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ABDOMINAL ORGAN GROWTH IN INTRAUTERINE GROWTH RETARDATION: FETAL "PROGRAMMING" CAUSING "METABOLIC SYNDROME" IN ADULT AGE

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Background/aims: Fetal growth retardation may be associated with diseases and disorders in later life. This risk may be due to some impairment of the development of such organs as liver and kidney. In addition to general malnutrition of the fetus, preferential blood flow to the brain and the heart may furthermore deprive such organs as liver, spleen, and kidney on oxygen and macro- and micronutrients. As a consequences these organs may not develop normally, which predisposes to impaired outcome of the fetus. Persisting metabolic dysfunction may then cause such diseases as hypertension, cardiovascular disease, osteoporosis, schizophrenia, mental depression, breast cancer, and polycystic ovary syndrome in adult age. The aim of this study was to investigate the effects of maternal undernutrition on the growth of some abdominal organs. The size of the kidneys, spleen and liver in adequate for gestational age newborn infants (AGA) has been compared with that in small for gestational age (SGA) infants.

Methods: A total of 25 randomly selected AGA [M:14, F:11; gestational age: 34.5± 5.02 (range:25–40) weeks; birth weight: 2318±965 g (range: 680-3800)] and 25 SGA infants [M:8, F:17; gestational age: 34.2±4.2 (range:25–39) weeks; birth weight: 1562±644 g (range: 440-2400)] entered the study. The sizes of the liver, kidneys and spleen were determined by the use of ultrasonography. The volumes were estimated using the standard ellipsoid formula (longitudinal x antero-posterior x transverse diameter x <240/6). Liver/kidney, liver/spleen, and kidney/spleen ratios were determined in three gestational age groups of the infants (<30, 30–36, 37–40 weeks).

Results: The volumes for the kidneys and the liver differed significantly between AGA and SGA infants in all 3 groups (p≤ 0.0018, p≤0.029, respectively); whereas the spleen volume only differed in the 37–40 weeks group (p=0.0002). The correlation between the liver volume and the birth weight differed significantly between SGA and AGA infants (r=0.56 vs. 0.84, p=0.04). On the other hand, the ratios between the 3 organs were the same in all groups (p≥0.15).

Conclusions: Our findings support the view that fetal growth of the liver and the kidneys is impaired in intra-uterine growth-retarded infants. Impaired fetal development of these organs may cause metabolic dysfunction which predisposes to diseases included in the so-called metabolic syndrome or syndrome X. Fetal environmentally caused "programming" may increase the risk of functional defects and diseases in later life.

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ABDOMINAL ORGAN GROWTH IN INTRAUTERINE GROWTH RETARDATION: FETAL"PROGRAMMING" OF DISEASES LATER IN LIFE

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Background: Fetal growth retardation has been associated with diseases and disorders later in life. It has been suggested that this is caused by the impaired development of abdominal organs. Besides general malnutrition of the fetus, preferential bloodflow to the heart and brain may further deprive organs, such as liver, spleen, and kidney, of nutrients. As a result these organs may not develop properly, thus predisposing to higher morbidity and mortality rates, as well as a possible contribution towards late sequelae, such as hypertension, cardiovascular disease, osteoporosis, schizophrenia, depression, breast cancer, and the polycystic ovary syndrome in adulthood. The aim of this study was to investigate the effects of maternal undernutrition on abdominal organs growth, comparing kidney, spleen and liver sizes in adequate for gestational age (AGA) and small for gestational age (SGA) infants.

Methods: A total of 25 AGA [M:14, F:11; gestational age: 34.5± 5.02 (range:25–40) weeks; birth weight: 2318±965 g (range: 680-3800)] and 25 SGA infants [M:8, F:17; gestational age: 34.2± 4.2 (range:25–39) weeks; birth weight: 1562±644 g (range: 440-2400)] participated to the study. Intraabdominal organs sizes (liver, kidney, spleen) were determined using ultrasonography during neonatal period. Liver, kidney, and spleen volumes were estimated using the standard formula for ellipsoid (longitudinal x antero-posterior x transverse diameter x <240/6). Liver/kidney, liver/spleen, and kidney/spleen ratios were also determined. For better comparisons the infants were subdivided into three gestational age groups (<30, 30–36, 37–40 weeks).

Results: Kidney and liver volumes were significantly different between the two groups at all ages (p≤ 0.0018, p≤0.029, respectively); while spleen volume differed in the 37–40 weeks group (p=0.0002). The correlation liver volume vs. birth weight was significantly different between SGA and AGA infants (r=0.56 vs. 0.84, p=0.04). On the other hand, the ratios among intraabdominal organs were unchanged (p≥0.15).

