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HYPERPIPECOLIC ACIDEMIA (HPA): CLINICAL, BIOCHEMICAL AND PATHOLOGIC FEATURES. Barbara K. Burton (Spon. by W. B. Lorentz, Jr.). Bowman Gray School of Medicine, Dept. of Pediatrics, Winston-Salem, N.C.

HPA is a unique metabolic disorder previously described in only 2 unrelated infants. A 5 mo. old male (Pt. 2) was suspected of having HPA when he presented with hepatomegaly, retinopathy and developmental delay. A previous sib, also male (Pt. 1) died at 18 mo. with a similar disorder progressing to liver failure and seizures. The diagnosis of HPA was supported in Pt. 2 by a serum pipecolic acid (PA) level of 1.10 mg% (nl .17 ± .05) and confirmed by a markedly abnormal response to an oral PA loading study. Since PA is a metabolite of lysine, protein restriction was begun and decreasing intake of protein was accompanied by decreasing serum PA. On 0.9 g/kg/day, however, serum PA remains 2-3 x normal. The pt. has grown well and has had no apparent progression of his liver disease but remains developmentally delayed and visually impaired at age 14 mo.

The PA level in frozen liver from Pt. 1 was 2.41 mg/g prot (nl .36-.87). Unique pathologic changes were found in liver and fibroblasts from Pts. 1 & 2 and in brain from Pt. 1.

Unless suspected clinically, HPA may be missed by routine metabolic screening. 2-dimensional TLC revealed a PA spot in the urine of Pts. 1 & 2 but no PA peak was detected in serum or urine on an autoanalyzer. HPA is clinically similar to Zellweger's syndrome which has also been associated with elevated serum and urine PA in some patients. The primary metabolic defect in these disorders may be closely related.

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THE POSSIBLE ROLE OF CATECHOLAMINES IN THE PATHOGENESIS OF SHOCK IN ACUTE MAGNESIUM (Mg) DEFICIENCY IN YOUNG RATS. Joan L. Caddell and David Lagunoff (Spon. Patricia Monteleone), Dept. Pediatr-Adolesc Med. and Pathology, St. Louis U. Sch. Med. and Cardinal Glennon Hosp., St. Louis, Mo.

The sudden potentially fatal episode occurring in the young Mg deficient rat appears to be a form of shock with neurological components; the pathogenesis is unknown. Pathologic changes include acute pulmonary edema, which may be hemorrhagic (Ped. Res. 12:1157, 1978); this suggested the possible role of massive catecholamine release in this syndrome (Cheng, Cardiovasc. Res. 9:105-11, 1975). Male weanling 35 g rats were fed purified diets with 40% casein and sufficient (S) Mg (150.8±1.1 mg/100 g(3)) or deficient (D) (6.0±0.1 mg/100 g) (3). Group D rats became hyperirritable; of 10, three died spontaneously between days 10 and 12. On days 12 to 13, urine was collected in 7 rats per group and analyzed for 24 hr catecholamines. Bone Mg was determined by atomic absorption spectrophotometry. US Bureau Stds. liver was reference.

GROUP	WT GAIN	FEMUR Mg	URINARY CATECHOL.	URINARY CATECHOL.
RATS	g/13 da	mg/kg dry	ug/24 hr urine	ug/24 hr/kg b.wt.
S	108.6±2*	4066±94	0.80±0.13	7.5±1.3
D	72.4±2	846±39	1.22±0.12	16.6±2.0
P Value**	<0.001	<0.001	<0.025	<0.0025

*Mean±SEM; ** Student's t test. Reduced growth and bone Mg values in group D rats confirmed Mg deficiency. We conclude that there is an abnormality in catecholamine metabolism which may contribute to the pathogenesis of shock in acute Mg deficiency in young rats. Support: Life Seekers and Cardinal Glennon Hosp. Res Funds.

