not clearly distinguish the patients' sera from normal sera, nor did these studies indicate clearly the tissues sources of serum enzymes. We conclude that abnormalities of AP do exist in hypophosphatasia, and that most of the AP in sera of patients is derived from tissues other than bone.

61 In vivo *Kinetics of Polysaccharides in the Hurler and Sanfilippo Syndromes.* CHRISTOS S. BARTSOCAS and HUGO W. MOSER, Harvard Med. Sch., Massachusetts Gen. Hosp., Children's and Neurology Services, Boston, Mass. (introduced by John D. Crawford).

FRATANTONI and NEUFELD have shown that cultured skin fibroblasts of patients with the Hurler and Hunter syndromes are deficient in their ability to degrade polysaccharides. We have studied *in vivo* polysaccharide turnover and have found this technique to be of value for the detection and delineation of the metabolic defects in this group of disorders. In these studies, 25 microcuries of ^{35}S Na_2 SO_4 were injected intravenously, and the specific activities of urinary polysaccharide and inorganic sulfate measured serially for 3–21 days. In 6 control patients urinary polysaccharide and inorganic sulfate reached isotopic equilibrium within 12 to 36 hours after injection; thereafter, the rate of disappearance of radioactivity from polysaccharide and inorganic sulfate was identical.

In 3 patients with the Hurler syndrome, the rate of disappearance of radioactivity from urinary polysaccharides was much slower than normal, suggesting impaired degradation. The same result was obtained in a clinically similar patient with normal urinary polysaccharide levels, who at postmortem was found to have polysaccharide storage and diminished beta galactosidase activity. The most striking defect in polysaccharide degradation was found in a patient with combined sulfate and polysaccharide storage who was later shown to have a generalized deficiency of arylsulfatases A, B and C. In contrast, 2 twins with the Sanfilippo syndrome and a 10-fold increase of urinary heparitin sulfate, had a normal polysaccharide turnover time, and thus by this technique showed no evidence of a degradative defect.

62 *Effective Treatment of Hypophosphatemic Vitamin D Resistant Rickets (VDRR) with 25-Hydroxycholecalciferol (25-HCC).* J. R. SEELY, HARRIET COUSSONS, J. D. SMITH, Univ. of Okla. Med. Center, Children's Mem. Hosp., Dept. of Ped., and Clin. Res. Center, Okla. City, and HECTOR F. DELUCA, Univ. of Wis., Dept. of Biochem., Madison (introduced by Harris D. Riley, Jr.).

From the demonstration by DELUCA *et al.* that 25-HCC is the active form of D_3, it was postulated that some forms of VDRR may result from a decreased ability to convert D_3 to 25-HCC and should respond to it. Following oral administration of tritiated D_3, 4 patients with VDRR failed to develop significant plasma concentrations of labeled 25-HCC compared to controls ($< 1\%$ vs. $> 4\%$ at 24 h and $< 3\%$ vs. $> 10\%$ at 48 h). Five patients 3 with VDRR and 2 with osteomalacia) from two pedigrees with hypophosphatemic VDRR have been treated for periods of 2 to 8 months with increasing oral doses of 25-HCC in oil. All have responded symptomatically, chemically and radiographically (X-ray unchanged in 1 patient adequately treated less than 1 mo.). 4,800 U/day appears to be a minimal effective 'healing' dose. Maintenance dose has not been established. No toxicity has been observed. Observations during unplanned transient periods off treatment indicate that the duration of action of 25-HCC in man is short compared to D_2 or D_3. These findings indicate that 25-HCC will prove to be an effective, safe form of therapy for VDRR.

63 *A New Syndrome of Keto-acidemia in Infancy.* MARVIN CORNBLATH, GRANT MORROW III, LOUIS A. BARNESS, GARY A. FLEMING, ROBERT L. GINGELL and ALLAN T. LEFFLER, Univ. of Maryland, Dept. of Ped., Balto., Md. and Univ. of Pennsylvania, Dept. of Ped. Philadelphia, Penna.

Following unexplained tachypnea in the first month of life, C.C., a Negro male born of healthy, unrelated parents, presented at 6 weeks of age with recurrent tachycardia, hyperpnea and dehydration. Severe metabolic acidosis, ketonuria, ketonemia and aminoaciduria were present, yet the free fatty acids, glycerol and glucose values were normal. These episodes consistently lasted 72 h and required intense hydration (200–250 cc/KG/24 h) and alkalinization (up to 40 mEq $NaHCO_3$) therapy. Methylmalonic acidemia, hyperglycinemia, glycogen storage disease, diabetes mellitus and salicylism were eliminated as the etiology. Episodes of keto-acidosis occurred spontaneously with soy formula feedings; but with carbohydrate feedings alone, the child remained clinically normal and relatively ketone free. The administration of soy protein precipitated keto-acidosis within three h. This incident was characterized by the rapid production of a metabolic acidosis, rise in serum ketones from 36 mgm% to over 100 mgm%, excretion of up to 4.94 gm of urinary ketone/24 h, and the development of reversible amino-aciduria, consisting primarily of lysine, glycine and phenylalanine. Measurement of the serum amino acids during ketosis revealed mild elevations in proline, lysine and glycine. The child succumbed at age 26 weeks. Continued studies of h, cultured skin fibroblasts indicate normal utilization of propionate, methylmalonate, β-hydroxybutyrate and aceto-acetate. It is postulated that this child represents a previously undescribed form of keto-acidosis due to the excessive production of ketones from amino acids.

64 *Thiamine-dependent Neonatal Lactic Acidosis with Hyperalaninemia.* M. G. BRUNETTE, B. HAZEL, C. R. SCRIVER, F. MOHYUDDIN and L. DALLAIRE, Univ. of Montreal, Maisonneuve Hosp. and McGill Univ., Montreal Children's Hosp. Res. Inst. Montreal, Canada.

The 'vitamin dependencies' comprise a rapidly developing group of metabolic diseases. We describe a recurring disorder of pyruvate metabolism responsive to thiamine supplements. Severe neonatal metabolic acidosis was observed in a child who subsequently developed psychomotor retardation and infantile spasms. The acidosis was accompanied by increased concentrations of lactate, pyruvate and -alanine in plasma and urine. Spontaneous acidosis has been intermittent, three episodes being recorded since birth. In later life, thiamine (25 mg i.v.) given after correction of acidosis with bicarbonate, provoked a severe metabolic alkalosis. The last episode could be induced by high carbohydrate diet, corrected in 4 days by thiamine (5 mg i.m.), and controlled by a low carbohydrate, high protein diet. Nutritional deficiency of thiamine has been ruled out. Since -ketoglutarate levels were