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LONGITUDINAL PATTERN OF MACRONUTRIENTS IN BREAST MILK DURING THE FIRST SIX MONTHS OF BREASTFEEDING: AN ITALIAN STUDY

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Aim: Few longitudinal data are available on macronutrient breast milk composition during lactation. There are no studies from Italian lactating mothers.

Methods: Thirty lactating mothers (enrolled according to major criteria of normality for mother, delivery and infant) were followed up to 6 months of delivery. Breast milk samples were taken at 1 (T1), 2, 3, 6 (T6) months, at the first feeding in the morning. Fore- and hind milk were collected and frozen (-20 C) until analysis, when were mixed. Total fats were determinated gravimetrically and fatty acid (FA) methyl esters extracted from lipids according to Folch were separated by GLC. Total protein and carbohydrate content were evaluated by turbidimetric assay and HPLC, respectively. Breast milk macronutrient concentrations were further categorized in tertiles. Statistics: Analysis of variance for repeated measures and Friedman test. Significance: $P<0.05$.

Results: Concentration of breast milk macronutrients changed significantly over time for protein ($P<0.0001$), total fat ($P=0.026$) but not for lactose ($P=0.169$). Among total fat, variation was significant for saturated FA ($P=0.022$) but not for either monounsaturated ($P=0.189$) or polyunsaturated ($P=0.218$) FA. Significance of difference between T6 and T1 was $P<0.0001$ (mean [SD], 9.6 [1.6] vs 11.6 [1.5] g/l) for protein and $P=0.05$ (mean [SD], 27.1 [12.5] vs 32.0 [12.7] g/l) for total fat. No significant longitudinal within-subject change was found with respect to tertiles of any macronutrient concentration (protein, $P=0.47$; fat, $P=0.96$; lactose, $P=0.89$).

Conclusions: In this study we have found a reduction in breast milk protein concentrations over time, in agreement with previous studies. Differently than other studies, we further have found significant variation in total fat concentrations. The lack of a specific, detectable within-subject trend in pattern of macronutrients in breast milk confirms that many factors may influence the milk composition in the first six months of lactation.

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PPAR-GAMMA2 PRO12 ALA VARIANT, INSULIN SENSITIVITY AND PLASMA FATTY ACIDS IN CHILDHOOD OBESITY

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Background: The relationship between Pro12Ala variant of peroxisome-proliferator-activated receptor-gamma2 (PPAR-gamma2), insulin sensitivity and plasma fatty acids is unclear.

Aim: To examine whether an association of PPAR-gamma2 Pro12Ala with insulin sensitivity and plasma fatty acids may exist in obese children.

Methods: One-hundred and twelve obese children (mean age [SD], 10.4 [2.8] y), were included into this observational study. Obesity was defined in accordance with the International Obesity Task Force. BMI z scores were calculated and adjusted by using the LMS-method of Cole. Fasting blood samples were taken for measurements of glucose, insulin levels, lipid profile, total and HDL cholesterol, triglycerides, fatty acids (FA) composition. Insulin resistance (IR) was estimated by the homeostatic model assessment (HOMA-IR). Genomic DNA was obtained from peripheral blood using standard methods, and the Pro12Ala PPARgamma2 variant was detected by PCR polymorphism analysis.

Results: Prevalence of Ala carriers was 19%. Multiple logistic-regression analysis disclosed that the Pro12Ala genotype was independently associated with lower values of 1. fasting insulin levels ($p=0.032$), 2. HOMA-IR ($p=0.05$), 3. plasma levels of C20:3n-9 ($p=0.004$) and 4. n-6/n-3 PUFA ($p=0.063$) compared with Pro/Pro. Mean [SD] values of fasting insulin levels, HOMA, C20:3n-9 and n-6/n-3 PUFA in Pro/Pro and Pro12Ala groups were, respectively, : 21.7 [13.1] vs 13.1 [6.6] mU/ml, 4.7 [3.9] vs 3.0 [2.0], 0.17 [0.15] vs 0.09 [0.02] mg/dl and 14.2 [3.3] vs 12.7 [2.2].

