55 BILIRUBIN REVERSIBLY REDUCES SYNAPTIC TRANSMISSION IN RAT HIPPOCAMPAL SLICES.

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Bilirubin increases latencies and reduces amplitudes in the auditory brainstem response (ABR). However, the basic mechanisms involved are not known. The aim of the present study was to investigate the neurotoxic effects of bilirubin on synaptic transmission in an in vitro system. Hippocampal slices were prepared from 5-7 weeks old male Sprague-Dawley rats and incubated at 30-33°C in an artificial cerebrospinal fluid equilibrated with 95% O_2 and 5% CO_2 to pH 7.4. We stimulated the Schaffer collaterals of the CA3 cells. Recordings were made of the amplitudes of the presynaptic fibre volley (PV) and the field excitatory postsynaptic potential (EPSP) in the apical dendritic layer of the CA1 region, and of the population spike (PS) in the corresponding cell body layer. The slices were exposed to bilirubin at concentrations up to 1mM, in an 8:1 molar ratio with bovine serum albumin (BSA). Over periods of 30-120 minutes a gradual reduction in the field EPSP amplitude was noted. In parallel with this the peak latency of the PS increased. The stimulus/response relationships were examined with stimulus voltage from 1.0 to 3.4V. Bilirubin caused the PV/EPSP curve to shift to the right, while the EPSP/PS curve shifted to the left. These changes were reversed when bilirubin was removed from the perfusion fluid. The effect of bilirubin on rat hippocampal slices consists of a gradual and reversible decrease in synaptic transmission. This is consistent with the findings reported from ABR studies.

56 ONE YEAR SUCCESSFUL TREATMENT OF INFANTILE PRIMARY HYPEROXALURIA TYPE I;

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The first child of consanguineous parents died at the age of 6 months in renal failure due to oxalosis despite treatment with pyridoxine since the age of 4 months. The 3rd child of this family was found to have hyperoxaluria type I at the age of 3 weeks: plasma oxalate 60 µmol/l (n:3-23), plasma glycollate 1157 µmol/l (n:7-33), urinary oxalate 1650 mmol/mol creat. (n:15-85), urinary glycollate 463 mmol/mol creat. (n:25-164), inuline clearance (IC) 32 ml/min/1,73m^2, creatinine clearance (CC) 28 ml/min/1,73 m^2, normal i.v.pyelography and ultrasound investigation of the kidneys.
Treatment consisted of pyridoxine-HCl (100-1000 mg/d), magnesiumoxide (0.25-0.8 mmol/kg/d) and a high oral fluid intake also by nocturnal gastric drip.
Treatment was complicated by encephalopathy during high pyridoxine dosage. Dosis reduction (400mg/d) resulted in normalisation.
At the age of 1 year there are slight signs of renal calcification on ultrasound. However, renal function is near normal : IC 69 ml/min/1.73m^2, CC 96 ml/min/1.73m^2.

57 CARDIOMEGALY RESPONSIVE TO CARNITIN (C) SUBSTITUTION IN THE NEONATE OF A CARNITIN DEFICIENT MOTHER

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We report on a male Turkish neonate of 38w gestation with a birthweight of 2500 g. After normal adaptation, clinical and radiological signs of cardiomegaly were noticed on the 2nd day in the absence of muscular hypotonia. Echocardiography revealed hypertrophy involving mainly the right ventricle (RV) and the septum but less the left ventricle: RV anterior wall diameter and septum thicknesss were 6.0 and 6.5 mm, resp. (normal $\bar{x} \pm SD$ 2.0 ± 0.3 and 2.5 ± 0.4, resp.) on days two and seven. Serum C levels were low on day two (total C 15, free C 6.5 µmol/l, resp.; normal: 36 - 62 and 21 - 56, resp). Oral substitution with L-carnitin (100 mg/kg bw/day) was given from day 7 to 28. Cardiomegaly, echocardiographic parameters and serum C normalized within 10 days and remained normal for the following 3 mos. Since placental C transfer is a passive process we considered C deficiency in his mother. Four weeks after delivery, her serum C was 20 and 12 µmol/l, the muscle tone was normal, ketogenesis unimpaired and urinary excretion of dicarbonic acids absent. Excessive renal loss was ruled out (tubular reabsorption >99 %). However, a low alimentary intake due to a self-imposed exclusion of meat during the whole pregnancy alone, or in combination with a decreased C synthesis, may have lead to C deficiency in the mother. We conclude that neonatal cardiomegaly and hypertrophic cardiomyopathy can be clinical manifestations of C deficiency in the mother amenable to restitution by short-term C substitution.

