

# ESPR EUROPEAN SOCIETY FOR PEDIATRIC RESEARCH

Stockholm, Sweden  
September 19-22, 2004

1

## FATTY ACID PROFILE IN A BLOOD DROP COLLECTED IN 3-DAY OLD INFANTS: COMPARISONS WITH ADULT SUBJECTS AND CORRELATIONS WITH PHYSIOLOGIC PARAMETERS

L Colombo<sup>1</sup>, F Marangoni<sup>2</sup>, G Sivali<sup>1</sup>, E Riva<sup>1</sup>, C Galli<sup>2</sup>, C Agostoni<sup>1</sup> <sup>1</sup>University of Milan, San Paolo Hospital, Department of Pediatrics, Milan, Italy; <sup>2</sup>University of Milan, Department of Pharmacological Sciences, Milan, Italy

**Background:** Long Chain Polyunsaturated (LCP) Fatty Acid (FA) status in the newborn may affect post natal growth and development, but data in newborns are limited due to difficulties in sample collection.

**Methods:** A new method for FA analysis in a drop of whole blood absorbed on a strip of Chromatography Paper (Marangoni et al, Anal Biochem 2004;326:267) was applied to a population of 110 infants, by analyzing blood samples collected from the heel within 72 h after delivery (37-41 wks post-conceptual age).

**Results:** Comparisons with data from an unrelated, healthy adult population (100 subjects), analyzed with the same technique, showed lower levels of linoleic acid (LA) and alpha-linolenic acid (ALA) together with higher LCP (mainly arachidonic acid, AA, and docosahexaenoic acid, DHA, 22:6 n-3) levels, and markedly higher proportions of > 22 C FA of all FA families in the newborns, revealing major differences in FA intake, metabolism and incorporation in lipid pools between the two groups. Differences in FA profiles occurred also within the newborns, in relation with 1. gender (higher LA in females) 2. gestational age, with lower AA and DHA levels in the highest decile (10 s) for post-conceptual age at birth (41.2 weeks, SD 0.1) compared to the others 3. birth weight, with higher DHA levels in the lowest (10 s) vs the highest (12 s) decile (%: 4.2, SD 0.4, vs 3.4, SD 1.0, Mann-Whitney U test: P = 0.002) and 4. maternal life style (higher 22:5 n-6/22:6 n-3 ratio in smoking vs non-smoking mothers).

**Conclusion:** The new method of FA analysis provides valuable information on the FA status and biochemical features related to FA at very early stages of post natal development, an age that has not been adequately investigated so far.

2

## POLYCHLORINATED BIPHENYLS AND LEVELS OF POLYUNSATURATED FATTY ACIDS IN HUMAN MILK

F Grandi<sup>1</sup>, I Brunetti<sup>1</sup>, G Radaelli<sup>2</sup>, B Vergani<sup>1</sup>, M G Bruzzese<sup>1</sup>, E Riva<sup>1</sup>, M Giovannini<sup>1</sup>, C Agostoni<sup>1</sup> <sup>1</sup>San Paolo Hospital, University of Milan, Department of Pediatrics, Milan, Italy; <sup>2</sup>San Paolo Hospital, University of Milan, Department of Medical Statistics, Milan, Italy

**Background:** Environmental contaminants such as persistent organic chlorines may contaminate human milk and negatively affect neural development. To what extent organic chlorines might influence levels of polyunsaturated fatty acids (PUFA) in milk has not been investigated yet. In this study we have investigated whether concentration of polychlorinated biphenyls (PCBs) may be associated with PUFA levels in human milk.

**Methods:** Subjects: 25 healthy women (mean [SD, range] age 33 [6, 23-42] y., pre-pregnancy body mass index <25kg/m<sup>2</sup>, 88% smoking during pregnancy, 24% primiparous, 32% who had been living in Milan or surrounding areas for at least 20 years and who delivered full term singleton infants participated in the study. Mothers exclusively breastfed for at least 4 months. Samples from colostrum, the first 2 days after delivery, and mature breast milk after 1 and 3 months were collected. The samples were analyzed for PCB 105, 118, 138, 153, 156 and 180, and for C18:2 n-6 (linoleic acid), C18:3 n-3 (alpha-linolenic acid), C20:4 n-6 (arachidonic acid), C20:5 n-3 (eicosapentaenoic acid), C22:6 n-3 (docosahexaenoic acid) by means of gas-chromatographic techniques.

**Results:** The concentrations of all examined contaminants were highest in colostrum and then declined (P<0.001). PUFA levels did not show a definite smooth trend, except C20:4 n-6 and C22:6 n-3 whose concentrations declined (P<0.001). The concentrations of PCBs in milk were associated with mother's age, correlation coefficient (r) 0.57 < r < 0.86, P < 0.001. No significant association was found between levels of PUFAs and mother's age, P > 0.14. No significant association was found of PCBs with PUFAs in human milk: colostrum, -0.16 < r < 0.25, P > 0.19; 1 month, -0.34 < r < 0.20, P0.10; 3 months, -0.27 < r < 0.33, P0.11.

