INVESTIGATIONS IN CHILDREN WITH CEREBRAL SALT LOSING SYNDROME. J.R.Bierich & M.Muller, Tübingen.

5 children with acute brain disease showed heavy urinary salt losses which were considered related to the cerebral lesions as renal and adrenal function was unimpaired. Lowest serum Na levels were 110-118 mval/L, lowest Cl levels 69-82 mval/L, serum K was normal. NaCl administered in large amounts did not raise serum Na but was excreted in the urine. Symptoms of dehydratation were absent; plasma volume blood pressure and serum N were normal. Red cell volume was increased by 20-30%. Symptoms of water intoxication in accordance with analogous intracellular oedema in the brain were observed in 2 cases and were temporarily relieved by NaCl infusions. - Presumably the disorder corresponds to the syndrome of Schwartz & Bartter which is characterised by enhanced endogenous ADH production and water retention. The heavy salt losses are considered as the results of a compensatory "3rd factor" activity. Determinations of ADH, renin, 3rd factor and aldosterone will be reported. Similar findings-water retention, hyponatriaemia, increased urinary NaCl excretion-were observed in a girl with diabetes insipidus treated by Pitressin, two large doses.

MINERAL METABOLISM AND TREATMENT OF METABOLIC DISORDERS

MENKES' KINKY HAIR DISEASE: CONFIRMATION OF COPPER DEFICIENCY. K.Baerlocher, A.Nussbaumer (St. Gallen) & E.A.Werder, M. Spycher (Zürich)

The typical symptoms of the X-linked inherited kinky hair disease are present in a 6 year old boy: growth failure, severe mental retardation, pili torti, hypothermia & osteoporosis.

Since 1968 the content of copper in serum & urine of the patient was repeatedly determined. The mean value of serum copper was 52 µg/100ml (n=6, controls 70-140 µg/100 ml) & of urinary copper 56.5 µg/24hours (n=5). Caeruloplasmin was 13 IU (n=8, controls 36-74 IU), the copper content of the liver 0.0068 and 0.0070 µg/mg wet weight (controls 0.0042-0.017 µg/mg. Recently, Danks et al. reported a defect in the intestinal absorption of copper in this disease (Pediatrics 50,188,1972, Science 179,1142,1973). The copper deficiency can well explain the symptoms present in the disease.

Absorption studies of copper in the patient, the heterozygous mother & other family members will be reported as well as the effect of parenterally administered copper on the patient's behaviour.

CYCLIC 3'-5'-ADENOSINE MONOPHOSPHATE IN HYPOPITUITARISM AND SILVER-RUSSELL SYNDROME. M.Vanderschueren-Lodeweyckx, G. Van den Berghe, W.Proesmans, L.Corbeel, E.Eggermont and R.Eeckels, Louvain, Belgium.

The urinary excretion of cyclic 3'-5'-adenosine monophosphate (c-AMP) was studied in 5 patients with idiopathic hypopituitarism during two -day periods before and during administration of 5 mg of human growth hormone (HGH) per day. In 4 out of these 5 patients the urinary excretion of c-AMP was normal and not modified by the administration of HGH. In one patient, however, urinary c-AMP was found to be absent during 2 consecutive days following an insulin tolerance test performed in the control period. The effect of dibutyryl c-AMP (0.2 mg/kg.min during 60 min) on plasma glucose, immunoreactive insulin (IRI), growth hormone (GH) and cortisol was investigated in 8 patients with idiopathic hypopituitarism and in 2 patients with the Silver-Russell syndrome. Plasma glucose and IRI increased markedly in all patients. An increased level of cortisol was also observed except in 1 hypopituitary patient presumably having ACTH deficiency. Although the 2 Silver-Russell patients showed a net increase of plasma GH at 120 min., 7 out of the 8 hypopituitary patients failed to increase the level of plasma GH above 1 ng/ml. In 1 patient, however, the cyclic nucleotide provoked an increase of plasma GH up to 5 ng/ml. The significance of these findings for the investigation of GH-deficiency is discussed.

IS NUTRITIONAL RICKETS A HEREDITARY DISEASE?
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Previous work by others and us suggested that nutritional rickets may have a genetic basis. The present paper attempts to obtain further evidence for the hereditary nature of the disease. Biochemical investigations were performed on 22 rachitic infants before and after treatment and on 23 of their parents. The results obtained were a) increased a-amino-nitrogen excretion was found in 1/3 of the infants a long time after healing of rickets b) in the 9 rachitic infants examined abnormal values of pattern amino-acid excretion were found c) 9 of the parents were found to have abnormally high a-amino-nitrogen excretion, 12 abnormally high phosphorus clearance and 10 abnormally high urine phosphorus-urine creatinine concentration d) all 10 examined parents had raised values of the pattern of aminoacid excretion for 1-7 of the aminoacids e) the comparison of the abnormal excretion of individual aminoacids between infants and parents showed that there is a correspondence between them. Our findings suggest that in some at least cases of nutritional rickets there is a genetic element manifesting itself only under adverse environmental conditions.

HORMONAL IMBALANCE IN THE DIENCEPHALIC SYNDROME.
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The findings of cachexia with lack of subcutaneous tissue, euphoria, hyperkinesis, nystagmus, optic atrophy pallor without anemia, and large hands and feet are characteristic of the diencephalic syndrome. Extreme starvation and undernutrition may be associated with high concentration of serum growth hormone (GH). This has also been observed in patients with diencephalic syndrome (DS) after glucose administration and arginine infusion. A 2y old girl is described with proven spongioblastoma of the 3rd ventricle and the classical symptoms of DS. Arginine infusions were performed before, after and during irradiation therapy to determine GH and insulin response. Basal GH was elevated and increased further after arginine. During X-ray treatment the arginine-induced GH increase was considerably enhanced but decreased toward the end of X-ray therapy. 4 weeks after irradiation was finished no increase of GH was elicited upon arginine infusion but GH rose to extremely high levels during sleep. Insulin levels were always low normal, T_4 at the upper limit of normal, plasma cortisol and diurnal variation normal. Extension of tumor or treatment may explain GH changes.

ACID-BASE STATUS IN DIETARY TREATMENT OF PHENYLKETONURIA
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Blood acid-base status, serum electrolytes and urine-pH were examined in 64 PKU-patients receiving 3 different low-phenylalanine protein hydrolysates and 2 synthetic amino acid mixtures. The different formulae caused significant differences in acid-base status, K and Cl in blood- and in urine-pH. Metabolic acidosis seemed to be correlated to an excess of anions (Cl^-) and a high content of the sulphur containing amino acids. Balance studies were done in two children. In 6 balance periods 4 formulae were given. Formula A had an excess of cations, whereas formula B_1 showed an excess of anions. Both were commercially available products. Formulae B_2-B_3 were modifications of formula B_1 with a reduction in the content of Cl, cystine and methionine. We found an increasing metabolic acidosis from A (blood-pH 7.45, serum HCO_3 25.8 mval/L) to B_3 (7.41, 24.0), B_2 (7.39, 19.3) and B_1 (7.36, 17.0). Urine-pH decreased (A 7.25, B_3 6.22, B_2 5.65, B_1 5.6) and total H excretion in urine increased (A 0.3, B_3 2.7, B_2 3.3, B_1 4.4 mEq/Kg/24h). In the formulae B_3, B_2 and B_1 the difference in total H^+ excretion correlated with the different Cl^- and S^- content of the diet and the different Cl^- and SO_4^- content of the urine. We propose that formulae should have an excess of cations and that organic sulphur intake should not exceed 1mM S/Kg/24h.