oxygenation, which may play a role in the multifactorial pathophysiology of necrotizing enterocolitis (NEC).

The aim of this study is to evaluate by NIRS the effects of bolus and continuous enteral feeding on splanchnic and cerebral oxygenation in preterm infants with normal feeding tolerance.

Methods Eighteen healthy preterms (GA 27–32 weeks), tolerating at least 100 ml/kg^{-1}/day^{-1} of fortified human milk or preterm formula, underwent a 6-hours simultaneous monitoring of cerebral and splanchnic oxygenation using NIRO-200 oximeter. Sensors were placed on frontal and sub-umbilical region. During the monitoring they randomly received a 10-minutes bolus meal and a 3 hours continuous meal.

Recorded values of cerebral and splanchnic Tissue Oxygenation Index (TOI) were clustered in 5-minutes intervals and compared between different feeding techniques using Wilcoxon Signed Ranks Test. Statistical significance was set at p≤0.05.

Results Splanchnic oxygenation significantly decreased (p<0.05) during continuous feeding, from 1.30' hour after the beginning to almost the end of the feed. No differences were found on cerebral oxygenation.

Conclusions To the best of our knowledge, this is the first study comparing the effect of different feeding techniques on splanchnic and cerebral oxygenation in preterms. A significant reduction in splanchnic oxygenation was observed during continuous enteral. A possible role of these findings on the multifactorial NEC pathogenesis remains to be investigated.

347 IS FOLIC ACID SUPPLEMENTATION REALLY NECESSARY IN PRETERM INFANTS WITH ≤32 WEEKS OF GESTATION?

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Background and Aims The main goal of this study was to determine the necessity of folic acid supplementation in preterm infants.

Methods Infants born ≤32 weeks of gestation were included in the study with parental consent. Blood samples for the determination of serum folate levels were obtained on days 14 and 28 postnatally, as well as 36 weeks postconceptionally (or just before discharge if patients are discharged before 36 weeks) - samples A, B and C, respectively. Infants were divided into three groups based on mode of feeding; human breast milk (HBM), fortified HBM or preterm formula (PF).

Results A total of 162 preterm infants were enrolled in the study, 17(10.5%) of whom received HBM alone, 94(58%) received fortified HBM and 51(31.5%) were fed with PF. Comparisons between groups revealed that preterm infants in the fortified HBM and PF groups to have significant higher serum folic acid levels in samples C compared to those receiving HBM alone (p<0.001 for both). None of the preterm infants included developed folate deficiency during the study period.

Conclusion This is the largest and most comprehensive clinical study to date evaluating the need for folic acid supplementation in preterm infants who were fed using either modern PFs or milk fortifiers mixed with HBM. Our results suggest that fortified HBM use in preterm infants can alleviate the need for further folic acid supplementation. On the other hand, in preterm infants who are unable to receive HBM folic acid support can be provided with PFs.

348 EFFECTS OF GLUTAMINE SUPPLEMENTATION ON BRAIN DEVELOPMENT OF VERY PRETERM CHILDREN: A FOLLOW-UP STUDY AT SCHOOL-AGE

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Background and Aims The amino acid glutamine has been shown to reduce the number of serious neonatal infections in very preterm children (< 32 weeks of gestation), which may benefit long term brain development. The aim of this study was to elucidate potential effects of glutamine supplementation on brain development in very preterm children at school-age.

Methods First, we investigated growth trajectories of head circumference, weight, and length in the first year for 65 very preterm children that originally participated in a randomized controlled trial on enteral glutamine supplementation between day 3 and 30 of life. Second, we measured brain structure volumes and white matter integrity for 52 very preterm children at school-age, using magnetic resonance imaging (MRI) and Diffusion Tensor Imaging (DTI), respectively. Furthermore, differences in functional outcomes were explored. Group differences were tested using ANOVA statistics.

