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The protein sparing of exogenous lipid during i.v. alimentation.

The prerequisites of a rational nutritional design for premature receiving total parenteral nutrition (TPN) are the:

(a) estimation of coverage of the energy cost of basal metabolism muscular activity, chemical thermogenesis and growth by the metabolizable energy (ME) intake.

(b) estimation of the desirable protein and fat deposition for optimal growth and development.

Using nutrient balance, indirect calorimetry (IC) and urinary nitrogen output (UN), the coverage of energy metabolism by carbohydrate (CHO), protein (P) and fat (F) were determined by studying 36 infants during (TPN). The majority of patients were 2-3 day postoperative surgical; mean gestational age 36 weeks, birth weight 2600 g, postnatal age 16 days. During initial hypocaloric infusion (18-35 Kcal/kg/day) of glucose (GL) the nitrogen balance was negative (-70 mg/kg/day). GL + amino acid (AA) infusion resulted in a positive nitrogen balance and correlated significantly with the daily protein intake ($y = 0.61 X + 0.17$; $r = 0.54$; $p < 0.01$; n=19) which varied between 0.5 - 3.5 g/kg/day. By increasing the caloric intake with Intralipid (IL) at a fixed protein intake nitrogen retention was increased (51 mg/kg/day), resulting in 0.3 g/kg/day extra protein deposition. Over 50-60% of the IL was oxidized. These results suggest that this protein sparing is attributable to the preferential utilization of fat for energy metabolism.

59 L. SANN, M. MATHIEU*, Y. LASNE*, A. RUITTON*. Hopital Debrousse, Lyon, France. Hyperglycemic effect of an oral load of triglycerides in preterm neonates.

A nasogastric load of 2,7 g/kg of lipids with 67 % of medium chain triglycerides and 30 % of grape seeds oil was given at the age of 48 hours to 20 preterm neonates (mean bw = 2164 g ; gest. age : 35 weeks). Its effect on the concentrations of plasma glucose free fatty acids (FFA), serum B-OH-butyrate (BOHB) and lactate was compared to their evolution in 11 control preterm infants (mean bw 2102 g ; gest. age : 35 weeks). The basal levels were similar in both groups. In the supplemented group, plasma glucose increased from (mean ± SD) 57 ± 7 to 74 ± 11 mg/dl at 30 min. ($p < 0.001$) and to 80 ± 11 mg/dl at 60 min. ($p < 0.001$) while no significant change was recorded in the control group. At 60 min., serum BOHB had increased in the supplemented group from 339 ± 165 to 631 ± 230 µmol/l ($p < 0.01$) and it was higher than in the control group : 439 ± 200 µmol/l ($p < 0.05$). Plasma FFA decreased from 303 ± 178 to 199 ± 90 µlEq/l ($p < 0.05$) in 60 min. in the control group while no significant change was observed in the supplemented group. Serum lactate decreasedin 30 min. from 1777 ± 809 to 1257 ± 375 µmol/l in the supplemented group ($p < 0.05$) while the change (from 1820 ± 600 to 1581 ± 438 µmol/l) was not significant in the control group. In 7 supplemented infants, there was no change of serum insulin or glucagon concentration and no change of serum glycerol levels in 6 other supplemented infants.

These data suggest that in preterm infants 1)this load of triglycerides can provide glucose and ketone bodies which could be available for the neonatal brain 2)this hyperglycemic effect independant of hormonal influence is probably achieved through gluconeogenesis.

60 A. NIEDERWIESER*, J. BIERI*, B. BLEHOVA*, H.-CH. CURTIUS*, A. MATASOVIC*, F. REY*, B. SCHIRCKS*, M. VISCONTINI* (Intr. by A. Prader) Dep. Pediatrics and Org. Chemistry, University of Zurich; Detska Klinika, Prague; Hôp. des Enfants Malades, Paris. Urinary pterins in atypical phenylketonuria.

Three further patients with atypical PKU caused by tetrahydrobiopterin deficiency were investigated: D.K. (B. Blehová), A.C. and T.Y. (F. Rey). Pterin analyses in urine were performed by two-dimensional high-voltage electrophoresis/paper chromatography as well as by gas chromatography-mass spectrometry. The trimethylsilyl derivatives were analyzed by gas chromatography on a 20 m OV-1 glass capillary column and detected by a nitrogen detector as well as by mass fragmentography at m/e 409. Mass spectra were identical with those of the pure reference compounds. All three patients excreted high amounts of neopterin and smaller quantities of dihydroxanthopterin in urine but no biopterin or dihydrobiopterin. This pterin pattern was the same as in the first two patients (M.K. and Z.Y.) shown to suffer from dihydrobiopterin synthetase deficiency (A. Niederwieser et al. Lancet I: 131, 1979; H.-Ch. Curtius et al. Clin. Chim. Acta 93: 251, 1979). Neopterin was shown to be of D-erythro and not of threo configuration. Furthermore, the patients' elevated serum phenylalanine level was normalized by oral administration of L-erythro-tetrahydrobiopterin bishydrochloride, 2.5 mg/kg body weight. Conclusion: Analysis of urinary pterins is of value for the early detection of atypical PKU and - in combination with pterin administration tests - for the localization of the corresponding enzyme defect.

