxidant activity increases significantly.

## * 222

BONE MASS IN CHILDREN WITH CONGENITAL HYPOTHYROIDISM

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**Backgroud**: Bone loss may complicate hypothyroidism and hyperthyroidism; we evaluted if children with Congenital Hypothyroidism (CHT) treated with T4 from the neonatal period can have a modification of bone mass.
**Subjects**: 18 children (10 girls) with CHT aged 3.1-12.1 (mean ± SD: 6.1 ± 5.2): all were diagnosed by screening in neonatal period. The causes of CHT were: 7 athyreosis, 1 dyshormonogenesis, 9 ectopic, 1 hemiagenesis. The initial L-T4 dose was 7.8 ± 1.2 μg/Kg, at time of testing was 4.52 ± 1.3 μg/Kg and values of T3, T4, FT3, FT4 and TSH were normal. Physical and neurological developments of the children were normal. Controls (C): 36 sex and age matched healthy children.
**Measurement**: Bone mineral Content (BMC) was measured by double photon densitometry with $I^{125}$ (Osteoden-P, Nin, Italy) and expressed as BMC divided by bone width (g/cm²).
**Results**: Biochemical values of children with CHT and C were similar: (CHT vs C: PTH 25.1 ± 9.2 hg/l vs 24.9 ± 9.9; CT 39.14 ± 18.1 pg/ml vs 38.71 ± 17.1; 25OHD 27.41 ± 4.8 ng/ml vs 26.67 ± 3.7; 1,25 (OH)2D 103 ± 41 pmol/l vs 107 ± 52. No significant difference of BMC was found: 0.45 ± 0.11 vs 0.46 ± 0.12 g/cm².
**Conclusions**: Children with CHT diagnosed and treated from birth of various etiology, had no abnormalities of the main parameters of calcium metabolism and show a normal BMC.

## † 223

GROWTH HORMONE SECRETION IN CHILDREN WITH PRECOCIOUS PUBERTY TREATED WITH DEPOT GnRH ANALOGUES

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**Background:** Treatment of children with Precocious Puberty (PP) with Depot GnRH analogues can be associated with a significant decline in growth velocity (GV) and GH secretion. It is unknown if GH secretion is responsible of the very slow GV of children during treatment with GnRH analogues.
**Patients:** 8 children (6 girls) with PP before and after treatment with depot GnRH analogues (60 μg/Kg i.m. every 4 weeks for 6 months).
**Measurements:** GnRH testing done within 5 days before the third GnRH administration, indicated sustained gonadotropin suppression. GH secretion has been evaluated within 28 days of previous Depot GnRH analogue dose by administration of clonidine (CLON) and pyridostigmine plus GHRH (PD + GHRH) in two consecutive days.
**Results:** No difference was observed in GH secretion (GH peak) between children with GV < 4 cm/year (Group A) and those with GV > 5 cm/year (Group B) (CLON: 16.4 ± 5.8 vs 18.2 ± 7.3 μg/l; p > 0.05 - PD + GHRH: 37.3 ± 12.7 vs 40.1 ± 15.4 μg/l; p > 0.05). Also IGF levels were similar in the two groups.
**Conclusions:** GnRH analogues induces, particularly in some children, a significant decrease of GV; GH secretion is normal both in slow- and in normally-growing subjects.

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*IN VITRO* EFFECTS OF MAGNESIUM SULPHATE IN THE PULMONARY AND MESENTERIC ARTERIES FROM NEONATAL PIGLETS.

