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INSULIN-LIKE GROWTH FACTORS AND THEIR BINDING PROTEINS IN EARLY MILK FROM MOTHERS OF PRETERM AND TERM INFANTS AND THEI BIOLOGICAL RELEVANCE

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Background: Breast fed preterm infants often show a better neurological outcome than formula-fed. The benefit of human milk is partly ascribed to it's content of the growth promoting insulin-like growth factors (IGFs). The aim of this study was to investigate, whether the content of IGFs und Their binding proteins (IGFBPs) is higher in human milk from mothers of preterm infants than of term infants and to test their biological relevance.

Methods: In a prospective study we investigated the concentrations of IGF-I, IGF-II and their binding proteins IGFBP-2 and IGFBP-3 in human milk from mothers of 30 preterm infants (<31 SSW) and of 19 term infants (>37 SSW) at day 7 and 21 after birth by means of an RIA, and the protein content of human milk by the Bichinonic acid (BCA) method. We analyzed the specific proteolysis of IGFBP-2 in human milk and the stability of 125I-IGF-I and 125IGFBP-2 in the presence of gastric juice from neonates.

Results: Mean concentrations (±SD) of IGF-I(2,8 ± 0,2 vs. 2,3 ± 0,1 ng/ml), IGF-II (12,0 ± 0,4 vs. 12,2 ± 0,5 ng/ml) and IGFBP-3 (100,0 ± 5,1 vs. 80,0 ± 5,8 ng/ml) did not differ in human milk of preterm versus term infants on day 7. The content of IGFBP-2 (3144 ± 172 vs. 2428 ± 188 ng/ml) was higher in preterm human milk ($p<0,05$). IGF-I ,IGF-II and IGFBP-2 did slightly change until day 21. IGFBP-3 decreased from day 7 to day 21 by 41%/ 27% in human milk of preterm/ term infants ($p<0,05$). The protein content in human milk of preterm infants was on day 7 (2,5 ± 0,1 g/dl) higher than on day 21 ($p<0,05$). On day 21 the protein content was equal to term infants (1,9 ± 0,1 g/dl). Preterm human milk contained about 42% more IGFBP-2- fragments of 14 und 25 kDa ($p< 0,05$). Incubation with gastric juice led to a complete digestion of 125IGFBP-2 and a partial digestion of 125I-IGF-II, while complexation with each other protected IGF-II and IGFBP-2 from cleavage.

Conclusion: We suggest that IGF-II and IGFBP-2 play a role in the nutrition of preterm infants. Both are found in a constant level in human milk and IGF-2 showed a higher concentration in preterm than in term human milk for the first 3 weeks. IGFBP-2/IGF-II-complexes can partly pass the stomach and may exert their promotive effects in the intestine. Taken together it can be concluded that preterm infants profits best from breast milk of it's own mother.

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THE "NEW"BRONCHOPULMONARY DYSPLASIA. EPIDEMIOLOGICAL STUDY ON THE EURONEONET DATABASE

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Background: Bronchopulmonary dysplasia (BPD) has classically been related to the use of high oxygen concentrations and mechanical ventilation in infants with respiratory distress syndrome (RDS). However, an increasing number of very low birth weight infants (VLBWI) develop BPD without having acute RDS, which has been termed "new" BPD.

Aim: To identify the characteristics of VLBWI who develop this "new " form of BPD.

Methods: This is a multicenter, prospective, longitudinal study of a cohort of 1798 VLBWI born in 2001 and 2002, at one of the 30 Spanish NICU included in EuroNeoNet initiative. The database, including demographic characteristics, risk factors, interventions and outcomes, was searched to identify babies alive at 36 weeks PMA (n=1549). BPD was diagnosed (need of oxygen at 36 PMA) in 221(14%) babies, 32 of who did not have RDS. An univariate and logistic regression analysis was used to asses the risk factors for BPD

Results: In comparison to the classical BPD, babies with the "new" BPD were more mature, had a higher birthweight, needed less resuscitation manoeuvres and respiratory support, had a lower incidence of PCA, but a higher one of early sepsis (7.4 vs. 12.5%) and NEC (6.9 vs. 21.9 %). Multifactorial analysis in infants without RDS (n=804), showed an increased risk for BPD related to use of CPAP (OR 3.6; 95% IC 1.5–8.8) and mechanical ventilation (4.8; 1.9–11.8), and to the presence of both, early sepsis (9.1; 1.9–42.4) and late sepsis (4.8; IC 2–11.1). However, in patients with RDS (n=745) we showed an increased risk related to CPAP, mechanical ventilation, late sepsis and PDA (1.7, 1.1–2.6), but not with early onset sepsis.