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Reduction of serum phenylalanine levels in PKU rats with intestinal absorption inhibitors of phenylalanine (PHE).- It has been often suggested that inhibition of the intestinal absorption of PHE would be a new approach for PKU treatment. We have previously shown that a PKU model for dietetic studies is obtained by means of the synergistic inhibition of Phenylalanine-Hydroxylase with p-chlorophenylalanine + cotrimoxazole (daily intraperitoneal injection of the 2 inhibitors leads to hyperphenylalaninemia without need for a phenylalanine load). Addition of beta-2-thienylalanine (THI) or phenylalaninol (PHE-ol) to the diet (1g%) significantly reduced phenylalaninemia: PHE: 1.30 ± 0.30, + THI : 0.70 ± 0.27, + PHE-ol:0.87 + 0.29 mmol/l. However, the effectiveness of THI or PHE-ol was mainly dependent on diet quality: with 5 isonitrogenous-isoosmotic diets (amino acids, lactalbumin & its hydrolysate, casein & its hydrolysate), decrease of serum PHE with THI or PHE-ol only occurred with high PHE diets (inhibitor/PHE molar ratio 1.4), without significant difference between results with intact or hydrolysed protein diets. It has been claimed that amino acid (AA) changes in serum, liver and brain, induced by hyperPHE, could explain disturbed protein synthesis in PKU; we confirm such changes in our PKU model (mainly: essential AA decrease in serum, liver and brain), however AA imbalance did not disappear on THI or PHE-ol supplemented diets. These data suggest that PHE analogues (such THI or PHE-ol)used in diets to decrease intestinal absorption of PHE cannot ensure serum PHE reduction comparable to that obtained with PHE restricted diets.

62 D.MICHALK*, H.SCHMIDT*, G.MITTERMAIER*, P.WONG*, P.LUTZ: University Children's Hospital, Heidelberg, FRG. Homocystinuria due to 5,10-methylenetetrahydrofolate (THF) reductase deficiency: clinical presentation and treatment.

In 5,10-THF-reductase deficiency, first described by Mudd et al. in 1972, homocystinuria with normal plasma methionine is clinically associated with mental retardation, behavioural abnormalities and proximal muscular weakness. We observed a family with 7 children. Two of them, a 17 yrs old boy and a 19 yrs old girl, presented with mental retardation from early childhood and progressive muscular rigidy, mainly of extrapyramidal origin with onset at school age. Two other siblings with similar symptoms suddenly had died prior to our investigation at the age of 13 and 21, respectively. A marked homocystinuria (3 mmol/d) was found in our patients. Plasma homocystine ranged between 100 and 200 µmol/l; methionine, however, was subnormal. The determination of the 5,10-THF-reductase in lymphocytes and fibroblasts revealed a very low activity. (15-30% in LC and 0-7% in fibroblasts)

A therapeutic trial with leucovorine (5-formyl-THF) resulted in a prompt reduction of urinary homocystine excretion accompanied by an improvement of the neurological disturbances.

63 L.R. GARIBALDI*, I. REZVANI*, H.G. ARTMAN*, C.S. PHILLIPS*, and A.M. DIGEORGE*(Intr. by P. Durand). Temple Univ. Sch. Med., Dept of Ped.,St. Christopher's Hospital for Children, Philadelphia, Pa., U.S.A. Excessive suppression of serum dehydroepiandrosterone sulfate (DHEAS) in patients treated for congenital adrenal hyperplasia (CAH).

Serum levels of DHEAS and 17-hydroxyprogesterone (17OHP) were measured in 20 females (2.5-22 yrs) and 11 males (2.5-16.5 yrs) with CAH due to 21-hydroxylase deficiency treated with oral hydrocortisone (HC) (non-salt losers, n=12), or HC and Florinef (salt losers, n=19). Adequacy of therapy was judged by clinical findings, growth rate, bone age, serum 17OHP, urinary 17 ketosteroids and pregnanetriol. These allowed separation of patients into 3 groups: A- poor control (n=11), B- good control (n=12), and C- mildly overtreated (n=8). The groups were comparable for sex ratio but mean age in group C (5.5±1.9 yrs) was lower than group A (13.7±2.1 yrs) or group B (11.4±6 yrs). In "optimally" treated patients (group B), whose serum levels of 17 OHP were consistent with adequate treatment (250±189 ng/dl), mean serum level of DHEAS was significantly lower than that in age matched controls (23±20 vs 82±42 µg/dl, P <0.01). Serum levels of DHEAS in group C were all below the sensitivity of the assay (<5 µg/dl). Serum levels of 17OHP were also suppressed in this group (12±5 ng/dl). In poorly controlled patients (group A), mean serum level of DHEAS was slightly but not significantly higher than controls (121±80 vs 92±39 µg/dl) while serum 17OHP levels were abnormally high (>1000 ng/dl). These data indicate that doses of HC necessary for "optimal" treatment of CAH result in oversuppression of serum levels of DHEAS. This supports the hypothesis that the secretion of DHEAS may be controlled by a hormone other than ACTH.

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An earlier retrospective study of children to alcoholic mothers showed correlation between size at birth and later mental performance. In a study of 23 children born by 15 presently alcoholic women (study group) with matched controls (sex, birthweight, gest. age, city area) the study group had slower growth after birth. Study children scored lower than controls in tests for intelligence (Griffith and WISC mean IQ 93.8 and 112.7 respectively, $p<0.001$), perception (Frostig test, $p<0.001$), gross motor age (score 91 and 105 resp., $p<0.005$) and fine motor age (score 89 and 105 resp., $p<0.005$).

Prospective tracing of alcoholic pregnancies was done in some areas of Göteborg. 28 alcoholic pregnancies were traced from May -77 to Nov -78. 5 legal abortions were done. 2 infants were still-