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142 Urinary cyclic AMP : A sensitive index for the healing of rickets.

The present work is concerned with studies of the renal tubular defect in advanced stages of rickets of infancy.The increased loss of phosphate in the urine in this disease is probably due to high plasma levels of parathyroid hormone (PTH). We therefore investigated urinary adenosine 3',5'-monophosphate (cAMP) which is partly formed in the renal tubules in response to PTH. An 8 months old boy with vitamin D deficiency rickets showed a pre-treatment urinary cAMP value of 31,3 nmol per mg creatinine (Normal values in this age group less than 11,0 with our method). On treatment with vitamin D_2 (2700 IU daily) urinary cAMP was normalized in the course of 4-5 months,concomitantly with a complete radiological healing. A 12 months old girl with vitamin D dependency rickets was treated with vitamin D_2(40.000 IU daily) for one year to obtain complete healing.During this time there was a steady decline of urinary cAMP from an initial value of 37,8 nmol per mg creatinine to values within the normal range.The patterns of urinary cAMP in the 2 types of rickets clearly reflects the time factor in the healing process,and the response to vitamin D.We conclude that urinary cAMP is a sensitive index for the healing of rickets,whether due to vitamin D deficiency or vitamin D dependency.

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143 HEPATIC GLYCOGEN SYNTHETASE DEFICIENCY: METABOLIC AND ENZYME STUDIES IN A NINE YEAR OLD GIRL

In the 13 yrs since hepatic glycogen synthetase (GS) deficiency was first described in identical twins no further cases seem to have been observed. We now report on K.S. who had suffered from morning convulsions since the age of 7. Three 24-h metabolic profiles showed fasting hypoglycaemia (mean 1.5 mM), hyperketonaemia (mean total ketones 8.5 mM) but normal lactate (mean 1.5 mM). One h after lunch the mean values were 11.7 mM glucose, 0.2 mM ketones and 6.0 mM lactate. The former levels reappeared after an 8 h fast. Glucagon (0.03 mg/kg i.m.) caused a rise in glucose (Δ:2 mM) 3 h after a meal with a fall in lactate and alanine. No effect was seen after a 12 h fast. Normal increments in glucose followed oral galactose or alanine. Liver and abdominal muscle biopsies were taken. Glycogen content was subnormal in liver: 0.65% (6 controls: 1-6%) but normal in muscle: 0.76% (2 controls: 0.70,0.72%). Glycogen synthetase (EC 2.4.1.11) was virtually absent from liver: 0.04 U/g wet wt. $\bar{c}$ G-6-P, 0.01 U/g $\bar{s}$ G-6-P (6 controls 1.99-3.60, 0.03-0.16) but fully active in muscle: 1.71 U/g wet wt. $\bar{c}$ G-6-P, 0.11 U/g $\bar{s}$ G-6-P (2 controls 1.52,1.24; 0.11,0.06). GS in K.S. liver extract was not activated by K.S. muscle extract nor by control liver or muscle. Liver extract of K.S. did not inhibit GS of K.S. muscle or of control liver or muscle. Hepatic GS deficiency causing fasting hypoglycaemia does indeed exist.

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144 Gyrate atrofy of the choroid and retina and ornithine-ketoacid aminotransferase deficiency.

In a 10 years old girl with gyrate atrofy of the choroid and retina plasma ornithine concentration was consistently elevated ranging from 1000-1250 µmol/l. The ornithine concentration of the spina fluid was similary increased. The concentration of the other amino-acids was normal in all samples. The urine showed a typical overflow aminoaciduria, with an increase in ornithine only The prenatal and postnatal history was generally uneventful. Nc clinical abnormality could be found; liver was not enlarged. Intelligence was normal. The following laboratory tests gave normal results: haematological examination, serum proteins and their electrophoretic pattern: SGOT, SGPT, LAP, γGT, bilirubin, ureum, creatinin, blood ammonia. A deficiency of ornithine ketoacid aminotransferase was found in cultured fibroblasts by radiochemical method. Pharmologic doses of Vit. B6 for 7 days and restriction of protein intake to 0.8 g/kg for 2 months did not result in normal plasma ornithine concentration. Normal ornithine concentrations were found in plasma of the parents and the healthy sibs.