58 HbAlab, A POSSIBLE MEANS OF METABOLIC CONTROL IN HEREDITARY FRUCTOSE INTOLERANCE (HFI) AND GALACTOSEMIA (G).

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About 5% of hemoglobin is linked to glucose resulting in a chromatographically distinct hemoglobin component, HbAlc, that is successfully used as a means of metabolic control in diabetic patients. It was the purpose of the present study to clear whether similar hemoglobin alterations can be expected in HFI and G. Minor hemoglobin components of patients with HFI (n=23), G (n=9), type I diabetes (n=14) and healthy controls (n=14) were separated by column chromatography on Bio-Rex 70 resin. In addition, purified hemoglobin was incubated during 4 days at different concentrations of glucose, fructose, galactose, fructose-1-phosphate and galactose-1-phosphate. The following concentrations of minor hemoglobins were obtained:

	HbAlab	HbAlc	HbAlabc	ab/c
Controls	2.47 ± 0.60	3.89 ± 0.64	6.44 ± 1.09	0.64
Diabetes	2.97 ± 0.96	5.65 ± 2.45	8.62 ± 3.26	0.58
Galactosemia	3.71 ± 1.45	4.08 ± 1.02	7.77 ± 1.99	0.94
HFI	3.27 ± 1.59	3.98 ± 1.41	7.24 ± 2.52	0.85

The patients were reportedly well controlled and presented no abnormalities of liver transaminases or blood coagulation at the time of presentation. The in vitro incubation of hemoglobin with glucose resulted in the expected increase of HbAlc. An increase dominating in the HbAlab fractions resulted after exposure to galactose respectively fructose-1-phosphate. We want to advocate the determination of HbAlab as an additional means in the metabolic control of patients with G and HFI.

59 STUDIES ON A KINDRED WITH APOLIPOPROTEIN A-I MÜNSTER 4

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Mutations of serum apolipoproteins may cause genetic dyslipoproteinemia and are used to study structure-function relationships of these proteins. Only recently some rare mutants of ApoA-I, the major apolipoprotein of HDL have been described. In our study 330 unrelated Austrian subjects were screened for genetic variants of ApoA-I by means of an isoelectric focusing method. One proband heterozygous for a mutant ApoA-I was detected HPLC and mass spectrometry of the tryptic peptides of the isolated Apo A-I variant revealed Lys at position 198 instead of usual Glu. So far only one patient with this ApoA-I mutant (ApoA-IMünster4) had been identified, family data had not been reported (1). In the present study 6 blood relatives heterozygous for the mutant (2 children, 4 adults) could be detected in 3 generations among 20 family members. The family data are consistent with an autosomal codominant inheritance of the trait. 3 of 6 heterozygous subjects and 6 of 14 unaffected family members were hyperlipoproteinemic (4 type IIa, 2 type IIb, 3 type IV). However, no relationship between the occurence of ApoA-IMünster4 and hyperlipoproteinemia could be shown. Serum levels of cholesterol (C), triglycerides, LDL-C, HDL-C, VLDL-C, ApoA-I, A-II and B were not significantly different in probands with the mutant from those in unaffected family members. In conclusion, ApoA-I Münster4 is inherited in an autosomal codominant way and does not appear to be causally related to dyslipoproteinemia. Nevertheless this ApoA-I mutant may be of interest for studying the interaction of ApoA-I with cell receptors for HDL.

1) Assmann et al., J Clin Chem Clin Biochem 22:585(1984)

60 ELEVATED PLASMA SORBITOL LEVELS IN CATARACT PATIENTS WITH SORBITOL DEHYDROGENASE DEFICIENCY

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Two male patients in a family with congenital cataracts were found to have a deficient sorbitol dehydrogenase (SD) activity in erythrocytes (J. Inher. Metab. Dis. 7 Suppl. 2, 151, 1984). The concentrations of sorbitol and galactitol were determined by a stable isotope dilution assay using gas chromatography-mass spectrometry (Pediatr. Res. 18, 714, 1984). The sorbitol level was elevated significantly in plasma of the patients (5.58 and 12.98 µmol/L compared to the normal values (0.60-1.84, n=16). On the other hand the galactitol concentration in plasma was in the normal range (0.08-0.40 µmol/L). The elevation in sorbitol is comparable to that in diabetes where the accumulation of sorbitol in the lens and peripheral nerves is considered to contribute to cataract and neuropathy development. The patients, however, do not show any neuropathy but severe neonatal cataracts. This difference may be explained by tissue specific isoenzymes of SD and aldose reductase. Further studies with SD from sheep liver and erythrocytes showed that galactose, galactitol and galactose-1-phosphate have no effect on SD, while xylitol inhibits and xylulose activates SD.