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BACKGROUND: Magnesium sulphate ($MgSO_4$) has been proposed to be an efficient treatment in persistent pulmonary hypertension of the newborn (PPHN). We compared the ability of $MgSO_4$ to inhibit the responses to several vasoconstrictors.
SUBJECTS: Isolated porcine pulmonary and mesenteric artery rings.
INTERVENTIONS: The vasorelaxant effect of $MgSO_4$ was evaluated under isometric conditions.
RESULTS: $MgSO_4$ (3-100 mM) produced a slight vasodilator effect in the pulmonary arteries (15.1 ± 3.7%, 20 ± 3.33% or 10.4 ± 0.9% in arteries precontracted with the thromboxane mimetic U46619, noradrenaline (NA) and KCl, respectively, n = 10). In contrast, in the mesenteric arteries $MgSO_4$ produced a marked endothelium-independent vasodilation (80.4 ± 4.0%, 93.1 ± 3.46% and 87.5 ± 1.93 in arteries precontracted with U46619, NA and KCl, respectively, n = 8). No differences were observed in the concentration-response curves to noradrenaline or U46619 nor in the vasodilatory effects of acetylcholine or sodium nitroprusside in pulmonary and mesenteric arteries under different $MgSO_4$ concentrations. In both arteries precontracted with U46619 removal of $Mg^{2+}$ from bath medium produced endothelium-dependent transient vasodilation.
CONCLUSIONS: $MgSO_4$ is a poor vasodilator of pulmonary arteries *in vitro*. Furthermore, $Mg^{2+}$ inhibits the endothelial production of NO. Thus, the beneficial clinical effects of $MgSO_4$ in PPHN do not appear to be related with a direct effect on pulmonary vascular smooth muscle.

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**The neurological and cognitive outcome of ELBW infants at the age of five to eight years: Prognostic value of CRIB, NICHD, gestational age and birth weight.**

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The increased survival of ELBW infants has led to search on early prognostic factors. We compared Apgar score, birth weight and gestationa age with illness severity indeces (CRIB, NICHD) in relation to the outcome of survivors.

During the years 1982-1987 96 children (53%) with birthweight below 1000 g survived at our hospital. The median birthweight was 820 g (540-995) and gestational age was 26 wks (22-33). In the follow-up 91 (95%) of the children underwent neuropsychological and neurological evaluation at the age 5-8 years. Cognitive functions were evaluated using standardized tests. CRIB and NICHD illness severity indices were calculated retrospectively for each infant. The median CRIB score was 5 (1-18) and the median NIHCD score was -0.1 (-1.9-1.6).

The risk of PIVH increased significantly with decreasing gestational age ($p$=0.001) and with increasing illness severity indices (CRIB, $p$=0.005; NICHD, $p$=0.008). PIVH was associated with abnormal neurological findings ($p$=0.02), abnormal cognitive functions ($p$=0.04).

Decreasing birthweight was associated with poor general outcome($p$=0.03), poor cognitive functions ($p$=0.03) and high risk of ROP ($p$=0.01). Similar associations were observed with low gestational age (general outcome, p=0.01; cognitive functions $p$=0.05; ROP, $p$=0.002). Of the illnes severity indices high CRIB-score was associated with poor general outcome ($p$=0.01) and poor cognitive functions ($p$=0.01) but not with ROP. The associations with NICHD were stronger (general outcome $p$=0.001, cognitive functions $p$=0.005, ROP $p$=0.02). Neurological findings could not be predicted from any of the early findings. The year of birth was not associated with any of the outcome variables.

Despite the increasing amount of surviving ELBW infants the amount of children with neurological handicap from this group did not increase. The prognostic value of the early findings was limited, but NICHD score seemed most promising. Although about half of the children had some problems, most of them were minor.

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MIDDLE EAR FUNCTION-CHANGES AFTER BIRTH

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**Hypothesis:** The middle ear of the fetus is said to be filled by fluid or by mesenchyme, or both. Air-conducted hearing should improve postnatally eather fast, if only fluid has to be replaced, or slowly, if mesenchyme is present. **Study design:** 20 healthy newborns were examined by click-evoked brain stem potentials in a 1st session 2 to 5½ and in a 2nd one 49 to 109 hours after birth. A more precise time schedule was not possible due to the sometimes delicate feelings of parents. Clicks were applied by head-phone and by a contact-transducer over the temporal bone. **Measurement:** Latencies of waves III and V were measured and plotted individually against stimulus intensities. Latencies corresponding to the same intensities from session 1 vs. session 2 were compared, and in the same way stimulus intensities corresponding to the same latencies, elicited via air-conduction and via bone-conduction as well. **Results:** Latencies from session 2 were sometimes equal, mostly shorter and never longer than latencies from session 1 (p < 0.0001). Intensities for gaining the same latencies were never higher, but mostly lower and rarely equal in session 2 vs. session 1. Differences of latencies between air- and bone-conducted stimulation were less clear due to physical difficulties with the contact-transducer. **Conclusion:** Middle-ear function of newborn babies improves markedly within hours or days after birth due to replacement of fluid in the tympanon by air.