Results Glutamine supplementation was associated with improved growth trajectories of head circumference in the first year of life (d=0.66, p=0.03). Furthermore, glutamine supplementation increased white matter (d=0.54, p=0.03), hippocampus (d=0.47, p=0.02), and brain stem (d=0.54, p=0.04) volumes at school-age. All differences were strongly related with the number of serious neonatal infections (all p<0.02). Glutamine supplementation did not influende measures of motor, cognitive, and behavioral functioning at school-age.

Conclusions We found evidence that reduction of serious infections by neonatal glutamine supplementation improves head growth in the first year of life, as well as brain structure volumes at school-age. This suggests an early programming effect of nutritional intervention with enteral glutamine.

349 EFFECTS OF POSTNATAL ENERGY AND MACRONUTRIENT INTAKES ON GROWTH IN EXTREMELY PRETERM INFANTS: A POPULATION-BASED STUDY

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Background Extremely preterm infants often experience growth failure and adequate nutritional supply may be difficult to achieve. It is still debated to what extent nutrition affects growth at an early stage in life. The aim of this study was to explore associations between energy and macronutrient intakes and growth.

Methods The study population consists of extremely preterm infants born in Sweden during 2004–2007. Detailed data of nutritional intakes and anthropometric measurements were retrieved from hospital records.

Results Infants (n=602) had a mean±SD gestational age of 25.3±1.1 weeks and birth weight 765±171g. From birth to 70 days of age, energy and protein intakes were 119.3±11.3kcal/kg/day and 3.2±0.4g/kg/day respectively. Infants showed postnatal growth failure: mean standard deviation scores (SDS) decreased by 1.5 for weight, 2.3 for length and 0.8 for head circumference.

The following confounders were included in the multivariate analyses: Gestational age, CRIB-score, duration of mechanical ventilation, days on postnatal steroid and antibiotics treatment, infant

sex and baseline anthropometrics. Energy intake was significantly correlated with weight gain (r=+0.31, p<0.001), length gain (r=+0.20, p<0.001) and head circumference growth (r=+0.26, p<0.001). In addition, protein intake was independently positively associated with weight gain, and the effect of macronutrient intakes on growth varied with postnatal age.

Conclusions Extremely preterm infants in Sweden received lower macronutrient intakes than recommended and showed postnatal growth failure. We found significant positive correlations between intakes of energy and macronutrients and growth. This suggests that optimized energy and macronutrient intake is important to prevent growth failure in these vulnerable infants.

350 EFFECTS OF DIFFERENT FATTY ACIDS ON RED BLOOD CELL MORPHOLOGY

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Background and Aims Recently echinocytosis and subsequent haemolytic anaemia was described in a premature infant receiving omega-3 fatty acids (Omegaven) in parenteral nutrition. It was presumed that omega-3 fatty acids caused echinocytosis. No study has been done to compare the effect of different fatty acids used in parenteral nutrition on human red blood cell (RBC) morphology. We therefore studied the effect of omega-3 fatty acids (Omegaven) and omega –6 fatty acids (Intralipid) at different concentrations on RBC in vitro.

Methods Blood samples were obtained from 12 healthy adult volunteers. Aliquots with 0.5 ml of washed RBC resuspended in autologous plasma to a hematocrit of 48% and containing 0%, 5%, 10%, 20%, 30% and 40% of Omegaven or Intralipid were prepared and incubated for 30 min at 37 °C. The cells were then fixed with 1% glutaraldehyde and inspected under an inverted brightfield microscope. The extent of echinocytosis was quantified by means of the morphological index (MI), calculated according to the standard protocol.

Results It was found that at concentrations equal to and higher than 20%, Omegaven produced significantly higher RBC morphological index (MI) than Intralipid: mean MI at 20% for Intralipid was 0.61±0.24 and for Omegaven 1.12±0.43 (p<0.01), whereas at 40% MI was 1.47±0.37 and 2.48±0.66 for Intralipid and Omegaven, respectively (p<0.01).

