79 TREATMENT OF HEREDITARY TYROSINEMIA

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Two major problems exist in the management of Hereditary Tyrosinemia (HT); the acutely ill infant with liver failure and the development of hepatoma in the older child and young adult. Most dietary programs have failed in treating the acutely ill infants and in preventing hepatoma, and the question may be asked whether the diets have been strict enough. The clarification of the enzymatic defect and the possibility to measure the main metabolite quantitatively, make it possible to monitor the therapy more rationally.

One 2 months old acutely ill infant treated with a marked restriction in the intake of phenylalnine and tyrosine and large supplements of potassium and phosphate, survived and is living 5 years old. Two other children with start of diet 1/2 and 1 year of age, are both living on a very strict diet. The youngest child has on normal serum tyrosin concentration still succinylacetone in the urine, indicating a risk for hepatoma. So far liver transplantation is the only way to prevent or treat hepatoma.

A liver transplantation was performed in a 23 years old woman. She is living and well 6 months after the operation. Following the operation the metabolic derangements were almost normalized, but she still excretes the main metabolite, succinylacetone in the urine. The importance of this observation is uncertain.

80 URINARY ACYLCARNITINES IN VARIOUS ORGANIC ACIDEMIAS ANALYZED BY MASS SPECTROMETRY AND ^{1}H-NUCLEAR MAGNETIC RESONANCE SPECTROSCOPY.

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Patients with organic acidemias may have low plasma free carnitine concentrations and urinary acylcarnitines may be elevated. A concomitant muscular carnitine deficiency has been thought to contribute to the frequently observed hypotonia in these patients. Oral supplementation with carnitine could restore normal carnitine concentrations and promote the removal of 'toxic' short-chain fatty acids as acylcarnitines. We analyzed urinary acylcarnitines by means of ammonia desorption chemical ionization mass spectrometry and also by 500 MHz ^{1}H-nuclear magnetic resonance spectroscopy. The latter technique gives accurate information about the structures of the carnitine esters; their molecular weights are derived from the mass spectrometric measurements. Various urinary acylcarnitines were identified: propionylcarnitine in propionic acidemia and methylmalonic acidemia, isovalerylcarnitine in isovaleric acidemia, octanoylcarnitine in medium-chain acyl-CoA dehydrogenase deficiency. Isovalerylcarnitine increased considerably in a patient with isovaleric acidemia after oral supplementation with carnitine (1g/day), but it did not reach the level of that of isovalerylglycine. The amount of propionylcarnitine in patients with propionic acidemia was much lower than that of other propionyl-CoA metabolites such as methylcitrate. In general carnitine supplementation did not prevent metabolic decompensation, but resulted in normalization of plasma free carnitine. A positive effect on the muscle tone was observed in one patient.

81 EFFECT OF SOY BEAN PROTEIN ON LIPOPROTEINS AND APOLIPOPROTEINS IN CHILDREN WITH FAMILIAL HYPERCHOLESTEROLEMIA

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Children heterozygous for familial hypercholesterolemia (FH) usually are placed on a fatmodified diet (FMD) in an attempt to lower the elevated serum levels of atherogenic LDL. Results on a cholesterol lowering effect of soy bean protein diet (SBPD) in adults are controversial and studies on SBPD in children with FH have not been performed so far.
We determined serum cholesterol (C), triglycerides (TG), lipoprotein-C and apolipoproteins (Apo) A-I, A-II and B in 10 children heterozygous for FH (age 2-16yrs.) before and during 2 weeks of diet in a controlled clinical situation. 8 children received FMD (total fat<35J%, P/S ratio>1,5, C<300mg/day) and 6 received SBPD (FMD+partial replacement of dietary protein by 20g of purified soy bean protein/day). 4 of the 10 children completed a crossover study receiving both diets for 2 weeks in hospital followed by 2 months of outpatient treatment. Results (mg/dl, x±sd):

	C	VLDL-C	LDL-C	HDL-C	TG	B	A-I	A-II	n
before FMD	302±52	14±7	242±46	47±6	92±20	155±39	104±23	37±10	8
after FMD	279±40	10±10	231±49	38±7	95±33	128±38	92±18	35±5	8
P	n.s.	n.s.	n.s.	<0,05	n.s.	n.s.	n.s.	n.s.	
before SBPD	348±99	8±2	279±97	52±6	80±29	180±61	93±33	37±6	6
after SBPD	285±90	11±5	235±53	38±7	76±42	155±50	88±26	43±10	6
P	<0,025	n.s.	n.s.	<0,025	n.s.	n.s.	n.s.	n.s.	