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PREGNANCY OUTCOMES IN MOTHERS WITH IDDM: A POPULATION BASED STUDY IN NORTHRHINE, GERMANY.

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**Background:** Studies from centers of Diabetes care suggest and almost normal prognosis for children of mothers with IDDM. How do population based outcome measures compare to thes standards?.
**Population and Methods:** This study was performed in the Northrhine area with ≈ 100 000 births anually from 1988-93. Data from a perinatal quality assessment plan will used. Outcome parameters: perinatal mortality, macrosomia, cord blood pH > 7.1. Explanatory variables for poor outcomes: maternal smoking, education, use of prenatal care, ethnicity.
**Results:** For 2402 of 595 393 prenancies (0.4%) IDDM was noted as a known condition before pregnancy. Outcomes in IDDM versus NonIDDM mothers were: perinatal mortality: 2.7 versus 0.6%; macrosomia: 27.5 versus 9%; cord pH < 7.1; 3.1 versus 1.4%. The following parameters were associated with poor pregnancy outcomes: smoking, low education, use of prenatal care below average. **Conclusions:** A population based assessment in an area covering 1/8 of the German annual births shows a considerable excess in perinatal mortality and asphyxia in children of in mothers with IDDM. The high standards from centers of diabetes care have not yet been achieved for all children.

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THYROTROPIN(TSH), FREE THYROXINE(FT4), TRIIODOTHYRONINE(T3) AND REVERSED T3 (rT3) LEVELS IN PRETERM INFANTS BORN AFTER PLACENTAL INSUFFICIENCY.

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**Background:** Fetal thyroid hormone levels are determined by fetal thyroid function and perhaps by placental transfer of maternal thyroid hormones. Reduced fetal thyroid hormone levels may be found in placental insufficiency.
**Subjects:** 30 Preterm infants (gest.age 28-34 wks): 15 were born after placental insufficiency (study group), 15 served as controls (control group).
**Interventions:** TSH, FT4, T3, and rT3 in cord blood, and at day 1,3,5,7.

| Results (mean + s.d.): | | study group | control group | P (t-test, two-sided) |
|---|---|---|---|---|
| birthweight (g) | | 1040 ± 190 | 1445 ± 280 | 0.000* |
| gest.age (wks) | | 30.0 ± 1.4 | 29.6 ± 0.9 | 0.38 |
| cord blood: | TSH (mU/L) | 6.0 ± 2.9 | 18.9 ± 11.7 | 0.001* |
| | FT4 (pmol/L) | 10.8 ± 2.1 | 14.6 ± 3.3 | 0.001* |
| | T3 (nmol/L) | 0.33 ± 0.20 | 0.54 ± 0.42 | 0.109 |
| | rT3 (pmol/L) | 3870 ± 1124 | 4313 ± 1666 | 0.43 |
| first week: | TSH | 4.87 ± 2.06 | 4.18 ± 1.47 | 0.35 |
| | FT4 | 15.6 ± 3.4 | 15.6 ± 2.4 | 0.96 |
| | T3 | 0.75 ± 0.23 | 0.86 ± 0.27 | 0.28 |
| | rT3 | 2841 ± 673 | 2189 ± 384 | 0.007* |

**Conclusions:** Infants born after placental insufficiency had: 1) low FT4 levels in utero, which was not due to decreased placental transfer, 2) intact pituitary-thyroid axes, as was shown by the rapid increase of FT4 after birth, and 3) elevated rT3 levels after birth, suggesting an impaired hepatic deiodination pathway.
**Hypothesis:** Transient hypothyroxinemia is a common finding in very preterm infants, which may be treated by thyroxine (T4) supplementation. As deiodination of T4 to T3 may be decreased in preterm infants subjected to placental insufficiency antenatally, supplementation with T3, rather than with T4, may be preferred in these infants.