**Conclusion:** Within the population of this study, no evident association was found between concentration of PCBs and PUFAs, in human milk.

3

## INCREASED LIPOLYSIS IN LARGE FOR GESTATIONAL AGE INFANTS

F Ahlsson, B Diderholm, U Ewald, J Gustafsson Uppsala University, Department of Women's and Children's Health, Uppsala, Sweden

**Background:** During late gestation the fetus accumulates fat and glycogen for the immediate postnatal period. Newborn infants of diabetic mothers as well as other infants with hyperinsulinemia have particularly large energy depots and are at risk for hypoglycemia. Large for gestational age (LGA) infants, without known predisposing factors, also have increased energy stores. The relative proportion of this group of infants is increasing. Only limited data is available on the metabolic adaptation of these infants.

**Aim:** To study lipolysis and glucose production in infants born LGA of non diabetic mothers.

**Methods:** Eight term LGA infants, were studied at a postnatal age of 19±8-h. Gestational age was 40±1.5 w and birthweight 4.87±0.44 kg. Rates of lipolysis and glucose production (GPR) were analysed by gas chromatography-mass spectrometry following constant rate infusion of [2-13C]-glycerol and [6,6-2H2]-glucose.

**Results:** Plasma glucose and glycerol averaged 3.8 ± 0.6 mmol . L-1 and 418 ± 190 ± mol . L-1, respectively. Glycerol production, reflecting lipolysis, was 13.2±2.9 imol . kg-1 . min-1 and GPR averaged 5.5±0.9 mg . kg-1 . min-1 (30.6±5.1 imol . kg-1 . min-1). The fraction of glycerol converted into to glucose was 54±22 % contributing to 11±6 % of the total glucose production. Lipolysis and GPR correlated to birth weight. Plasma concentrations of insulin and glucagon averaged 11±3 mU . L-1 and 39±4 pmol . L-1, respectively.

**Conclusion:** The results show that term LGA infants have a markedly increased lipolysis during the first day of life as compared to term infants born appropriate for gestational age (AGA). The correlation to birth weight indicates that the degree of lipolysis is dependent on the amount of stored fat in the LGA infants. GPR was similar to that observed in AGA infants. There was no pronounced hyperinsulinemia, which contradicts the occurrence of insulin resistance in this particular group of infants.

4

## INSULIN-LIKE GROWTH FACTOR ATTENUATES APOPTOSIS AND MUCOSAL DAMAGE IN HYPOXIA/REOXYGENATION-INDUCED EXPERIMENTAL NECROTIZING ENTEROCOLITIS

M Akisu<sup>1</sup>, S Ozen<sup>1</sup>, M Baka<sup>2</sup>, M Yalaz<sup>1</sup>, E Y Sozmen<sup>3</sup>, A Berdeli<sup>1</sup>, N Kultursay<sup>1</sup> <sup>1</sup>EGE University, Pediatrics, Izmir, Turkey; <sup>2</sup>EGE University, Histology, Izmir, Turkey; <sup>3</sup>EGE University, Biochemistry, Izmir, Turkey

**Objective:** The aim of present study was to investigate whether hypoxia-reoxygenation (H/R)-induced necrotizing enterocolitis (NEC) was due to increased apoptosis of the intestinal mucosa in the young mice and whether pre-treatment of the animals with recombinant human Insulin-like growth factor-I (IGF-I), known anti-apoptotic factor, could protect the intestinal cells from H/R-induced apoptosis or intestinal injury.

**Study design:** Young mice were divided into three groups; Group 1 mice (H/R) were hypoxia-reoxygenation; Group 2 mice (H/R + IGF-I) were treated with recombinant human IGF-I by intraperitoneal injection (1 µg/g BW; once daily) for 7 days; Group 3 mice were served as control. Hypoxia was induced by placing young mice in Plexiglas chamber, consisting 10% oxygen for 60 min. After hypoxia, the young mice were reoxygenated for 10 min with 100% oxygen. Intestinal generation of substances reactive to thiobarbituric acid (TBARS) and active caspase-3 were measured in H/R-induced intestinal injury.

**Results:** Increased numbers of apoptotic cells (apoptotic index) across the villi in young mice subjected to H/R were observed with the TUNEL reaction whereas few apoptotic cells existed in the control animals. In addition, H/R-induced intestinal damage in H/R + IGF-I group was greatly attenuated, with necrosis limited partially to the mucosa. Tissue active caspase-3 levels in H/R group were found to be significantly higher when compared with that of H/R + IGF-I group of mice and control. However, TBARS concentrations in the intestine were similar in H/R groups when compared to the intestine of control animals.

**Conclusion:** The present study suggests that both necrosis and apoptosis via mechanisms occurring oxygen-derived free radicals and activation of caspase-3 play a role in the pathogenesis of H/R-induced NEC. We also show that IGF-I protect intestinal mucosa from necrosis and apoptosis from intestinal H/R injury.