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

not increased, a specific thiamine-dependent defect in pyruvate decarboxylase was considered. Assay of this enzyme in fresh peripheral leucocytes, or after phytohemagglutination stimulation, at low and high concentrations of pyruvate, with and without thiamine added, revealed no abnormality. Negative results were also obtained with cultured skin fibroblasts. A phenotypic variant of the traits described by BLASS and TADA, but limited to liver in this case, is proposed. (Research supported by Grants MRC 1085 and NHW 604-7-643.)

65 *Low Phosphorylase Activity: A Symptom but not a Diagnosis.* GEORGE HUG, WILLIAM K. SCHUBERT and GAIL CHUCK, Children's Hosp. Res. Fndn. Cincinnati, Ohio.

Since our initial description of deficient activity of hepatic dephosphorylase kinase and increased liver glycogen [Science *153:* 1535, 1966], we have studied a total of 7 patients with this condition. Five of these patients have been reported [J. clin. Invest. *48:* 705, 1969]. They and the 2 additional patients, brothers age 4 and 1 ½ years, always had greatly reduced liver phosphorylase activity (about 10% of control) that could be increased to normal by addition of kinase. This rules out phosphorylase deficiency, or type VI glycogenosis. On the basis of 'one enzymatic defect for one type of glycogenosis', we called deficient kinase activity type IX glycogen storage disease. In type IX glycogenosis there is no hyperlipemia, hypoglycemia, acetonuria, or evidence of X-chromosomal inheritance. There is a typical light and electron microscopic appearance of the liver. Biochemically, the skeletal muscle is normal as is the blood sugar response to glucagon. In contrast, in a girl with hepatomegaly and low hepatic phosphorylase activity there is increased glycogen concentration in the skeletal muscle as well as the liver and the glucagon tolerance curve is flat. In her skeletal muscle the amount of *total* phosphorylase is normal but all of it is in the *inactive* form. Phosphorylase kinase is present in this muscle but we found evidence for deficient activity of 3′5′-AMP dependent kinase that normally activates phosphorylase kinase [J. biol. Chem. *243:* 3763, 1968]. Therefore, we have named this new type of glycogen storage disease with a hitherto undescribed enzymatic deficiency type X glycogenosis. (Supported by NIH grants No. AM 13903 and No. RR 00123.)

66 *Human Liver Galactose-1-phosphate Uridyl Transferase: Activity in the Negro Galactosemic.* STANTON SEGAL and SHIRLEY ROGERS, Children's Hosp. of Philadelphia, Pa.

Since the Negro with congenital galactosemia can metabolize substantial amounts of galactose, assays for the deficient enzyme, gal-1-p uridyl transferase, were performed in homogenates of punch biopsies of liver from two Negro patients. Kinetic characteristics of the normal enzyme were determined in homogenates of liver from four non-galactosemic patients undergoing abdominal surgery and in two 50-fold purified preparations of liver obtained within 24 h of death. Kinetic parameters including concentration dependence and Km were similar in the crude homogenates and partially purified normal enzyme. The specific activity of transferase in mμmoles/min/mg protein was 12 and 1.6 in crude homogenates of the normals and galactosemics, respectively. The latter activity was linear with incubation time but showed no concentration dependence on uridine diphosphoglucose. No uridine diphosphogalactose pyrophosphorylase activity, a possible alternate pathway, was detected in the liver of Negro patients and transferase activity with thymidine diphosphoglucose as substrate was negligible. Either these patients possess a non-nucleotide pathway of galactose metabolism or the residual transferase activity accounts for their galactose metabolic capability. Results of *in vivo* metabolic studies with labeled galactose suggests the latter is most likely.

67 *Idiopathic Hypomagnesemia and Osteochondritis.* WILLIAM G. KLINGBERG, Dept. of Ped., West Virginia Univ. Sch. of Med., Morgantown, W.VA.

A previously asymptomatic 5-year-old boy presented with classic carpopedal spasm of 6 h duration. On examination he also had papilledema, decreased DTR's and a negative Chovstek. Serum Mg was 0.8 and K was 2.8 mEq/L. All other serum electrolytes, proteins, enzymes, Ca, PO_4, Glucose, BUN and Creatinine were normal. The EMG and PEG were normal. The EEG showed a few non-specific low waves and mild disorganization. Unexpectedly x-rays of bones showed a mild osteochondritis of shoulders, knees and hips (Legg-Perthes-like). Creatinine clearance was 70 ml/min/1.73 M^2. Gross renal tubular function was normal by concentration and acidification.

A 6-day balance study showed minimal negative Mg balance. When 20 mEq magnesium acetate (MgA) was added *per os* daily, another 6 day balance study showed a positive balance, but barely so (intake 174 mEq, output 132 mEq = +42 mEq). Little is known regarding Mg balance and metabolism in children, but adults with hypomagnesemia given MgAc would excrete very little in the urine. This child continued to excrete 5–9 mEq/day during the balance studies. Potassium was also in negative balance although not enough to be significant. Other ions were in normal balance.

When MgAc orally was increased to 40 mEq/day serum Mg rose to normal. After 6 months therapy the bony lesions have reverted almost to normal. MgAc therapy is still required as hypomagnesemic tetany again occurred when inadequate therapy was given. Is this a specific, partial renal tubular defect in Mg absorption.

68 *Evaluation of Adenine Therapy for Lesch-Nyhan Syndrome.* JOSEPH D. SCHULMAN, MARTIN L. GREENE, WILFRED Y. FUJIMOTO and J. EDWIN SEEGMILLER, NIH, Univ. of Washington, Seattle, and Univ. of California, San Diego (introduced by W. L. Nyhan).

The use of oral adenine to prevent the devastating neurologic consequences of the Lesch-Nyhan syndrome has a sound theoretical basis, and has been proposed for management of this aspect of the disease. We have attempted therapy of two patients with adenine begun in one patient, during the first month of life. Preliminary experiments in rats explored the toxicity of adenine; pretreatment with allopurinol (10 mg/kg) reduced the nephrotoxic effects of the insoluble adenine metabolite, 2,8-dioxyadenine, at adenine doses of 70 mg/kg. Two patients, a 13-year-old male with established neurologic disease and self-mutilation, and a normal-appearing one-month-old boy with documented hypoxanthine-guanine phosphoribosyltransferase (PRT) deficiency, were given adenine in doses up to 65 mg/kg/day. Toxicity was monitored by daily esti-