## ● 229

Title Diabetes incidence and ascertainment in children under 5 years for the UK, the Netherlands and Germany

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Background The reported incidence of type I diabetes varies widely, and increases have recently been reported in several countries. The aim of the study was to assess and compare the incidence and ascertainment rates for children under 5 in each country.
Subjects All children diagnosed under 5 years with primary insulin dependent diabetes 1992 in the UK and 1993 in the Netherlands and Germany.
Interventions Monthly reports of cases seen were made by paediatricians in each country through their respective Paediatric Surveillance Units. The diabetes association, specialist nurses, regional health authorities and office-based physicians provided secondary source data for validation.

| Results | UK | The Netherlands | Germany |
|---|---|---|---|
| Year of study | 1992 | 1993 | 1993 |
| Number of cases | 387 | 113 | 269 |
| Population under 5 | 4,183,970 | 967,083 | 4,440,677 |
| Incidence/100,000/yr | 9.3 | 11.7 | 6.1 |
| Ascertainment | 99% | 87% | 96% |

Conclusions The observed differences in incidence may help in the search for environmental factors involved in the development of type I diabetes. The study also shows that incidence, even of a relatively common disease, can be successfully assessed, with a high level of case ascertainment using the Paediatric Surveillance Unit framework.

## ● 230

**Measurements of Feto-Placental Blood Volume in Haemolytic Disease**

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***Background:*** Direct measurement of Red Cell Volume (RCV) and Blood Volume (BV) would help assess severity of fetal anaemia. Estimation of BV is possible at intravascular transfusion (Tx) with adult blood for anaemia. Calculation using changes in haematocrit (hct)[1], or HbF[2] or RhD+ proportions[3,4], may be compared. Hct changes under-estimate the true BV because of plasma extravasation.
***Subjects and Intervention:*** 15 Txs for fetal Rh haemolytic disease.
***Measurement:*** RCV measurement based on dilution of autologous red cells with transfused cells[1,2,3,4] and BV computed from RCV divided by pre-transfusion Hct (BV therefore not subject to error from changes in plasma volume (PV) after Tx).
***Results:*** **1.** BV predicted from HbF/HbA fits the regression equation $BV = 0.51 \times GA^2 - 165$.
**2.** After red cell Tx to human fetuses, plasma extravasation and decline in plasma volume (PV) accompany intravascular Tx so that total BV shows little change after Tx.
**3.** Changes in PCV predict a smaller BV than changes in HbF/HbA or in D+/D- proportions. The difference in calculated BV depends on the age of the fetus e.g. from near 0 at 20 weeks to almost 200 ml at 34 weeks gestation.
***Conclusions:*** Estimation of RCV and BV in the fetus with haemolytic disease may make the timing and magnitude of Tx more rational. If fetal erythropoiesis can be suppressed, neonatal jaundice may be reduced.

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## † 231

CUTANEOUS REFILLING TIME (CRT) AND HAEMODYNAMICS IN NEONATES

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Background, aim : The purpose of this study was to evaluate whether CRT measured in neonates is correlated to hemodynamic data obtained by Doppler-echocardiography.
Subjects: 95 neonates (without congenital cardiopathy) admitted to the NICU were included in this study (gestational age 32.3 ± 4.7 weeks; birthweight 1.6 ± 0.9 kg).
Interventions : CRT was measured after a pressure of around 100 mmHg for 3 seconds. Echocardiographic and pulsed-Doppler measurements were: aortic diameter (Ao), left atrial diameter (LA), LA/Ao ratio, shortening fraction, left ventricular output (LVO), flows in aorta, in left pulmonary artery and in patent ductus arteriosus (PDA). We had 3 groups of babies: no PDA (I), PDA without (II) or with (III) reversed flow in descending aorta (DAo). Low cardiac output (CO) was defined as <260 $ml.kg^{-1}.mn^{-1}$ in NN with PDA and <200 $ml.kg^{-1}.mn^{-1}$ in others; CRT was considered prolonged over 4.5 sec (mean CRT + 2 SD).
Results: In group I, CRT was correlated with LVO ($r = 0.734$; $p < 0.001$) and to calculated systemic arterial resistance (SAR) ($r = 0.538$; $p < 0.001$). A less strong correlation of LVO to CRT was found in groups II and III. The sensitivity and the specificity of CRT > 4.5 sec in the diagnosis of low CO are respectively 83% and 37.5%. A low CO is found in 5% of babies with CRT < 4,5 sec in group I, against 7% in groups II and III. Neonates in group I with CRT > 4.5 sec and LVO > 200 $ml.kg^{-1}.mn^{-1}$ have significantly higher SAR than neonates having a CRT < 4,5 sec and LVO > 200 $ml.kg^{-1}.mn^{-1}$.
Conclusions : Aortic flow appears to be the factor better correlated with CRT especially in the absence of PDA. Our results show that CRT < 4,5 sec is reassuring in neonates because it nearly allows one to rule out low CO. A prolonged CRT should lead to a complete hemodynamic evaluation. It does not always correspond to a low CO, and an increase in SAR can sometimes be found.