Conclusion: Our findings support the concept that abdominal organs development mainly for liver and kidney is impaired in intra-uterine growth-retarded infants and may contribute to impaired organ function, thus possibly predisposing to late sequelae in childhood and adulthood. As a consequence, fetal "programming"may increase susceptibility to diseases later in life.

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INTUBATION LENGTH AS A PREDICTOR OF BRONCHOPULMONARY DYSPLASIA

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Background: Bronchopulmonary dysplasia (BPD) continues to be one of the most common long-term complications associated with preterm birth. Although its pathogenesis is changing, BPD is very often preceded by the use of mechanical ventilation early in life. To date, little information exists on the role of a prolonged intubation in developing lung injury.

Methods: Here, we compared the frequency of oxygen-dependency ≥28 days (BPD 28-d) and/or oxygen-dependency ≥36 weeks postmenstrual age + oxygen-dependency ≥28 days (BPD 36 wk) in 121 very low birth weight infants (M:63, F:58, gestational age: 27.4±2.5 weeks, birth weight:. 954±261 g) from our neonatal intensive care unit (NICU), commonly using a minimal intubation approach, to 121 gender and gestational age-matched newborns (M:59, F:62, gestational age: 27.9±2.8, birth weight:. 1005 ± 310 g) from a NICU of comparable size, commonly using a standard intubation policy.

Results: A significantly reduced prevalence of BPD-28d (15.7% vs. 29.7%, p=0.014) and BPD-36 wk (0.8% vs. 18.2%, p<0.0001) in the minimal intubation policy population was observed. Minimal intubation policy showed a significantly protective effect on both BPD-28-d (Odds Ratio=0.50; 95% C.I.: 0.26–0.95; p=0.0034) and BPD-36 wk (O.R.=0.044; 95% C.I.: 0.0058–0.33; p=0.0025), as compared to the standard intubation strategy. After correction for possible confounding variables, BPD-28d was significantly associated to intubation duration (O.R.=7.06, 95% C.I.: 3.22–15.52, p<0.0001) and Clinical Risk Index for Babies (CRIB)-II score (O.R.=5.22; 95% C.I.: 2.35–11.57, p<0.0001), while BPD-36wk was associated to intubation duration (O.R.=11.03, 95% C.I.: 3.62–33.59, p<0.0001) and gestational age (O.R.=4.61; 95% C.I.: 1.48–14.37, p=0.0083).

Conclusion: These findings strongly suggest that a minimal intubation policy may be effective in reducing the BPD risk in VLBW infants, with the potential impact of a shorter intubation length being significantly stronger on BPD-36 wk than BPD-28d.

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INCREASED CONCENTRATIONS OF IL-6 AND FAS-LIGAND IN CEREBROSPINAL FLUID OBTAINED FROM NEWBORN INFANTS FOLLOWING CEREBRAL HYPOXIC-ISCHAEMIC INJURY

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Background: Perinatal hypoxia-ischaemia (HI) in term human infants is a major cause of neurodevelopmental impairment and disability. Inflammatory cytokines have been implicated as a major cause of brain injury. Among these Fas ligand plays a major role in apoptotic cell death, while IL-6 acts predominantly as an anti-inflammatory cytokine. The objective of this study was to investigate the cytokine profile in cerebrospinal fluid (CSF) samples from human infants with cerebral Hypoxic-Ischaemia (HI) and to correlate these data with clinical evaluation and outcome in comparison to appropriate controls.

Methods: Cytokine concentrations were measured in CSF by enzyme-linked immunosorbent assay (ELISA) from a cohort of 40 newborn infants comprising 20 patients with HI and 20 controls (newborn infants with suspected infection but negative cultures in CSF). From 10 of the patients in the HI group two consecutive samples were obtained at 12 hours post-partum and at 3 days of age.

Results: The concentrations of the inflammatory cytokines IL1- , TNF- , IFN- , IL-10 and IL-12 did not differ between the patient and controls. The concentrations of IL-6 and Fas ligand were higher in the HI group than in the controls (p<0.01) (Figure 1). A significant correlation (r = .92; p<0.01) was observed between IL-6 levels in CSF samples taken 12 hours after birth and the concentration of Fas ligand in CSF from the same patient, 3 days later.

