137 SELENIUM INTAKES IN PHENYLCETONURIC (PKU) CHILDREN ON PHENYLALANINE RESTRICTED DIET. CORRELATION WITH BLOOD SELENIUM, PHENYLALANINE AND GLUTATHION PEROXIDASE ACTIVITY.

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In Western Countries , the major sources of selenium (SE) are protein rich products such as meat, fish, eggs and bread. One could expect that in patients with phenylketonuria on a protein restricted diet, the SE intake will be dramatically reduced. To objectify this, we decided to measure the daily intake of 5 PKU children's , aged 7 to 19 year, during a PKU summer camp. Daily consumption was duplicated, homogenized and frozen. Se was measured with an atomic absorption spectrometry method after hydride generation. Results: Se intake from allowed natural foods and drinks ranged from 1.3 TO 10.7 µg/d. The synthetic diet products (Phenyldon, PKU2,PKU-Drink, low protein biscuits) provided < 0.5µg/d (detection limit). The mean total SE intake was 2.8±2.2 µg/d (mean±SD.N:35). The mean Se plasma level was 38±13.7 ng/ml (age matched control: 77±13ng /ml) and the glutathion peroxidase activity was 0.062±0.014 U/ml (n=0.301±0.019). These 5 patients with PKU, all symptom free, had a SE daily intake far below the recommended allowances (40-60µg/day).

138 BILIRUBIN PHOTOISOMERIZATION PRODUCTS IN URINE FROM A CRIGLER-NAJJAR TYPE I PATIENT

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Crigler-Najjar type I syndrome (C.-N.s.) is a rare anomaly of bilirubin (BR) metabolism characterized by life-long hyperbilirubinemia.Phototherapy (PT) is the only treatment of value in the long-term management of C.-N.s.. In this study, we have analyzed the BR photoisomer composition in urine of a 18 year-old girl with C.-N.s., before, during and after PT administered with Philips F40T12/BB 'special' blue fluorescent lamps. The HPLC analysis of serum samples indicates that only native BR and its configurational isomer, 4Z,15E-BR, were present, with a relative steady-state concentration of about 24% of 4Z,15E-BR during PT. In urine, both configurational and structural [lumirubin, (15Z-LR+15E-LR)] isomers were found before and, with increasing concentrations, during PT. Before PT, the total amount of structural isomer pool (15Z-LR+15E-LR) was as much as 3 times higher than configurational pool (4Z,15E-BR+4E,15Z-BR+4Z,15Z-BR). This proportion did not change when the patient was exposed to PT light, although the total pigment concentration in urine increased markedly. This study suggests that the BR photoproduct elimination in this adult with C.N.s. is significantly different than in the neonates. In fact, 15Z-LR (1-4%) and traces of 4E-15Z-BR are detected in serum of icteric babies exposed to PT, along with 4Z,15Z-BR and 4Z,15E-BR. On the other hand, the urine of icteric infants contains very small concentrations of the configurational pool. These evidences show that in C.-N.s. mechanisms exist to excrete all BR photoisomers. The existence of a relevant fraction of configurational photoisomers in urine suggests that their contribution to the mechanism of action of PT in C.-N.s. is not negligible.

139 PORTOSYSTEMIC ENCEPHALOPATHY DUE TO PERSISTENCE OF AN OPEN DUCTUS VENOSUS ARANTII

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A girl was followed from birth to age 6 y because of congenital heart defect and persisting hypergalactosemia without enzyme defect. An open ductus venosus was suspected, remained undetected by conventional 2-dimensional ultrasonography but was demonstrated by combined color and pulsed wave Doppler sonography at age 4 y. Average forward flow in the portocaval shunt was 240 ml/min; intrahepatic venous flow or other intra- or retroperitoneal venous collaterals were not seen. Episodes of sleepiness, withdrawal, apathy, occasional vomiting, complaints of headache inbetween, starting at age 3.5 y, were first misinterpreted as migraine. After age 4, she occasionally smelled of ammonia, had mild intention and head tremor, dysmetria, rubeosis of face, hands and feet, insecurity of gait, moderate hyperammonemia, elevated liver enzymes in serum. Her liver remained small, by ultrasound. She was treated with low-protein diet, lactulose, sodium benzoate, with limited success. Tentative treatment with flumazenil is in progress. Hypergalactosemia without enzyme defect is an early sign of duct persistence. The early onset of portosystemic encephalopathy correlates with the large volume of shunted splanchnic blood.