Conclusion: As previously reported (1), we showed risk factors of developing DBP in infants with and without RDS are CPAP, mechanical ventilation, and late sepsis. Nevertheless, in babies without RDS, BDP is associated with early sepsis, and in those with RDS with PDA. Despite the small number of patients without RDS who developed BPD in our cohort, the higher incidence of early sepsis and NEC point out toward prenatal factors related to fetal inflammatory disease (2). (1) Rojas MA et al. J Pediatr 1995;126:605–10. (2) Lyon A. Eur J Pediatr 2000;159:798–802.

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COMPARISON OF RESUSCITATION OF PIGLETS WITH 21% AND 100% OXYGEN AFTER EXPOSURE TO INFLAMMATION AND HYPOXIA

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Objective: To assess if endotoxin increases vulnerability to hypoxia and if resuscitation with 100% O2 increases brain damage in the presence of inflammation. **Method:** After anaesthesia and surgery, newborn piglets (n=31) were randomized to four interventional groups. Two groups received pretreatment with saline for 60 min followed by hypoxia and resuscitation with 21% (Group I, n=8) or 100% oxygen (Group II, n=8). The other two groups received pretreatment with endotoxin for 60 min followed by hypoxia and resuscitation with 21% (Group III, n=7) or 100% oxygen (Group IV, n=8). Hypoxia was administered until base excess (BE) reached –20 mmol/L. Reoxygen with either 21% oxygen or 100% oxygen was administered for the first 30 minutes, followed by 21% oxygen for 150 min for all groups. During the experiment, we measured extracellular brain tissue glucose, glycerol, and lactate/pyruvate by microdialysis, brain tissue oxygen tension and laser doppler flow.

Results: Administration of endotoxin caused a reduction in the time to reach BE –20 by median 31.5 minutes compared with saline ($p<0.05$). We found no differences in biochemical markers, brain tissue microcirculation or brain tissue oxygen tension between piglets pretreated with saline or endotoxin and resuscitated with room air or 100% oxygen in the four groups

Conclusion: Endotoxin and hypoxia acted synergistically in inducing arterial acidosis. In the presence of experimental inflammation, 21% seems as safe as 100% O2 in reoxygenating newborn piglets.

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BABYLINK - A WEB BASED TOOL TO IMPROVE COMMUNICATION BETWEEN CLINICIANS AND PARENTS IN A NEONATAL UNIT

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Background: There is an ever-increasing demand for improved communication with parents and their families. At present, parents gather information from multiple sources, which can lead to incorrect and/or inconsistent advice and information being received. The aim of this project was to develop, and evaluate a system that gives parents secure access via the internet to clinical information, extracted automatically from the electronic patient record and presented in a format appropriate to parents. **Method:** Software has been written that searches the electronic record for any information specified by the system administrator, such as diagnoses, treatments and records of communication. The system then links automatically to a library of short parent information templates and creates a parent report that is clinically relevant to the problems of the individual baby. The administrator can define the format of the reports, as well as the frequency and time interval sampled. Reports are encrypted and sent to an internet server. Parents access the reports on the Babylink website (www.babylink.info/edinburgh), using their own log-in and password. They can also view their baby's diary, which contains photographs and non-clinical messages written by the staff. The web-site has an open area providing general details about the neonatal unit and generic information about common neonatal problems. As part of data validation, reports have been checked manually for accuracy. Parents can comment or ask specific questions about their baby on-line. This feedback has been used to develop the website and the content of the reports. The project was approved by the local ethics committee and parents give written, informed consent before information is forwarded to the website.

Results: The reports and diaries have been successfully implemented. To date the system has been live for 6 weeks. 23 families have been accessing reports on the internet. Two refused to be involved. There has been no negative feedback, with parents expressing very positive views. Many constructive comments have helped develop the website and the parent reports.

Conclusions: This system offers the facility for parents to access specific, up to date information about their baby. It can be used with any electronic record system from which data can be exported. Further developments include prospective tailored information about discharge planning and care of the baby at home. The effect of the system on parental perceptions of communication is being evaluated.

