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PPA values ranging from 6.6 mg % to 11.6 mg % on a regular diet. Case 4 is an infant with a PPA value of 45 mg % at 4 days and 76.4 mg % at 2 ½ weeks. She was treated with low-phenylalanine diet for 15 months and then returned to a regular diet. For the past 7 months on a regular diet, the PPA has ranged between 4.6 mg % and 10.7 mg %. Cases 3 and 4 may be viewed as hyperphenylalanemia without PKU.

Phenylalanine hydroxylase was determined by the method of LaDu and Zannoni and fresh liver obtained by biopsy. The results expressed as μM tyrosine¹⁴C formed/Gm protein/45 minutes were as follows:

	6 controls	Case I	Case 2	Case 3	Case 4
Without DMTHP* With DMTHP*	3.0 ± 1.6 57.0 ± 10.0	0	0	1.6 24.7	0.6 6.0

These data suggest that the 'classical' and 'mild' form of PKU probably have the same basic metabolic lesion. They show that hyperphenylalanemia without PKU is not caused by cofactor deficiency and represents a true 'partial' PKU as reflected by slightly elevated PPA, delayed clearance of phenylalanine by tolerance test and decrease of phenylalanine hydroxylase in liver. (APS)

*2-amino-4-hydróxy-6,7-dimethyl-tetrahydropteridine

73 The In Vitro Control of Calcification in Osteogenesis Imperfecta. CLIVE C. SOLOMONS*, Univ. of Colo. Med. Ctr., Denver, Colo. (introduced by Donough O'Brien).

Previous work has implicated bone collagen obtained from patients with osteogenesis imperfecta as a potent inhibitor of the in vitro formation of bone mineral. The present investigation further examines the mechanism of inhibition and suggests a possibility for therapy. It was observed that the citrate-soluble fraction of bone collagen from two patients with the disease had a pyrophosphate content of 1.4 µm/mg collagen which is four times the normal value. Urinary excretion of pyrophosphate was also elevated. As pyrophosphates are thought to be inhibitors of calcification both in vitro and in vivo (Fleisch, H. et al. Nature 212: 903-3 [1966]), the abnormal collagen was treated with the enzyme pyrophosphatase in the presence of Mg as cofactor during the in vitro mineralization procedure. It was found that Mg alone significantly increased the catalytic properties of osteogenesis imperfecta collagen and this effect was doubled when pyrophosphatase was present. These results suggest that collagen-bound pyrophosphate is partly responsible for the failure of bone matrix to calcify. The possibility that these pa-tients need a high level of Mg as cofactor for their pyrophosphatase activity is being investigated. (Supported by U.S.P.H.S. AM 08757-03) (SPR).

74 Hyperexcretion of Urinary Amino Acids and Phosphorus in the Vitamin D-Deficient Holtzman Rat.

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Hyperexcretion of urinary phosphorus, and free amino acids, resulting from diminished net tubular absorption, occurred in rats fed for 6 weeks or more, from weaning, on low calcium diets (0.02 %) and normal phosphorus intakes. The intensity of renal dysfunction was proportional to the degree of hypocalce-

mia below 6.5 mg %; the Vitamin D content of the diet was immaterial to the relationship; controls pairfed on 0.4 % calcium diets did not develop renal dysfunction. Intrapetitoneal calcium injected and parathyroidectomy suppressed the urinary hyperexcretion of amino acids and phosphorus; injection of parathyroid extract (LILLY) enhanced it. Rickets and bound hyperaminoaciduria also occurred in hypocalcemic animals; hydroxyproline, proline and glycine were particularly prominent in the bound fraction. Parathyroid glands showed increased mitoses and cellular hypertrophy, proportional to the severity of hypocalcemia, and irrespective of Vitamin D intake. The data imply that excess circulating parathyroid hormone, rather than Vitamin D deficiency itself, accounts for the bound aminoaciduria and impaired membrane transport of amino acids and phosphorus in Vitamin D deficiency. (Supported by M.R.C. Grant, MT-1085, and N.I.H. Grant, AM-05117) (SPR)

75 Effect of Copper on Serum Ceruloplasmin Concentration. Neil Holtzman*, George Graham*, Patricia Charache* and Robert Haslam*, Johns Hopkins Univ. Sch. of Med., Baltimore, Md. (introduced by Robert E. Cooke).

The effects of the oral administration of copper were studied in 1. infants with nutritionally induced cooper deficiency; 2. children receiving copper sulfate as an emetic after toxic ingestions. 1. Seven marasmic infants were rehabilitated with a high calorie-adequate protein-low copper diet. In 2 of them where initial determinations were performed, serum ceruloplasmin con-centration was normal. With recovery and rapid growth, copper deficiency developed, and all 7 exhibited hypoceruloplasminemia. The intact metalloprotein was deficient both by oxidase and immunochemical assays. Apoceruloplasmin could not be detected immunochemically. Thus both the copper prosthetic group and the apoprotein were deficient. In each of the 7, ceruloplasmin levels rose after the administration of copper, 0.10-0.30 mg/kg/day. 2. Copper sulfate, 250 mg, was administered orally as an emetic to 4 children after toxic ingestions. Although vomiting occurred within 5 minutes, a rise of serum copper of 14, 22, 30 and 71µg % was observed. Serum ceruloplaxmin concentration increased significantly in 3 of the children within 12 hours. Thus it appears that copper either stimulates de novo synthesis of ceruloplasmin or combines with apoceruloplasmin in the liver to form the metalloprotein which is then released into the peripheral blood. It is possible that in Wilson's disease this mechanism may be impaired. Because copper is corrosive and absorbed, even after prompt emesis, it does not appear to be a safe emetic, as recently advocated, particularly when the agent ingested has the same effects as toxic doses of copper. (APS)

76 Energy Substrates in the Normal Premature Newborn.
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Recent studies indicate the importance of lipid substrates in normal premature infants (Van Duyne, 1959; Persson et al., 1966). To determine the relationship of acid-base status to energy substrates, sequential arterialized pH, PaCO₂, BE (mEq/L) and venous FFA (mEq/L), ketones (mEq/L), and glucose (mg%) were determined in 36 newborns (1250–2500 gm)