140 METABOLIC CHANGES IN LIVER AFTER INTRAVENOUS FRUCTOSE IN ADULTS WITH DISORDERS OF FRUCTOSE METABOLISM AND IN HEALTHY CONTROLS, FOLLOWED BY PHOSPHORUS MAGNETIC RESONANCE SPECTROSCOPY

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The effect of fructose on liver metabolism was studied by in vivo magnetic resonance spectroscopy in fasting healthy controls and in adults with inherited disorders of fructose metabolism, essential fructosuria (EF), hereditary fructose intolerance (HFI), and fructose-1,6-diphosphatase deficiency (FDD). Novel procedures of spectrometer calibration and spectrum analysis allowed accurate measurements of absolute concentrations of phosphorous compounds in liver. In healthy controls, after fructose infusion (200mg/kg, 20% solution, 2.5min), a fructokinase-mediated, rapid increase of fructose-1-phosphate (F-1-P) from 2.9 to 7.8 mmol per liter of liver was seen, while ATP dropped from 2.7 to 1.8 and inorganic phosphorus (Pi) from 1.4 to 0.3 mmol/l. The subsequent return of F-1-P, mediated by fructaldolase, to its initial concentration was accompagnied by an overshooting rise of Pi up to 2.7 mmol/l. In a patient with EF, concentrations of F-1-P, ATP, and Pi remained unchanged confirming that fructokinase was indeed inactive. In a patient with HFI, initial metabolic changes were as in controls, but baseline concentrations were reestablished only after a tenfold delay indicating weak fructaldolase activity. In a patient with FDD, i.e. the most distal of the three defects, initial metabolic changes occured as in controls at the normal rate and normalization was only slightly delayed.

141 PATHOGENESIS OF HEREDITARY TYROSINEMIA TYPE I: METABOLIC DISORDERS IN CULTURED HEPATOCYTES FROM TRANSPLANTATION PATIENTS

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Tyrosinemia is a disorder of tyrosine metabolism caused by deficiency of fumarylacetoacetase (FAA) enzyme activity. The disease is characterized by progressive liver failure, transplantation is the only effective treatment. We have cultured patient hepatocytes to study the effect of FAA-deficiency on cellular metabolism. Livers from two patients were used to isolate hepatocytes, cultivation was successful in only one case. Viability of those hepatocytes was 90%, EM micrographs showed lipid inclusions and asymmetric organelle distribution. Cultures were stable, lactate dehydrogenase was normal. Protein and S-adenosylmethionine (S-adoMet) synthesis were 30% of control values, no FAA-protein was synthesized. Previously we had found in patient liver tissue mRNA levels less than 10% of control values and low concentrations of spermine and spermidine. Experiments will be discussed to show that low S-adoMet concentrations are possibly limiting for mRNA methylation and polyamine synthesis.

142 ^{13}C NUCLEAR MAGNETIC RESONANCE (NMR) EVALUATION OF GLYCOGEN CONTENT IS USEFUL IN THE DIAGNOSIS OF GLYCOGEN STORAGE DISEASES IN CHILDREN.

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Case report: a 10 month-old infant was admitted to hospital for stunted growth (-4SD). The diagnosis of glycogen storage disease (GSD) was suspected. RBC phosphorylase kinase activity was found to be normal. Liver needle biopsy confirmed the diagnosis of GSD and excluded GSD type I. ^{13}C NMR was then performed. GSD type VI was later proved by the enzymatic assay.
Methods: Ten minutes ^{1}H decoupled ^{13}C spectra of calf muscles and liver were obtained at 2T. Spectra were acquired with a 180° pulse at the coil center repeated every 200ms and with a 40ms acquisition time. The glycogen content was evaluated from the area of the glycogen C_1 peak at 100.5 ppm. It was normalized to the area of the creatine peak at 157 ppm.7 normal subjects and 11 patients suffering from GSD (3 type Ia, 2 type III, 4 type V, 1 type VI and 1 type VII) were studied.
Results: The muscular glycogen/creatine ratio,R, was 2.0±0.7 in normal subjects and 2.1 in GSD type I. It was 13±1.7 in type V, 13.5 and 15 in type III, and 11.2 in type VII. In our patient, R was found to be 2.0. Semi quantitative (no internal reference for liver) evaluation of hepatic glycogen indicated high levels in the liver of our patient, as observed in GSD affecting the liver (types I, II, and VI).
Conclusions: NMR allowed to exclude type III and strongly argued for type VI. Therefore, in vivo ^{13}C NMR is able to distinguish GSD affecting the muscle from those not affecting it and also appears to detect abnormal hepatic glycogen content.