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**INFLUENCE OF EARLY NUTRITION AND FATTY ACID STATUS ON LATER DEVELOPMENT IN LOW-BIRTH-WEIGHT INFANTS**

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**Hypothesis:** Is fatty acid status 6 weeks postnatally associated with development in low-birth-weight(LBW) infants?
**Subjects:**87 LBW infants, mean birthweight 2036 g (1120-2500g)
**Setting:**Prospective cohort study in a secondary newborn unit.
**Interventions:** From postnatal day 10 up to day 42 12 infants received mother's-own-milk and 75 one out of three different preterm formulas. Plasma-cholesterol-ester(CE) and red-blood-cell(RBC) fatty acid contents were measured on postnatal day 42. At 18 months a Bayley development test was performed.
**Results:** Univariate regression analysis showed significant ($p<0.050$) relationships between both Bayley indices and CE and RBC long-chain-poly-unsaturated-fatty-acids(LCPUFA)ω3+ω6 contents,CE LCPUFAω3, CE C20:3ω6(dihomo-γ-linolenic acid),RBC C20:4ω6(arachidonic acid) and RBC LCPUFAω6 contents,and ratio RBC C22:4ω6(adrenic acid)/ C22:5ω6(docosapentaenoic acid).
**Conclusion:** In 6 weeks old LBW infants LCPUFA status correlates with later development. Ω6 fatty acids appeared to be more important than ω3 fatty acids. If not fed human milk, LBW infants may benefit from preterm formulas with LCPUFA.

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**RANDOMISED TRIAL OF FFP AND VOLUME EXPANSION IN VERY LOW BIRTHWEIGHT AND SICK PRETERM INFANTS.**

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**Background:** 25% of neonatal units in Britain and Ireland use Fresh Frozen Plasma (FFP) for the prevention of Intraventricular Haemorrhage (IVH), based on a previous randomised controlled trial. This did not show a significant change in clotting and concluded that improvement in outcome may have been due to volume expansion. We wished to test this hypothesis and to look at the effect on cerebral parenchymal lesions.

**Subjects:** 164 infants ≤ 1500 grammes or ≤ 34 weeks gestation at birth and ventilated within the 48 hours.

**Method:** Infants were randomised to either FFP, 4.5% Human Albumin Solution, 0.9% Saline or no extra routine fluid. Treatment was given as 10 mls/Kg over one hour within the first few hours after admission, repeated at 24 hours. Infants were eligible to receive further colloid as required for hypotension or acidosis according to our unit protocol. The main outcome was serial cranial ultrasound scan lesions.

**Results:** There was no significant difference between the groups in cerebral parenchymal lesions or IVH. There was a lower mortality in the colloid groups.

**Conclusions:** These findings do not support the routine use of Fresh Frozen Plasma in this group of infants for the prevention of intracranial lesions. We suggest that further investigation into the use of colloid is appropriate.

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**NEEDLELESS INJECTION DEVICES - HOW DEEP DO THEY GO?**

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**Background:** Spring-driven needleless injection has been used in paediatric insulin delivery. The physical distribution of the dose is poorly described.

**Subject:** 7 day old piglet under anaesthesia

**Method:** The device studied was the Vitajet, marketed in the UK for diabetic use. 4 sites were injected. Site A; water soluble dye, Indocyanin Green 0.3mls (equivalent to 30 units of insulin), site B; particulate India ink, 0.3mls. The piglet was then killed. Sites C and D were injected post mortem with India ink, 0.2mls and 0.3mls respectively. Tissue blocks were prepared and formalin fixed.

**Results:** The injection penetrated dermis and subcutaneous fat to a depth of 10 -15 mm. At the fascial plane spread was 10 to 25 mm. At site B inadequate device application led to superficial distribution of the ink with no significant penetration of subcutaneous fat. There was no difference in pre and post mortem dye distributions, 0.2 and 0.3 ml volumes nor between the soluble dye and particulate ink.