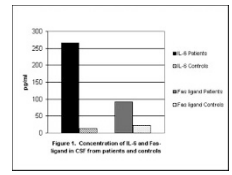

Figure 1. Concentration of IL-6 and Fas-ligand in CSF from patients and controls

Conclusion: The results support previous data that concentration of IL-6 is increased in CSF after birth asphyxia. The increased concentration of Fas ligand in CSF may be an indicator of the degree of apoptotic brain cell death. The association between Fas ligand in the first sample and IL-6 in the second sample might indicate that activation of Fas ligand in the central nervous system induces production of IL-6 in humans.

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PREVALENCE OF OVERWEIGHT AND OBESITY AMONG GREEK CHILDREN AT THE AGES OF 7 AND 18Y BY GENDER. A LONGITUDINAL STUDY

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Background: The obesity epidemic has alarmed consciousness against it in aim to prevent future mortality and morbidity. **Objectives:** : To investigate longitudinally the prevalence of overweight/ obesity among Greek children by gender. Population and methods: Data was obtained from a prospective follow-up study of 2000 children from birth to 18 y of age. Information was gathered by self-completed questionnaires. The age and sex specific BMI cut off points of the International Obesity Task Force were used to define overweight and obesity in 7 and 18 year olds.

Results: 1 out of 3 overweight/ obese 7y old children remain overweight/ obese at 18y. More specifically 1 out of 2 boys and 1 out of 4 girls do so. Logistic regression revealed no significant factors for boys who remain overweight/obese during adolescence. On the contrary, 7y old overweight/ obese girls are 7 times more likely to become normal at 18y when they have an incorrect impression of their body shape and consider themselves overweight (33%). Also girls with overweight/ obese mothers run a 3 times higher risk of remaining overweight/obese during adolescence. No other factor from those entered into the regression appeared to be significant.

Conclusion: Prevalence of obesity in both genders is similar and high (22–25%) at 7 years. 1 out of 2 overweight/ obese boys will become an overweight/ obese adolescent. This is not predictable so far. Girls are liable to psychosocial aspects of modern lifestyle and manage to lose their excess body weight.

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LOW LEVELS OF CYSTEIN ARE ASSOCIATED WITH INCREASED PROINFLAMMATORY ACTIVITY, ARTERIAL HYPOTENSION AND SEVERE INTRAVENTRICULAR HEMORRHAGE IN PRETERM INFANTS

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Background: Increased proinflammatory activity is associated with oxidative stress, hemodynamic impairment and tissue damage. Cystein is an essential amino acid in preterm infants and metabolized to glutathione which is one of the most important intracellular antioxidant systems. Plasma levels of isoprostane are considered a stable marker of oxidative stress. Aim: To evaluate if plasma levels of cystein and isoprostane at 6 h of age are associated with proinflammatory activity and with subsequent morbidity in preterm infants.

Methods: A two year prospective cohort study including inborn infants delivered at < 32 +0 gestational weeks after antenatal informed consent and excluding infants with major anomalies. 74 infants were enrolled with a mean (SD) gestational age of 27.1 (1.9) weeks. Blood sampling for analysis of proinflammatory (TNFá, IL-1 â, IL-2, IL-6, IL-8, IL-12, IFN- â) and modulatory (IL-4, IL-10) cytokines was performed from umbilical cord and at 6 h postnatal age. Plasma levels of cystein and isoprostane were determined at 6 h postnatal age. Continuous invasive measurement of arterial blood pressure (ABP) was digitally stored during the first 72 h. Ultrasound examinations of the brain were performed at day 1, 3 and 7, at 6 weeks and at term age.

Results: Levels of cystein in plasma at 6 h of age were positively related to gestational age at birth (r=0.46, p=0.001). Increased levels of IFN-ã, TNFá, IL-1â, IL-6 and IL-12 at 6 h were associated with a decrease in level of cystein (r=-0.37, p=0.002; r= -0.25, p=0.04; r=-0.45, p=0.000; r=-0.29, p=0.02 and r=-0.28, p=0.02 respectively). Level of cystein at 6h was positively related to average of mean ABP (0–6 h), r=0.38, p=0.004. Decreased levels of cystein at 6 h were associated with development of severe IVH (grade III + IV), OR (95 % CI) 0.93 (0.88–0.97), p=0.000. All associations remained significant after adjustment for gestational age and gender. Levels of isoprostane at 6 h were neither associated with cytokine levels in umbilical cord nor with those at 6h of age.

Conclusion: Increased proinflammatory activity, arterial hypotension and development of severe IVH are associated with low levels of cystein early after birth in preterm infants.