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ASYMPTOMATIC CONGENITAL CYTOMEGALOVIRUS INFECTION

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Background: Cytomegalovirus (CMV) is the most common congenital infection in developed countries with reported incidences varying from 0.15% to 2.0%. Congenital CMV infection may be a cause of a congenital syndrome or run without symptoms. Approximately 90% of congenitally infected infants are asymptomatic at birth but may still present handicaps at a later age.

Aims: The objectives of the present study were to evaluate the importance of this agent as cause of morbidity and long term sequelae, and to assess the utility of the different methods of congenital CMV infection screening

Methods: Between May and August 2002, 757 consecutive newborns were screened for CMV infection by Polymerase Chain Reaction (PCR) in cord blood and through the isolation of CMV by *shell-vial* from urine on the first two days of life. Epidemiological characteristics of the mothers and newborn were analysed from medical records. Follow-up was done at 3, 6, 9, 12, 15 and 18 months with neurologic, audiologic, ophthalmologic and development assessments.

Results: Asymptomatic congenital CMV infection was diagnosed in 5 out of 757 (0.7%) by means of a virus culture in urine. PCR in cord blood was negative in all cases. In three newborns, within the first 3 weeks of life, the clinical findings included: pneumonia (1); bone marrow failure (1); hepatitis (2); basal ganglia vasculitis (2). At 18 months, follow-up of two infants showed short stature (1), minor abnormal neurodevelopment (1) and partial hearing loss (1).

Conclusion: The incidence of congenital CMV infection was similar to that reported in other studies on highly immune populations. Urinary CMV culture is a reliable and convenient method, and may be a screening tool for the detection of congenital CMV infection. Infants with asymptomatic congenital CMV infection may have severe diseases that are not clinically evident at birth. In our series of studies, sequelae were found in 3 out of 5 (60%) children. Funded by Science and Technology Foundation

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EARLY FEEDING TOLERANCE IN VERY LOW BIRTH WEIGHT INFANTS WITH INTRAUTERINE GROWTH RETARDATION

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Background: It is unclear if special feeding guidelines are necessary for SGA infants and if the extent of intrauterine growth retardation (IUGR) should be considered an important factor in decisions about their enteral nutrition. We conducted a retrospective cohort study to evaluate whether IUGR (birth weight and/or length at least 1.28 standard deviations (SD) below the mean for gestational age) was independently associated with early feeding intolerance in VLBW infants

Methods: All infants admitted during 2000–2003 to our NICU who lived for at least 28 days were included in the study if they had BW ≤1500 g and no major congenital anomalies. They were fed following a standardized protocol beginning within 48 hours of age with ≤20 ml/kg daily increments. Feeding tolerance was assessed as the age at which full enteral feeds (150 mL/kg/d) were achieved. Multiple regression analysis was used to identify factors that might influence early feeding tolerance during hospitalization

Results: 78 SGA and 143 AGA infants met the inclusion criteria. SGA infants had a similar BW (1188±246 vs 1138±227 g), higher GA (31.7±1.7 vs 28.6±1.8 wks; $p<0.001$), lower birth Z scores (ZsW -1.65±0.64 vs -0.06±0.74, ZsHC-1.54±0.74 vs -0.16±0.67, ZsL -1.82±0.89 vs -0.13±0.65; $p<0.0001$) and lower CRIB score (1.0±1.7 vs 2.6±2.9; $p<0.0001$) than AGA infants. Thirty-nine (50%) SGA infants had all the 3 Zscores <-1.28 SD (Symmetric SGA) and 20 (16.7%) had 2 Zscores <-2 SD (Severe SGA). SGA infants reached full enteral feeding earlier than AGA infants (19.8±10.1 vs 24.9±12.2 days of life; $p = 0.018$) and showed shorter time to achieve full feeds after initiation of milk feeds (17.0±9.0 vs 21.4±11.8 days; $p =0.046$). No difference was found in percentage of human milk intake from the beginning of milk feeding until full enteral feeds were achieved (59.4±32.2 vs 52.6±31.8%). When confounding variables were controlled in a multivariate regression model (r2 0.52), Zscores at birth and simmetric or severe IUGR were not significantly associated with the age of full enteral feeds; independent predictors were GA (coeff -3.6, $p <0.0001$), CRIB score (coeff 0.65, $p =0.026$) and percentage of human milk intake (coeff -0.44, $p =0.017$)

Conclusion: In our population IUGR did not influenced early feeding tolerance of VLBW infants