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### BIRTHWEIGHT, GESTATIONAL AGE AND TYPE OF DELIVERY: COMPARISON BETWEEN TWO HOSPITALS WITH DISCREPANT RATES OF CAESAREAN SECTION.

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**Background:** Although caesarean sections are more common for heavier babies and for those who are preterm or post-term, caesarean rates have increased in all birthweight categories in several countries.

**Objective:** To analyse the distribution of birthweight and gestational age according to type of delivery in two maternity hospitals with discrepant caesarean section rates in Brazil.

**Methods:** The study was a retrospective analysis of all singleton live births at two hospitals in Ribeiryo Preto, Brazil, in 1999, corresponding to 70% of all deliveries in the city, one being public and the other private. Mean birthweight and mean gestational age and the distribution of birthweight and gestational age according to the type of delivery (vaginal or caesarean) were analysed in each hospital.

**Results:** The caesarean rate was 18.9% in the public maternity hospital and 84.3% in the private one. Mean birthweight in the public hospital was 3200g and 3279g for vaginal and caesarean delivery, respectively (p=0.074), and 3155g and 3158g (P>0.10) in the private hospital. The birthweight distribution in both hospitals followed a Gaussian distribution. In the public hospital, caesarean section was more common for babies with birthweight between 1500g and 2499g and over 3500g (p<0.001), whilst in the private one the higher rates were found for birthweights between 3000 and 3449g (p=0.073). The public maternity showed a gestational age distribution with a shift to the right, towards older gestational ages, with caesarean sections being performed mostly among post-term babies. The private hospital showed a peak around the gestational age of 38.5 weeks.

**Conclusions:** In the private setting, higher caesarean rates among babies with birthweight in the normal range and among those with gestational ages around the mean (38.5 weeks), who are at lower gestational risk, suggest that surgical deliveries were mostly performed without a medical indication at the private maternity.

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### DIFFERENT RISK OF ADVERSE NEONATAL OUTCOME: COMPARISON BETWEEN PRETERM INFANTS APPROPRIATE FOR GESTATIONAL AGE AND SMALL FOR GESTATIONAL AGE

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**BACKGROUND:** SGA (birth weight-BW <10 p for gestational age-GA) is frequently associated with an increased risk of preterm delivery and adverse outcome. Data regarding the association of SGA with different outcome variables are not always univocal and sometimes contrasting.

**AIM:** to determine the risk of incidence of adverse outcome (mortality, respiratory distress syndrome-RDS, bronchopulmonary dysplasia-BPD, severe intraventricular hemorrhage-IVH, periventricular leukomalacia-PVL, retinopathy of prematurity-ROP and necrotizing enterocolitis-NEC) related to preterm SGA vs AGA.

**METHODS:** between January 2001 and October 2003 we investigated all neonates born at 24-34 weeks' gestation and admitted to our NICU. We excluded twins and infants with congenital anomalies and we considered eligible a total of 170 neonates. All infants were defined AGA or SGA by neonatal growth standards. Neonates were stratified for GA: SGA 24-30 wks (n 19) mean BW 732±202 g (440-1280 g), mean GA 27±1.8 wks. SGA 31-34 wks (n 28), mean BW 1397±262 g (940-1835 g); mean GA 32±1wks. AGA 24-30 wks (n 41) mean BW 1196±289 g (680-1880 g); mean GA 28±1.8 wks; AGA 31-34 wks (n 82): mean BW 2000±301 g (1340- 2730 g); mean GA 32±1wks. Multiple logistic regression analysis were used to relate each outcome variable to SGA or AGA (SPSS 10.0 for Windows).

**RESULTS:** SGA 24-30 wks vs AGA 24-30 wks: RDS (OR 5; 95% CI 0.5-43), BPD (OR 1.7; 95% CI 0.47-6.4), IVH (OR 0.48; 95% CI 0.09-2.5), PVL (OR 1.5; 95% CI 0.22-9.7), NEC (OR 1; 95% CI 0.09-12); mortality (OR 3.3; 95% CI 0.7-14), ROP (OR 4.7; 95% CI 0.39-55). P=NS SGA 31-34 wks vs AGA 31-34 wks: RDS (OR 1.4; 95% CI 0.5-3.5); no cases of BPD, IVH, PVL, NEC, mortality in this group. P=NS

**CONCLUSIONS:** Although none of the comparisons resulted significant, SGA was a strong risk predictor for RDS, BPD, mortality and ROP in SGA <31 wks group.

