ACID BASE-
RENAL ELECTROLYTE

1 CALCIUM METABOLISM IN NEPHROTIC SYNDROME (NS) OF CHILDHOOD.

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Patients with NS have several disorders of calcium metabolism: hypocalcemia, hypocalciuria and probably decreased intestinal absorption of calcium. In order to evaluate the mechanisms responsible we have studied in 23 children, 3-12 years old, with NS and normal renal function, total and ionized calcium, calciuria, and blood levels of 25-hydroxyvitamin D and of Gc-protein. The studies were performed when proteinuria was > 200 mg/h/mq and repeated during remission of NS.
The blood levels of 25HCC and of Gc-protein were significantly lower than that in normal subjects ($p < 0.01$) and there was a direct correlation between albuminemia and plasma levels of 25HCC, and an inverse correlation between the degree of proteinuria and 25 HCC.
The loss of metabolites of vitamin D circulating bound to Gc-proteins seems the main cause of the disorders in calcium metabolism observed in NS. The need of vitamin D therapy in proteinuric nephrophaty is stressed out.

2 THEORETICAL MODEL TO ESTIMATE RENAL NET ACID EXCRETION,

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Natural food is originated from cell material with constant pH. Patients fed natural food show renal net acid excretion (NAE) far below maximum. During parenteral nutrition or under synthetic diets high NAE was observed. Therefore, a model was developed to calculate NAE under a synthetic diet from the analytical data of this diet. According to Relman (J.Clin. Invest. 40, 1621, 1961) NAE corresponds to the difference of urinary anions [sulfate (SO_4) + organic acids (OA) + chloride (Cl) + phosphate (P)] and urinary cations [sodium (Na) + potassium (K) + calcium (Ca) + magnesium (Mg)]. If urinary excretion of each parameter can be estimated from the data of intake, NAE can be predicted. In steady state conditions the urinary excretion of electrolytes correlates with their intestinal absorption, which can be estimated from intake and absorption rate. Absorption from the gut was estimated in the following way: Na + Cl: 100%; K: 90%; Ca: 0.17 x Ca intake (mg) + 60; Mg: 0.39 x Mg intake (mg) - 23; P: 0.642 x P intake (mg) - 11. 75% of the ingested organic sulfur (methionine and cystine) is oxidized to SO_4 and excreted in the urine. OA excretion is almost independent from the diet (38 meq/d/1.73m^2). The usefulness of this theoretical model to estimate NAE was demonstrated in acid-base studies of children with phenylketonuria receiving two synthetic amino acid mixtures (PAM with a high NAE of 4-6 meq/kg/d, PAM_{74} with a low NAE of 1 meq/kg/d).

3 FAMILIAL HYPOKALAEMIA AND HYPOMAGNESAEMIA. GITELMAN'S SYNDROME. REPORT OF 6 CASES.

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Six cases of renal wasting of potassium and magnesium are described in four families. Four patients presented with tetany, whilst two were asymptomatic siblings of these. One patient also suffered from a progressive external ophthalmoplegia syndrome and mental retardation, whilst the remaining five were normal in physical and intellectual development. One patient (now aged 31 years) has subsequently given birth to two normal children, but maintains very low serum levels of both potassium (2.0 mM) and magnesium (0.5 mM) when off electrolyte therapy. No abnormalities in calcium metabolism were found and there was no other evidence of tubular reabsorptive defect apart from slight defects in urinary concentration and acidification. In particular sodium chloride conservation appeared normal. Plasma renin levels were normal, or slightly raised in these patients and urinary aldosterone levels were normal, distinguishing this condition from Bartter's syndrome. Magnesium loading did not affect potassium wasting, nor did potassium loading alter the renal handling of magnesium. Spironolactone was able to improve tubular reabsorption of potassium, but not of magnesium.
Treatment consists of magnesium and potassium supplements to the diet. Despite continuing severe renal losses of both potassium and magnesium these patients show very few or no overt symptoms over many years, and renal function is otherwise well preserved. It is suggested that this condition be known as Gitelman's Syndrome.