**Conclusion:** The disruption of a cone of tissue may be causally related to blood frequently seen at the injection site; bruising is a common reason for stopping use of these needleless injection devices. An injection's physical distribution will affect both drug absorption and local side effects. Further study is required before these devices are promoted to paediatricians and families as a suitable alternative to needle injections.

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**EEG-Activity Suppression during ventilation in preterm infants as an indicator of increased risk for intracerebral complivations**

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Only little data exist on bioelectrical activity of the brain in preterm infants during the periods of increased risk of intracerebral complications during the first days of life.

In order to evaluate parameters influencing the EEG-activity, polygraphic recordings including EEG, $tcpO_2/pCO_2$, $SaO_2$, and blood pressure (RR), in 37 ventilated preterm infants (gestational age (GA) 25 to 34 weeks,$\chi$:29.6, birthweight 535 to 2640g, $\chi$:1364) and 7 spontaneously breathing infants (GA 29 to 32 weeks, $\chi$:31.1, birthweight 645 to 1850g, $\chi$: 1336) were performed during the first weeks of life. In the obtained 24 hour recordings, mean power (FFT), mean burst power, duration of bursts and interburst intervals, and power of interburst intervals within the discontinuous EEG patterns were calculated by means of computerized quantitative analysis. In constrast to spontaneously breathing infants, a drastic EEG activity suppression, characterised by increased interburst intervals, was found in all ventilated infants on the first 10 days of life. In addition to gestational age, several other factors affected EEG activity significantly: Application of surfactant correlated with an EEG power decrease and interburst-interval prolongation.

Moreover periods of milder hyperventilation, sedation, the occurance of a severe sepsis and low blood pressure levels correlated with an interburst-interval prolongation and decrease of interval EEG-activity (Wilcoxon Rank Test, $p<0.05$). After an initial major EEG activity suppression in ventilated infants a high incidence of pathological ultrasound findings was encountered (Mann Whitney Rank Sum Test, $p<0.05$) during the following 5 days.

Conclusions: Changes of homeostasis of bloodpressure and blood gases during ventilation significantly diminish EEG activity. Suppressed EEG-activity might point to an increased risk for structural brain lesions. Suppression of bioelectrical brain activity might be accompanied by impaired autoregulation of cerebral perfusion and thus by an incresed risk for intracranial hemorrhage. This study was supported by the Deutsche Forschungsgemeinschaft WU 171 1-1.

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PERIPHERAL VENOUS OXYHAEMOGLOBIN SATURATION (SvO2) REFLECTS CENTRAL SvO2 IN SICK NEONATES.

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**Background**: Central SvO2, a flow weighted average of SvO2 from all vascular beds, is a guide to the adequacy of tissue oxygenation, but is a technically difficult measurement in sick neonates. Peripheral SvO2 may be better as peripheral blood flow is more affected when circulation is impaired. We compared central SvO2 with a non-invasive measurement of peripheral SvO2 by Near Infrared Spectroscopy (NIRS) with venous occlusion.

**Subjects:** Neonates undergoing intensive care.

**Interventions**: Eighteen measurements of central SvO2 by co-oximetry of right atrial blood were compared with simultaneous measurements of peripheral SvO2 by NIRS with venous occlusion.

**Results**: Median (range) central SvO2 was 81.5% (60.2% to 93.7%). Median (range) peripheral SvO2 was 67.3% (56.2% to 77.8%). There was a significant correlation between the two measurements, n=18, r=0.59, p<0.01.

**Conclusions**: Frequent non-invasive measurements of peripheral SvO2 are possible using NIRS with venous occlusion. We have found a reasonable relationship between central SvO2 and peripheral SvO2. This method may provide useful information about the adequacy of tissue oxygenation.

## † 237

IN VITRO ACTIVATION OF CLASSICAL AND ALTERNATIVE PATHWAY OF THE COMPLEMENT SYSTEM IN TERM AND PRETERM INFANTS AND ADULTS

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**Background:** We studied the in vitro activation of alternative pathway (APW) and classical pathway (CPW) to asses the capacity of complement mediated antibody dependent (CPW) and antibody independent (APW) host defense in term and preterm infants.

**Subjects:** Healthy adults and 3 groups of infants of different gestational age (GA).

**Interventions:** Citrated plasma samples were incubated with either IgG aggregates, which primarily activates along the CPW, or zymosan (ZY), which mainly activates along the APW. The activation products C3a (CPW and APW activation), C1rsC1Ina (CPW activation) and C3bBbP (APW activation) were measured by EIA tests.