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### NEUTROPHIL CHEMOTAXIS IN NEONATES IS INFLUENCED BY THE MODE OF DELIVERY AND GESTATIONAL AGE SHOWN IN A NEW FLOW CYTOMETRIC ASSAY

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**Background:** Neutrophil adhesion and chemotaxis are early steps in the unspecific immune response. On the one hand bacterial infections are more common in newborns, on the other hand the neonates are prone to inflammatory tissue damage. We investigated neutrophil chemotaxis in neonates by means of a new functional flow cytometric assay to describe the early events of the unspecific immune response and to set up the basis for a potential impairment of the neonatal inflammatory response.

**Methods:** We analyzed the expression of the adhesion molecules CD11b and CD62L and the IL8-receptors A and B on neutrophils as well as functional parameters like shape change, spontaneous and IL8- or fMLP-induced transmigration of neutrophils.

**Results:** Cord blood neutrophils of healthy term newborns (n=20) differed significantly from those of healthy adults (n=30) in receptor expression and chemotaxis. Spontaneous migration was significantly higher (p=0.008) in cord blood neutrophils than in adults, whereas adult neutrophils could be more stimulated by fMLP (p=0.02) or IL8. We also found a significant influence of the mode of delivery on these parameters: Vaginally born neonates (n=20) showed a significantly higher chemotactic response compared to neonates after cesarian section without labor (n=35). Venous blood collected after the first hour of birth did not show these differences any more. Comparing term and preterm neonates (gestational age =>37 weeks vs. g.a. <37 weeks), the neutrophils of the mature neonates showed a higher spontaneous and fMLP- or IL8-stimulated chemotactic response.

**Conclusions:** The flow cytometric assay is a sensitive method to analyse functional differences concerning the chemotaxis of neutrophil granulocytes. Using this method we demonstrated significant differences between full-term neonates and adults and between full-term neonates delivered vaginally or by cesarian section. The process of labor and vaginal delivery seems to be a short-term preactivating stress-factor for the unspecific immune response.

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### DISRUPTION OF CEREBELLAR DEVELOPMENT AS A CONSEQUENCE OF PERINATAL RISK FACTORS AND NEURODEVELOPMENTAL FOLLOW UP

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**Purpose:** Very low birth weight infants (VLBW) are at high risk of suffering from adverse perinatal events with possible involvement of the central nervous system and lifelong disability. Due to the growing evidence of cerebellar involvement in higher cognitive processes cerebellar lesions have become of major interest concerning motor and cognitive deficits after prematurity.

**Patients:** We describe a series of 29 VLBW infants (mean 972g) born between 24 and 30 gestational wks (mean GA 26.6 wks) suffering from disruption of cerebellar development as a consequence of extreme prematurity.

**Methods:** In order to identify risk factors for the generation of cerebellar disruptive development the perinatal course of our patients was compared to an age (mean GA 26.0 wks) and weight (mean 828g) matched control group of 29 preterm infants with normal cerebellar development, confirmed by MRI > 3rd month of life. Outcome data of motor and cognitive development of our patients were compared to a control group of 19 former premature born infants matched for gestational age, birth weight and perinatal supratentorial brain lesions.

**Results:** VLBW infants with cerebellar involvement suffered significantly more often from intraventricular hemorrhage (p= 0,0023), posthemorrhagic hydrocephalus (p= 0,0006) and need for neurosurgical interventions (p= 0,0002). Furthermore they exhibited more hemosiderin deposits supratentorially (p= 0,015) and infratentorially (p< 0,0001). Catecholamine support was significantly higher than in controls (p= 0,03). No other differences in perinatal risks factors were found. Despite comparable motor deficits our patients exhibited a significantly poorer cognitive performance.

**Conclusion:** Our data show that the immature cerebellum has a high vulnerability suggested by the different amounts of hemosiderin deposits. Disruptive cerebellar development in premature infants was associated with major supratentorial brain injuries. VLBW infants suffering from disruption of cerebellar development exhibited both motor deficits and cognitive impairment.