Conclusions At concentrations over 20% Omegaven is more likely to cause echinocytosis than Intralipid. The higher concentrations may occur in vivo if Omegaven is given separately from other parenteral nutrition fluids (two-in one).

351 DIFFERENTIAL REGULATION OF CORD BLOOD NESFATIN-1 IN LARGE FOR GESTATIONAL AGE PREGNANCIES

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Background and Aims Large-for-gestational-age (LGA) infants are at increased risk for developing alterations in metabolic programming, which may lead to impaired glucose homeostasis during infancy, childhood and adulthood. Adipocytokines play an important role in short- and long-term energy balance, insulin resistance and fetal growth. The objective of the present study was to investigate circulating concentrations of nesfatin-1 (novel adipocytokine, also expressed by the gastric mucosa and pancreatic β-cells) in fetal samples from LGA and appropriate-for-gestational-age-(AGA) pregnancies and study their association with gender, parity, and delivery mode.

Methods Cord blood nesfatin-1 concentrations were prospectively measured by enzyme-linked immunosorbent assay in 40 LGA (9 born from diabetic mothers and 31 born from non-diabetic mothers) and 20 AGA singleton full-term infants.

Results Cord blood nesfatin-1 concentrations were lower in LGA compared to AGA neonates, after controlling for confounding factors (b= –0.206, p=0.005, SE 0.07). However, cord blood nesfatin-1 concentrations were elevated in infants born from mothers presenting with gestational diabetes mellitus (GDM), compared to those born from non-diabetic mothers, after controlling for group (b=0.190, p=0.050, SE 0.10). Finally, cord blood nesfatin-1 concentrations were lower in cases of vaginal delivery (b=0.11, p=0.042, SE 0.05).

Conclusions Down-regulation of nesfatin-1 in LGA fetuses probably represents a negative feedback exerted by adipose tissue on nesfatin-1 production. On the other hand, fetal nesfatin-1 concentrations are higher in cases of GDM, probably indicating the possible involvement of nesfatin-1 in the regulation of insulin secretion from pancreatic β-cells. Finally, vaginal delivery-associated inflammation could probably account for lower cord blood nesfatin-1 concentrations.

352 LONGITUDINAL INFUSION OF INSULIN-LIKE GROWTH FACTOR-I AND IGF-BINDING PROTEIN-3 COMPLEX TO FIVE PRETERM INFANTS - PHARMACOKINETICS AND SHORT TERM SAFETY

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Introduction In preterm infants, low levels of insulin like growth factor-I (IGF-I) and IGF binding protein 3 (IGFBP-3) are associated with impaired brain growth and retinopathy of prematurity (ROP).

Treatment with IGF-I/IGFBP-3 may be beneficial for brain development and decrease the prevalence of ROP.

Methods In a phase II pharmacokinetic and safety study, five infants (3 girls) with a median (range) gestational age (GA) of 26+6 (26+0 – 27+2) weeks and birth weight (BW) of 990 (900–1212) g received continuous intravenous infusion of rhIGF-I/rhIGFBP-3. Treatment was initiated during the first postnatal day and continued for a median (range) duration of 168 h (47–168) in doses between 21–111 μg/kg/24h.

Results Treatment with rhIGF-I/rhIGFBP-3 was associated with higher serum IGF-I and IGFBP-3 concentrations (p<0.001) than model-predicted endogenous levels. Out of 74 IGF-I samples measured during study drug infusion, 37 (50%) were within target range, 4 (5%) above and 33 (45%) were below. Predicted dose of rhIGF-I/rhIGFBP-3 to establish circulating levels of IGF-I within the intrauterine range in a 1000 g infant was 75–100 μg/kg/24 h. No hypoglycemia or other adverse effects were recorded.

Discussion Continuous intravenous infusion of rhIGF-I/rhIGFBP-3 was effective in increasing serum concentrations of IGF-I and IGFBP-3. Administration under study conditions was safe.

353 PRETERM BIRTH AND THE METABOLIC SYNDROME: A SYSTEMATIC REVIEW AND META-ANALYSIS

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