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TREATMENT OF AGRODERMATITIS ENTEROPATHICA(AE) WITH ZINC PICOLINIC ACID(ZnPA). Ralph Cash, Ingeborg Krieger, Gary Evans. Wayne State Univ. Dept. of Ped. Detroit, & USDA, Human Nutrition Research Cent. Grand Forks, ND

AE without hypozincemia(variant) was recently shown to respond to viokase which contains PA (Krieger&Evans, J.Pediatr.96:32,80). It promotes Zn absorption in the rat and concentrations in human milk are 20x higher than in cow's milk(Evans, Pediatr. Res.14:876, 80). The patient was treated successfully with 60mg Zn as the sulfate, then for 5 mo. with ZnPA(5mg Zn++) and 3 mo. with 8-20mg PA. Both maintained plasma Zn around 150ug/dl(N:112±13). This prompted a trial of ZnPA in 3 patients with "classical"AE. The minimum therapeutic dose of Zn sulfate that maintained normal plasma Zn was first determined and then discontinued until the rash appeared. ZnPA was then given, using 1/3 dose of Zn+. This caused rapid improvement and has maintained normalcy for 4-6 weeks.

Plasma PA was measured in 2 AE and 3 variant AE cases, age 1 to 9 yrs, while they were on 30-45mg Zn++ as the sulfate and well. Normal:1.2-2.0umoles/dl(4 children, 10 adults). Plasma PA in AE was 0.05±0.45 umoles/dl, and in variant AE 0.02-0.69 umoles/dl. These values were thus far below the normal range. Some variability can be attributed to different dietary content of PA since it was shown that oral PA raises plasma PA(in 1 case of AE from 0.05-1.24 umoles/dl). These data indicate that ZnPA decreases the requirements for Zn in AE, presumably because it acts as a ligand. A genetic defect of PA metabolism may be the cause of AE. Neither PA nor ZnPA are recommended for treatment until the metabolism of this tryptophan metabolite is better understood.

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ELEVATED SERUM 1,25-DIHYDROXYVITAMIN D (1,25OH₂D) LEVELS IN THE HYPERCALCEMIA OF SARCOIDOSIS: CORRECTION BY GLUCOCORTICOID THERAPY. Russell W. Chesney, Hector F. DeLuca, Sheldon Horowitz and Richard Hong, University of Wisconsin Medical School, University of Wisconsin Hospitals, Departments of Pediatrics and Biochemistry, Madison, Wisconsin.

It has recently been suggested that the hypercalcemia of pulmonary sarcoidosis could be related to high circulating levels of 1,25OH₂D (Bell et al, JCI 64:218, 1978; Papapoulos et al, Lancet i:627, 1979). However, this hypothesis has not been tested in a child. The evaluation of serum calcium levels of 12.4 to 14.8 mg/dl in a 9-year-old girl revealed a low normal immunoreactive PTH level, hypercalcuria, an abnormal Ca/Cr ratio (0.81) and a creatinine clearance of 20.5 ml/min/1.73 M². Because of hepatomegaly, cutaneous anergy and the presence of native macrophage suppressor activity, a liver biopsy was performed which revealed non-caseating granulomata. Vitamin D metabolite levels were: 25OH-D of 27-45 ng/ml (nl 30±5, SD); 24,25OH₂D of 2.3-2.7 ng/ml (nl 1.7±0.5), and 1,25OH₂D of 91 and 75 pg/ml (nl 42±15). Despite hypercalcemia, 1,25OH₂D levels were greater than +2 SD above mean value for age. Prednisone therapy (2 mg/kg/day) lowered serum Ca, urinary Ca/Cr ratio and Ca excretion (388 to 182 mg/day), and Cl_{Cr} rose to 128 ml/min/1.73 M². Levels of 1,25OH₂D fell to 23 and 28 pg/ml. The finding in this and other adults with sarcoidosis suggests that hypercalcemia and hypercalcuria are related to elevated circulating 1,25OH₂D levels. Serum elevations occur independent of PTH or other vitamin D metabolite levels and 1,25OH₂D overproduction and hypercalcemia in sarcoidosis can be reversed by glucocorticoids.