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### PROTECTIVE EFFECTS OF GALACTO- AND FRUCTOOLICO-SACCHARIDES ON NEONATAL JAUNDICE

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**Background:** Neonatal hyperbilirubinaemia occurs in approximately 8% to 20% of healthy, full-term newborn infants. Several mechanisms are implicated in pathogenesis of jaundice: decreased hepatic clearance, large hemoglobin mass degradation, and intestinal reabsorption. Reduction of bilirubin to urobilinoids by the intestinal microbial flora may be enhanced by modification of intestinal microflora.

**Aim:** To examine whether supplementing formula with oligosaccharide mixture would modulate bilirubin total (BT) levels in formula fed infants during the first weeks of life.

**Methods:** Fifty healthy full-term infants born at the maternity ward of San Giovanni di Dio Hospital, Crotone, Italy, and formula fed from birth participated in the study. Written parental consent was obtained. Infants were double blind randomly allocated into two groups to receive either supplementation of oligosaccharides mixture (galactooligosaccharides [gos-fo], derived from lactose, and long-chain fructooligosaccharides, derived from chicory) at the dosage of 0.8 g/100ml (n=27) or placebo (maltodextrine) (n=23), from birth through the first 28 days of life. BT level was determined by multiwavelength spectral analysis, using a portable BiliCheck device (SpectRx Inc, Norcross, GA), clinically equivalent to measurement of total serum bilirubin (transcutaneous bilirubin, TcB) within 2 hours after birth (T0), at 24, 48, 72 h and at completed 5, 7, 10, 28 (T8) days of life. Hematocrit (HT) was further determined by conventional methods.

**Results:** Groups were comparable for birth weight, gestational age, maternal age, type of delivery, baseline (T0) plasma TcB level (mean [SD; range], gos-fo 3.0 [0.7; 2.1-4.8] vs. placebo 3.0 [0.8; 1.6-5.0] mg/dl, and HT level. Pattern of TcB significantly differed between groups through the study (P<0.01; Anova for repeated measures). Infants in supplemented group exhibited lower plasma TcB levels than placebo group from 72 h of life onwards (0.01<P<0.02). At T8, mean [SD; range] TcB level was 2.4 [0.5; 1.1-3.6] mg/dl (gos-fo) vs. 2.8 [0.4; 1.8-3.8] mg/dl (placebo). HT significantly decreased from birth to day 28 in both groups (P<0.0001) but no difference between groups was found (P>0.55).

**Conclusions:** In formula fed infants, supplementation of a mixture of gos-fo significantly lowers bilirubin level after 72 hours of life. It may be hypothesize that stimulating the intestinal growth of bifidobacteria and lactobacilli enhances bilirubin excretion by reducing it to urobilinoids. Larger randomized trials would be of interest to evaluate prophylactic and therapeutic use of gos-fo in neonatal hyperbilirubinaemia.

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### TOTAL CEREBRAL VOLUME MEASUREMENTS FOLLOWING PRETERM BIRTH

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**Background:** Preterm infants have reduced cerebral tissue volumes in adolescence, and relative loss of some brain regions in early childhood, but it is unclear if this is due to perinatal or more prolonged growth failure. We therefore compared total cerebral tissue volume in preterm infants at term equivalent age and term born controls.

**Methods:** Subjects: We studied 89 preterm infants born at median 29.7 weeks GA without parenchymal lesions at median 40.57 weeks, and 20 term born controls (median 40.43 weeks GA). Image acquisition: a 1.5 Tesla MR system was used to acquire T1-weighted volume datasets with a voxel size 1x1x1.6mm, in addition to conventional and diffusion weighted imaging. Image processing: a non-rigid image registration algorithm transformed all images to a reference subject, and transformations were used to propagate region of interest (ROI) labels segmented in the reference anatomy to the corresponding structure in all subjects. The volume change for each ROI relative to the reference was computed, enabling cerebral tissue volume measurements (excluding CSF) to be calculated for each subject.

**Results:** Mean cerebral tissue volume in preterm infants at term was 404.9cm<sup>3</sup>; and in term controls, 401.1cm<sup>3</sup> (p=0.765). Diffuse white matter injury, oxygen requirement at 28 days, and intrauterine growth restriction were not associated with significant reductions in cerebral tissue volume.

**Conclusions:** Despite evidence of regional and later growth failure, total brain tissue volume in preterm infants at term is similar to term born controls.