Conclusions: In this study Pro12Ala polymorphism was related to higher insulin sensitivity and to an healthy plasma fatty acids pattern. We speculate that obese children carriers of the Ala12 allele might be protected from cardiovascular disease and type 2 diabetes by the phenotypic effect on insulin resistance and on plasma fatty acids metabolism.

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CHOLESTEROL SYNTHESIS IN VIVO IN PREMATURE INFANTS FROM DEUTERATED WATER (D2O)

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Background: Cholesterol is one of the main components of cell membranes and is required as precursor for many metabolically active compounds. To date cholesterol metabolism is uncompletely defined in premature infants. Using a 12 h i.v. constant infusion of 13C acetate, Renfurm (Pediatr Res 2004) studied de novo cholesterol synthesis in premature infants. This method required indwelling lines.

Objective: To assess if cholesterol synthesis can be measured with a less invasive method based on D2O as precursor (Matthan Lipids 2000).

Material and Methods: Cholesterol synthesis was studied in 15 newborns ($BW<1500$ gr, $age<48$ h) on parenteral nutrition without lipids. Subjects received orally a bolus of D2O (0.1 gr/kg), followed by 0.000625 gr/kg every 12 for 48 h. Urine and plasma samples (200 ul) were collected before study start and every 12 h thereafter till 48 h. Unesterified cholesterol was obtained from plasma lipid extraction and thin layer chromatography separation, and cholesterol deuterium enrichments measured by Gas-Chromatography-Isotope Ratio- Mass Spectrometry (GC-IRMS). Deuterium enrichment of urine samples were measured by GC-IRMS and regarded as the precursor enrichment pool. Cholesterol Fractional Synthesis Rate (FSR) and secretion time (ST) were measured as previously described (Matthan Lipids 2000). Data are given as mean±SD.

Results: Study weight was 1084±546 gr, gestational age 28±2 wks, mean age 23±19 h. Energy Intake was 30±8 kcal/kg/day. Cholesterol FSR was 16±12% and ST 11±11 h.

Conclusion: This method has the advantage that tracer can be given orally, steady state of precursor is easily achieved and very small amount of blood is needed. We measured cholesterol synthesis from D2O in vivo in premature infants and the calculated rate was approximately that found in adults (Jones J Lipid Res 1994). Given the high variability between patients larger study will better define factors related to endogenous cholesterol synthesis early in life.

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IMPROVING PERINATAL REGIONALISATION BY PREDICTING THE NEED FOR NEONATAL INTENSIVE CARE: A STUDY BASED ON THE EPIPAGE COHORT

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Perinatal regionalisation is organised in three ascending levels of care, fitting increasing degrees of pathology. Recommendations request that very premature infants be prenatally referred to level III facilities. Yet, not all very preterm neonates require level III intensive care. Some of them could thus be handled in maternity wards closer to their parents' home, avoiding useless intrauterine transfers.

Aim. To determine the antenatal factors predicting the need for neonatal intensive care in preterms, to fit the site of birth to the level of care required.

Methods. Our study sample is a cohort of preterm infants born in 1997, in nine French regions. We defined the need for neonatal intensive care as the requirement for mechanical ventilation for more than 48 hours, high frequency oscillation, inhaled nitric oxide, or transfer for more intensive care to a level III facility within the first two days of life, and early neonatal death. Triple pregnancies, pregnancies marked by foetal malformations or by intensive care requirement for mothers' purpose before delivery, were excluded.

Results. The need for neonatal intensive care decreased from 100% at 24 weeks' gestation (GA), to 54% at 29 weeks' GA and 13% at 33 weeks' GA. We hence focused our study on the 1267 neonates aged 30, 31 and 32 weeks' gestation, where the need for intensive care was 43, 34 and 23% respectively. Risk factors adjusted on gestational age for intensive care requirement were maternal arterial hypertension (aRR=1.12;95%CI=[1.04–1.20]), twin pregnancies (1.10;[1.04–1.17]), haemorrhagic pathology (1.06;[1.01–1.10]), foetal asphyxia (1.12;[1.01–1.23]) and infection (1.04;[1.01–1.08]). Antenatal corticotherapy (0.67;[0.55–0.80]) and premature rupture of membranes (0.81;[0.75–0.88]) were protective factors.