4 CHRONIC HYPERKALEMIA, METABOLIC ACIDOSIS AND SHORT STATURE IN TWO SIBLINGS-THE SPITZER-WEINSTEIN SYNDROME

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A three-year-old boy presented with the transient signs of disturbed consciousness, cyanosis and arrhythmia and was found to have hyperkalemia (K^+9.6), metabolic acidosis (pH 7.25, bicarbonate 17) and growth failure. Blood pressure was normal. Creatinine clearance, PSP excretion and urinary concentration were normal. Aldosterone level and plasma renin activity were also within normal ranges. Urinary acidification was normal, but the ability to excrete net acid appeared decreased. The renal threshold for bicarbonate was low. Administration of the sodium bicarbonate and acetazolamide showed poor response in reducing serum potassium, but serum potassium and bicarbonate returned to normal levels during the administration of a Thiazide diuretic. Hyperkalemia was also corrected by lasix, but serum bicarbonate remained unchanged. There were no significant weight changes during these treatments. When the diuretics were tapered or discontinued, hyperkalemia recurred while serum bicarbonate remained at normal levels. From these observations it appeared that this patient had impaired renal excretion of potassium. He has been on long-term Thiazide thereapy (1.3mg/kg) and his serum potassium and bicarbonate levels are kept within normal ranges, and he grew 9 cm in 18 months. Family studies revealed that his two-year-old sister had hyperkalemia (K^+6.8) and metabolic acidosis (pH 7.29, bicarbonate 16) with her height at fifth percentile and she is being worked up. His parents and an older brother are normal.

5 RENAL FUNCTION IN CONGENITAL HEART DISEASE (CHD),

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CHD is characterized by chronic hypoxemia and elevated hematocrit (HT). Both could affect renal hemodynamics and function. Renal clearance studies were performed before corrective surgery in 18 children presenting with CHD. Inulin clearance was normal (115 ± 5 ml/min x 1.73 m^2) while PAH clearance was significantly depressed (410 ± 25). Filtration fraction was elevated to 29%. A negative correlation was observed between PAH clearance and HT ($Y = 1355 - 17X$, $p < 0.02$) up to HT values of 60%. Free water clearance correlated with urine flow: the slope was similar in CHD and normal controls, thus reflecting normal Na transport in the distal tubule of CHD. Acidification studies demonstrated a state of proximal renal tubular acidosis with a bicarbonate threshold of 19.7 ± 0.6 mmol/l and a minimal urine pH of 5.15 ± 0.08. Urine PCO2 increased significantly above blood PCO2 during alkaline diuresis (ΔPCO2 = 29 mm Hg), thus demonstrating normal acidification by the distal tubule. It is concluded that chronic hypoxemia and/or elevated hematocrit present in CHD increase renal vascular resistance and decrease proximal bicarbonate reabsorption without affecting Na distal transport.

6 BIOLOGIC ACID THERAPEUTIC EFFECTS OF 1X-HYDROXY-VD_3 IN PATIENTS WITH FANCONI OR LOWE SYNDROME.

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The rachitis of the so-called Fanconi syndrome have been attributed mainly to disturbance of activation of vitamin D in kidney, renal tubular acidosis and failure of reabsorption of phosphate. Which of these factors plays a major etiologic role remains unknown. In this paper, the biologic and therapeutic effects of 1X-OHVD 3 in 6 patients with Fanconi or Lowe syndrome were studied.

Methods: Serum 1,25-dihydroxycholecalciferol. (1,25-$(OH)_2VD_3$) was determined by partial revision of the radioreceptor assay. ^{47}Ca uptake was estimated by modified Avioloi's method. Serum parathyroid hormone (PTH) was determined by usual manner. Results and Conclusion: 1X-$OHVD_3$ was administered to 6 patients with Fanconi or Lowe syndrome in order to evaluate its clinical effect. The dosage employed ranged from 0,25 to 6.0 ug. The effect of 1X-$OHVD_3$ proved to be 200-250 times as great as that of vitamin D_2. The plasma 1,25-$(OH)_2VD_3$ level was low but elevated rapidly as a result of treatment with 1X-$OHVD_2$. Calcium absorption was definitely diminished in patients with Fanconi or Lowe syndrome, except those with Lowe syndrome who had normal serum alkaline phosphatase level while on 1X-$OHVD_3$. It was thus suggested that calcium malabsorption due to failure of 1X-hydroxylation of 25-$OHVD_3$ in the kidneys, together with impaired regulation of acidbase balance and a defect in reabsorption of phosphate in the renal tubules, is involved in the pathogenesis of the rickets of so-called Fanconi syndrome.