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LACK OF SEASONAL VARIATION IN SERUM 1,25-DIHYDROXYVITAMIN D (1,25OH₂D) LEVELS DESPITE CHANGES IN 25-HYDROXYVITAMIN D (25OH-D) LEVELS. Russell W. Chesney, John F. Rosen, Alan J. Hamstra and Hector F. DeLuca, University of Wisconsin Medical School, University of Wisconsin Hospitals, Departments of Pediatrics and Biochemistry, Madison WI, and Albert Einstein College of Medicine, Montefiore Medical Center, Department of Pediatrics, Bronx NY.

The concentrations of 25OH-D (n=62) and 1,25OH₂D (n=231) were measured in the sera of normal subjects aged 18 months to 35 years. Samples were obtained in all months of the year to assess the effect of the seasons on serum concentration. Serum 25OH₂D was 16.3±7.0 ng/ml (SE) in Jan.-March and rose to 24.4±7.6 in April-June and to 31.2±8.5 in July-Sept., p < .001. In Oct.-Dec. it fell to 20.9±7.2, p < .01. Both total 25OH-D and 25OH₂D are higher during the months April-Sept. No seasonal variation in 25OH₂D ($\bar{x}$ ± SE = 7.3±5.2 ng/ml) or 1,25OH₂D ($\bar{x}$ = 43±2 pg/ml) were found. Age-related differences in 25OH₂D and D₃ were not apparent. The levels of 1,25OH₂D are higher in adolescents and increase from 35±19 pg/ml (SD) at 1.5 to 10 years to 54±21 pg/ml at 10-20 years. In adults, 20-35 years, the levels fall to 28±16 pg/ml. Despite a seasonal variation in the precursor of 1,25OH₂D, the levels of this most active metabolite of vitamin D do not vary with the seasons and presumed increased sunlight exposure. The levels of 1,25OH₂D are higher during a period of rapid growth. The absence of seasonal variation is further evidence of the tight feedback regulation of the hormonal form of vitamin D.

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HYPERTRIGLYCERIDEMIA INDUCED BY ZINC DEFICIENCY. Sandra Clejan, Mariano Castro-Magana, Vaddanahally T. Maddaiah, and Platon J. Collipp. Nassau Cty Med Ctr SUNY, Stony Brook Health Sciences Center, Dept. of Ped., E. Meadow, NY 11554.

Serum lipid abnormalities have been found to be associated with zinc deficiency (Zn-). We observed that serum triglycerides (TG) responded rapidly to alterations in zinc nutritional status. After 7 days on Zn- diet (Zn 1 ppm), TG were increased by 200%, whereas in rats fed a control (C) diet (100 ppm) no changes in TG levels were recorded. By continuing the Zn- diet the TG increased gradually to 600% of the initial value after day 28, when TG leveled off. Thus, the elevation in TG preceded clinical signs of Zn-, and the elevation in TG is higher in the more severely deficient rats. Zn- rats fed the C diet or a Zn enriched (Zn+) diet (500 ppm) were repleted with Zn rapidly and TG decreased to normal values. Thus, hypertriglyceridemia (HTG) of Zn- is reversible when dietary Zn is increased and body stores of Zn are repleted. The HTG may be related to the decrease in post heparin plasma lipoprotein lipase between Zn- (370 ± 98 DPM glycerol release/mg protein/30 min) and C (510 ± 124). To test the hypothesis that Zn- rats have a higher level of endogenous lipid production, *in vitro* liver metabolism experiments were undertaken. Liver slices were incubated with (¹⁴C) glucose or (¹⁴C) palmitate and their utilization for TG synthesis and ¹⁴CO₂ production was measured. The results showed higher incorporation into TG in Zn- rats which may be due to an abnormality in carbohydrate metabolism.