Conclusion. Infants <30 weeks' GA should be referred to level III facilities, since >50% require intensive care. Above 29 weeks' GA, decision of appropriate level of care could rely upon prenatal risk factors.

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RELAXANT EFFECTS OF THE SOLUBLE GUANYLATE CYCLASE ACTIVATOR AND NO SENSITIZER YC-1 IN PIGLET PULMONARY ARTERIES

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Background: The indazole derivative YC-1 has been characterized as an nitric oxide (NO)-independent and heme dependent soluble guanylate cyclase (sGC) activator, which also sensitizes sGC to NO.

Objective: To examine the effects of YC-1on vascular relaxation in newborn and 2 week-old piglet pulmonary arteries. The effect of YC-1 on the relaxation induced by exogenous NO was also analyzed.

Design/Methods: Isolated rings from third generation pulmonary arteries (outer diameter 500-1000 microm) and small distal pulmonary arteries (outer diameter 150–200 microm) were mounted in organ chambers for isometric tension recording. Arteries were precontracted with the thromboxane A2 mimetic U46619 (0.1 microM)

Results: YC-1 induced a concentration-dependent relaxation that was significantly greater in 2 week-old pulmonary arteries and was abolished by the sGC inhibitor ODQ (10 microM). YC-1 induced relaxation was similar in conduit pulmonary arteries and arterioles. In the 2-week-old pulmonary arteries, the response to YC-1 was significantly reduced when the endothelium was removed or after incubation with the NO synthase inhibitor L-NAME (0.1 mM). YC-1 (3 microM) augmented NO-induced relaxation in 2-week-old but not in neonatal pulmonary arteries.

Conclusions: YC-1 induced pulmonary vascular relaxation in conduit and resistance pulmonary arteries and these effects increased with postnatal age. In the 2-week-old pulmonary arteries and besides its direct activator of sGC, YC-1 produced endothelium-dependent relaxation and synergized with exogenous NO.

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KASABACH-MERRIT SYNDROME IN GIANT HEMANGIOENDOTHELIOMA OF THE LIVER IN A PRETERM INFANT

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Kasabach-Merrit syndrome, the association of a vascular lesion and consumptive coagulopathy represent a diagnostic and therapeutic challenge to clinicians. We report a case of an infant with a large mass of the liver diagnosed at 25 weeks of amenorrhea that started to bleed at 33 weeks of gestational age. A male newborn, 33 GW, 3170 gr of weight, was admitted to the neonatal intensive care unit for severe consumption coagulopathy caused by hepatic mass prenatally diagnosed. At the admission the clinical conditions were severe and so we decided for surgical treatment. He was then operated on at 3 hours of life. The operation was a total excision of the tumor with a left-side hemihepatectomy. Macroscopically the tumor was brown, encapsulated, elastic in consistency. The weight was 200 gr and the diameter 9 cm. Histological examination revealed an infantile hemangioendothelioma of the liver. The infant received a pre and postoperatively supportive care with transfusions of fresh frozen plasma and red blood cells and infusion protein C i.v. to stop the activation of coagulopathy. The postoperative course was uneventful. At 6 months after surgery the patient had no evidence of residual tumor or further coagulopathy. In 1940, Kasabach and Merrit first described the association of a large vascular tumor and trombocytopenia and termed this Kasabach-Merrit syndrome. This is a potentially life-threatening condition, with mortality estimates ranging from 20 to 30% as a result of severe sepsis, coagulopathy, or invasion of vital organs. Treatment modality have included corticosteroids, interferon alfa 2a or 2b, vincristine, cyclophosphamide, ticlopidine, aspirin, amicar, radiation therapy, and surgical excision. In our case the treatment of this life-threatening condition was aggressive surgery at birth associated to medical treatment of coagulopathy. To our knownledge our patient is the younger one in literature who underwent surgery for this lesion.