**Results:** (Medians, significance of differences by Kruskall Wallis test)

| incubation | activation product | A. adults n=24 | B. GA 37-40 weeks n=74 | C GA 32-36 weeks n=21 | D GA <32 weeks n=23 | difference |
|---|---|---|---|---|---|---|
| IgG | C3a ng/ml | 5833 | 6795 | 7489 | 4489 | A=B=C=D |
| IgG | C1rsC1Ina U/ml | 9.2 | 9.3 | 7.1 | 6.7 | A=B=C=D |
| ZY | C3a ng/ml | 12089 | 6136 | 3469 | 122 | A=B>C>D |
| ZY | C3bBbP U/ml | 103,4 | 41 | 12 | 8 | A>B>C=D |

**Conclusion**: There is no difference in the activation via CPW among the groups. However, preterm babies normally suffer from antibody deficiency. Thus, they may not be able to initiate sufficient CPW activation. On the other hand, the antibody independent APW activation is severely impaired in infants, especially in preterm babies.

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**INCREASED INTRAMITOCHONDRIAL AMOUNT OF MUTANT CARBAMYLPHOSPHAT SYNTHETASE (CPS) IN THE LIVER OF A SIBLING WITH MILD COURSE OF CPS DEFICIENCY IN COMPARISON TO HER SISTER WITH LETHAL OUTCOME**

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**Background:** We investigate whether hepatocytes can increase the intramitochondrial amount of mutant carbamylphosphate synthetase (CPS) postnatally. This cell biological process may contribute to the heterogeneity of urea cycle defects. Therefore, we compare the intramitochondrial amount of CPS in the liver of two siblings with CPS deficiency at different postnatal periods.

**Subjects:** We examine two sisters of consanguine parents. The CPS activity of both is 0 %. One sister has presented with excessive hyperammonemia and died on the 4th day of life. The younger sister has undergone early treatment and is doing well (liver biopsy after 1 month of life).

**Interventions:** Using a polyclonal antibody against CPS, the amount of mutant CPS is determined in the liver of patients with CPS deficiency and the control patient by western blot and immunoelectron microscopy. The labelling density over mitochondria and cytosol, volume density of nucleus and mitochondria, surface density of mitochondria, and the absolute volume of the nucleus are evaluated by stereological methods.

**Results:** Western blot analysis reveals that the amounts of mutant CPS are distinctly decreased in both patients in comparison to the control liver. However, the liver of the patient, who is doing well, contains more mutant CPS than the liver of her sister. The stereological evaluation indicates that this is mainly due to an increase in mitochondrial volume per hepatocyte.

**Conclusions:** Our results suggest that hepatocytes compensate a decreased enzyme activity of CPS by increasing the intramitochondrial amount of mutant enzyme in the first postnatal weeks.

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WOULD PARENTS IN THE NICU PREFER TO FOREGO CONSENT DECISIONS FOR ENROLMENT OF THEIR INFANTS IN CLINICAL TRIALS?

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**Background/aim:** Although the current doctrine of informed consent demands that competent subjects or their proxies be the primary decision makers after full education about the risks and benefits of the proposed study, it has not been shown that this involvement is desired by parents in the NICU. We determined how much parents wish to be involved in decisions to enrol their infants in clinical trials.
**Subjects:** 140 of 167 sets of parents who had been asked for consent to enrol their infants in 1 of 3 trials. Illness severity of the 140 infants ranged from very unstable to very stable. Mean BW (SD) was 1796 g (1112), mean GA (SD) 31.2 wks (4.9). Median age was 1 day.
**Methods:** After giving consent, or refusal, parents rated their agreement with the statement "I would prefer to have the doctors advise me whether my baby should be in the study, rather than asking me to decide", using a 7-point scale anchored at 1-strongly disagree and 7-strongly agree. This item was part of a more extensive questionnaire with good reliability and face validity.
**Results:** 32% of responders agreed or strongly agreed with the above statement. There was no significant correlation with this preference and the infant's illness severity, sociodemographic variables or other parental attitudes towards research.
**Conclusion:** Many parents in the NICU would prefer to forego consent decisions for enrolment of their infants in clinical trials.