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145 D-glyceric aciduria, an inborn error of serine metabolism?

An Afghanese boy is described who presented with severe metabolic acidosis, failure to thrive and recurrent infections in the neonatal period. Symptomatic treatment with bicarbonate, combined with a low protein diet, resulted in clinical improvement. Gas chromatographic analysis of organic acids (trimethylsilyl derivatives) in the patient's urine revealed high concentrations of glyceric acid (10 to 100 mM), confirmed by mass spectrometry. Amino acid excretion was normal, especially no excess of glycine was present. The optical configuration of glyceric acid was determined as follows: isolation of the acid by paper chromatography, esterification with L-menthol and acetylation of the OH-groups. Subsequent capillary gas chromatography, stationary phase SP-1000, yielded good separation of the enantiomers. Only D-glyceric acid was found in the urine.

Glyceric acid may be derived from carbohydrate or amino acids. To elucidate its origin we loaded the patient with fructose and L-serine. Fructose loading caused no increase of glycerate excretion. On the contrary, the loading test with 200 mg/kg L-serine resulted in a significant increase of glyceric acid excretion. 25% of the ingested serine was retrieved as glyceric acid. L-serine loading in a control led to the excretion of only a trace of glyceric acid. It is suggested that the enzyme defect is located somewhere in the serine degradation pathway.

At 1½ year the patient was moderately retarded and glyceric aciduria was persistent (~12 mmoles/day).

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146 University Children's Hospital III, 4 Düsseldorf, W-Germany. Selenium and reduced glutathione peroxidase activity in dietetically treated patients with metabolic diseases.

Selenium concentrations of serum, whole blood, hair and food were measured by instrumental neutron activation analysis in dietetically treated patients with maple-syrup-urine disease (M.S.U.D.) and phenylketonuria (P.K.U.) and in control children with normal food. Concomitantly glutathione peroxidase activity of erythrocytes as a marker enzyme of selenium deficiency was estimated. Follow-up studies showed that within 2 months of dietotherapy the serum selenium concentration fell from normal values at birth to very low values. The activity of the glutathione peroxidase of the erythrocytes also decreased to 50 per cent of the normal values. According to the intake the serum selenium concentrations and the activity of the glutathione peroxidase of the erythrocytes in 18 infants and children with P.K.U. and M.S.U.D. remained significantly lower during dietotherapy than those of normal children. The serum selenium concentration of the control persons showed an age dependency.

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147 REGULATION OF AN ENZYME ACTIVITY DURING MYELINATION BY MEMBRANE LIPIDS

Sulphatide, an acidic sphingolipid, is an important component of myelin. Its rate of synthesis changes significantly during development. In mouse brain, the synthesis starts at the 8th postnatal day, reaches a maximum at day 16 and declines until day 25, when a base rate of synthesis is achieved. To investigate the mechanism of the regulation of this developmental pattern, microsomes of mouse brain were delipidated and a lipid requirement of a key enzyme of the sulphatide-synthesis, the Cerebroside-Sulphotransferase (CST), could be shown. We could then demonstrate, that the residual activity of delipidated microsomes from brains of 8 to 25 day old mice remained at the same level, this in contrast to whole microsomes, where the CST-actvity pattern corresponded to the one found in vivo. Reconstitution experiments with delipidated enzyme preparations and the corresponding lipids of different ages showed a final CST-activity pattern depending on the age of the lipid and not on the age of the enzyme source. The results suggest, that the age dependent CST-activities are at least partly regulated by the lipids associated with the enzyme protein in the microsomal membrane.