These data show that diet alone is insufficient for normalizing LDL-C or ApoB in most children with FH. No marked difference between both diets concerning the effect on LDL-C or ApoB was apparent. Preliminary results of the crossover study suggest a favorable effect of SBPD on LDL-C.

82 MATERNAL SERUM GAMMA-GLUTAMYLTRANSFERASE IN THE PRENATAL SCREENING OF FETAL ALCOHOL EFFECTS

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In order to investigate prospectively the relationship between maternal serum levels of a biologic marker of alcohol and the outcome of pregnancy, we measured serum gamma-glutamyltransferase (GGT) in 628 women between 14 and 20 weeks of pregnancy. An abnormally elevated value was observed in 6.8% of the cases but only 16.2% of these suspected alcohol abusers admitted drinking practices during pregnancy. Analysis of obstetrical issue and blind examination of 541 newborns showed a significant correlation between raised GGT levels and an increased incidence of pre-/perinatal complications, congenital anomalies and intrauterine growth retardation. However, the sensitivity of this test is weak, limiting its use in the early recognition and prevention of fetal alcohol effects.

83 MATURATION OF THE HYPOTHALAMO-PITUITARY-GONADAL AXIS IN PRETERM GIRLS.

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We found oestradiol producing ovarian cysts and high serum concentrations of oestradiol in four very pre-term infants at a postconceptional age that slightly preceded the expected time of delivery.

To determine the maturation of the hypothalamo-pituitary-gonadal axis in these infants measurements of serum concentration of luteinizing hormone (LH) and follicle stimulating hormone (FSH) were made before and after an i.v. injection of luteinizing hormone releasing hormone (LHRH). At the time when the girls developed cysts, they had a postpubertal type of response to LHRH, i.e. the increase in LH was more marked than the increase in FSH. Some months later they had a prepubertal type of response and a low preinjection serum concentration of LH as expected at that age.

We then made a series of LHRH tests in all consecutive preterm girls born at a gestational age of less than 30 weeks at a postconceptional age of 32-33 weeks. All these girls had a postpubertal type of response to an LHRH injection, and the preinjection concentrations of LH and FSH were very high. When the tests were repeated at a date later than the calculated time of birth they all had a prepubertal type of response with low basal concentrations of FSH and LH. The oestradiol concentration was low on both occasions. Two girls developed very small ovarian cysts. The strong stimulation of the ovaries after birth may be a consequence of withdrawal of placental steroids. The feed-back system may be too immature in preterm girls to respond to low levels of oestradiol, resulting in high levels of gonadotrophins and an "ovarian hyperstimulation syndrome".

84 ERYTHROPOIETIN LEVELS IN NEONATAL HYPERVISCOSITY

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In order to investigate the role of erythropoietin in the neonatal hyperviscosity syndrome serum levels of the hormone were measured with an in vitro enzyme immunoassay in 10 full-term neonates with hyperviscosity and compared to those found in 10 normal newborns, 5 prematures and 10 normal controls. The neonates with hyperviscosity had venous Hct from 65-80% and in 4 of them partial exchange transfusion was performed. Erythropoietin levels were low in all cases of hyperviscosity (mean 14miu/ml) ranging from undetectable to 28miu/ml (Normal controls 45miu/ml, fullterms 47.6miu/ml, preterms 28-3miu/ml). Reevaluation of erythropoietin levels in 3 neonates with hyperviscosity 6 months later showed an increase of the hormone level (mean 45miu/ml mean Hct 36%). These results seem to indicate that in neonatal hyperviscosity erythropoietin is decreased but its feed-back production mechanism remains intact.