lated to the dosage of prednisone used for immunosuppression, the absence of growth potential at the time of transplantation and the development of chronic rejection.

- 57 *Nocturnal Enuresis: Correlation with Bacteriuria, Proteinuria and Dysuria.* WARREN F. DODGE, EVELYN F. WEST and LUTHER B. TRAVIS, Univ. of Texas Med. Branch, Dept. of Ped., Galveston, Texas.

Nocturnal enuresis has troubled parents and physicians at least since the 16th century. Theories as to its cause and cure have varied with the fad and fashion of the times and, until recent years, most studies have been remarkable principally for sampling bias and lack of controls. Myths which have been recently discarded include those relating it to deep sleep, lack of early toilet training, spina bifida occulta, low intelligence or common behavior problems. The present investigations of renal disease in school children presented a unique opportunity to evaluate the role of abnormal urinary findings in enuretic children and their non-enuretic classmates as well as re-examination of its association with sex, ethnic group, socioeconomic level, birth order and mother's level of education and marital status.

The prevalence of current bed-wetting for 6- to 10-year-old children was noted to be 18% for girls and 24% for boys ($p < 0.001$); and to differ significantly by ethnic group for girls but not for boys; by socio-economic level and family size for boys but not for girls; and for both sexes by mother's education but not by the other demographic characteristics examined. For girls, prevalence of significant bacteriuria increased in association with both presence and frequency of current enuresis ($p < 0.005$) and past complaint of dysuria ($p < 0.025$). No significant difference for prevalence of proteinuria in boys or girls was noted when analyzed by current enuresis or past complaint of dysuria.

- 58 *Measurement of Renal Function by Radionuclide Disappearance Curves.* GERALDINE I. SILKALNS, DONALD L. JECK, ADRIAN SPITZER, CHESTER M. EDELMANN, Jr. and M. DONALD BLAUFOX, Albert Einstein Coll. of Med., Dept. of Ped. and Radiol., Bronx, New York.

Reports based on adult patients suggest that either GFR or RPF can be measured accurately from the rate of disappearance of a radionuclide from the blood following a single intravenous injection. Although the advantage of avoiding urine collections in children is obvious, few attempts have been made to validate the method in this age group. Inulin, creatinine, and PAH clearances were performed and compared with simultaneous measurements obtained from iothalamate ^{125}I or orthoiodohippurate ^{131}I disappearance curves calculated as clearances by compartmental analysis (open, two compartment system). The results obtained in 31 patients ranging in age from 18 months to 16 years, with levels of renal function as estimated by C_{IN} between 20 and 158 ml/min/1.73 m 2 , were:

		n	ratio	r
^{125}I vs.	Inulin	12	0.96	0.93
	Creatinine	16	1.05	0.94
^{131}I vs.	PAH	6	0.81	0.97

No differences attributable to age or level of function were observed. It appears, therefore, that GFR or RPF can be estimated validly in children using the disappearance of a radionuclide from the blood.

- 59 *Hypersarcosinemia: New Observations.* F. H. GLO-RIEUX, F. MOHYUDDIN, D. T. WHELAN and C. R. SCRIVER, McGill Univ., Children's Hosp. Res Inst., Montreal.

Sarcosinuria was found in a 10-year-old French-Canadian boy with normal IQ, small stature ($< 3\text{rd}$ percentile) and bilateral contractures of lower limb muscles. Coexistent hypersarcosinemia ($0.18\text{--}0.34\text{ }\mu\text{M}$; normal $< 0.02\text{ }\mu\text{M}$) was unmodified by large supplements of folic acid, the coenzyme for the presumably abnormal apoenzyme, sarcosine dehydrogenase. It is appropriate to screen urine for this trait, since sarcosine is cleared rapidly by kidney ($8\text{--}35\text{ ml/min/1.73 m}^2$). The Tm sarcosine is about $160\text{ }\mu\text{moles/min/1.73 m}^2$ in the 'blocked catabolic mutant'. Sarcosine appears to interact weakly with a system shared by imino-acids and glycine. Sarcosine loading (100 mg/kg p.o.) produced 3 different responses in subjects. Normal: rapid disappearance of sarcosine from plasma ($t_{1/2} \sim 30\text{ min}$) with a fall in plasma glycine. Proband: greatly delayed disappearance of plasma sarcosine ($t_{1/2} \sim 153\text{ min}$) with no change in plasma glycine. Parents of proband: initial plasma sarcosine concentration normal but delayed disappearance of plasma sarcosine ($t_{1/2} \sim 68\text{ min}$) with a rising plasma glycine level. These findings suggest the trait is autosomal recessive in this pedigree. We were unable to detect sarcosine dehydrogenase activity in normal skin fibroblasts sub-cultured for 14 regenerations; consequently lack of activity in the proband's fibroblasts is of no significance. (Research supported by grants from Quebec MRC and MRC, Canada.)

- 60 *Studies on Alkaline Phosphatase in Hypophosphatasia.* YOUNG J. KIM and LYMAN A. PAGE, Dept. of Ped., Stanford Univ. Sch. of Med.

Central to an understanding of the pathogenesis of hypophosphatasia is the question of whether or not there is a deficiency of alkaline phosphatase (AP) activity in bone. A recently reported patient with the full syndrome had consistently normal total AP activity in serum and the suggestion was made that deficiency of phosphatase was not of primary pathogenic importance [SCRIVER and CAMERON, New Engl. J. Med. 281: 684, 1969].

We have studied two children who have the typical osseous and dental lesions of hypophosphatasia, markedly increased excretion of phosphoethanolamine, and total activity of serum AP in the normal adult range. AP was undetectable histochemically in leukocytes of the patients and was normal in family members. Extraction of the patients' leukocytes yielded extremely low activity. Electrophoresis of the patients' sera on polyacrylamide gel consistently yielded a single major band of phosphatase activity with a rate of migration intermediate between the rates of the two fast bands seen in normal sera. The two fast bands in normal sera have been identified as hepatic and osseous AP by comparison with extracts of tissues. Although the dominant band in the patients appeared to migrate differently from any seen in normal sera, there were no unusual isozyme patterns of AP from sera and leukocytes of family members. Studies of sensitivities of various AP to heat, *l*-phenylalanine, and urea did

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. BARTSOAS 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 $^{35}\text{S Na}_2\text{SO}_4$ 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 COUSONS, 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 CORNBATH, GRANT MORROW III, LOUIS A. BARNES, 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 alkalization (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